Amyotrophic Lateral Sclerosis and Frontotemporal Degeneration

ISSN: 2167-8421 (Print) 2167-9223 (Online) Journal homepage: http://www.tandfonline.com/loi/iafd20

ALSUntangled No. 36: Accilion

THE ALS UNTANGLED GROUP

To cite this article: THE ALS UNTANGLED GROUP (2016): ALSUntangled No. 36: Accilion, Amyotrophic Lateral Sclerosis and Frontotemporal Degeneration, DOI: 10.1080/21678421.2016.1215400

To link to this article: http://dx.doi.org/10.1080/21678421.2016.1215400

Published online: 09 Aug 2016.

Amyotrophic Lateral Sclerosis and Frontotemporal Degeneration, 2016; 1–6

Taylor & Francis
Taylor & Francis Group

RESEARCH ARTICLE

ALSUntangled No. 36: Accilion

THE ALS UNTANGLED GROUP*

ALSUntangled reviews alternative treatments for people with ALS (PALS). Here we review Accilion for ALS, a topic for which we have had 300 requests (1).

Overview

Accilion is a topical mineral cream advertised by Advanced Mineral Compounds, LLC (AMC, 2). It is one of several products with different names and websites (Table I) that trace their origin to a botanist named John Wayne Kennedy (20) and his patent entitled 'Bioavailable minerals for plant health' (19). Three of these products are topical mineral creams while a fourth is a mineral supplement marketed to be sprayed on agricultural crops to promote disease resistance and improve growth. These products appear to have similar ingredients and similar proposed mechanisms, and nearly identical description by which they claim to distinguish themselves from other mineral compounds (Table I). A representative from AMC has told us that these products are different in important ways including "zinc/copper ratios" and "redox", that there is a legal dispute underway between the current owners, and that "efforts to have these compounds independently assessed and thoroughly verified are now routinely obstructed" (21). Interestingly, the same cancer-patient testimonials appear for three of these products and the same ALS-patient testimonial appears for two of them (Table I).

Mechanism(s)

AMC explains the mechanism of Accilion as follows: 'Mutated or non-typical cells do not follow the Krebs cycle with only about 18 steps and absorb all foods (particularly sugars). These cells will also absorb minerals such as zinc and copper; however, the high concentrations (as included in our formulation) are toxic to these mutated, non-performing cells, causing them to die. The surrounding healthy tissues, following the Krebs cycle, take up the amounts of zinc and copper needed to function more efficiently and excrete the excess minerals. Following the Krebs 32 steps, versus the 18 steps that diseased cells follow, saves and replenishes minerals in normal healthy tissue while killing the mutated cells" (3). We found no studies proving that Accilion works this way in any human disease. It is doubtful that this proposed mechanism applies to ALS. While motor neuron death may not be cell autonomous (22), it is not yet clear that there is a particular type of damage-causing cell in any form of ALS that would make sense to attempt to destroy. Even if such a cell was identified, it is not clear how Accilion could be absorbed, cross the blood-brain barrier and target that cell within the central nervous

*The ALSUntangled Group currently consists of the following members: Richard Bedlack, Emma Fixsen, Colin Quinn, Chafic Karam, Alex Sherman, Lyle Ostrow, Orla Hardiman, Terry Heiman-Patterson, Laurie Gutmann, Mark Bromberg, Gregory Carter, Edor Kabashi, Tulio Bertorini, Tahseen Mozaffar, Peter Andersen, Josep Gamez, Mazen Dimachkie, Yunxia Wang, Paul Wicks, James Heywood, Steven Novella, L. P. Rowland, Erik Pioro, Lisa Kinsley, Kathy Mitchell, Jonathan Glass, Sith Sathornsumetee, Jon Baker, Nazem Atassi, Dallas Forshew, John Ravits, Robin Conwit, Carlayne Jackson, Kate Dalton, Katherine Tindall, Ginna Gonzalez, Janice Robertson, Larry Phillips, Michael Benatar, Eric Sorenson, Christen Shoesmith, Steven Nash, Nicholas Maragakis, Dan Moore, James Caress, Kevin Boylan, Carmel Armon, Megan Grosso, Bonnie Gerecke, Jim Wymer, Bjorn Oskarsson, Robert Bowser, Vivian Drory, Jeremy Shefner, Noah Lechtzin, Melanie Leitner, Robert Miller, 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, Michael Weiss, John Kissel, Jonathan Goldstein, Jeffrey Rothstein, Dan Pastula, Gleb Levitsky, Mieko Ogino, Jeffrey Rosenfeld, Efrat Carmi, Christina Fournier, Paul Barkhaus, Brett Morrison, Lorne Zinman, Eric Valor, Neta Zach, Ahmad Ghavanini, Yvonne Baker, Kristiana Salmon, Steve Perrin, Rob Goldstein, Fernando Vieira, Merit Cudkowicz, Hiroshi Mitsumoto.
Note: this paper represents a consensus of those weighing in. Every investigator in this group does not necessarily share the opinions expressed in this paper.

ISSN 2167-8421 print/ISSN 2167-9223 online
DOI: 10.1080/21678421.2016.1215400

Table I. Accillion comparison to other products.

Product name	Accilion	NDM Cream (FROST ZC-100)	CC Formula (Astridian 30)	BAM-FX (treatment for agricultural crops)
Company	Advanced Mineral Compounds	Biominix	CC Treatment	Zero Gravity Solutions
Website	Advancedmineralcompounds.com	Biominix.com	www.cancer-cell-treatment.com	www.zerogsci.com
Ingredients	'Water, Cetearyl Alcohol, Diacetyl Phosphate, Ceteth-10-Phosphate, Dimethyl Isosorbide, Caprylic/Capric Triglycerides, Butyrospermum (Shea Butter), Cetyl Alcohol, Sodium Hyaluronate, Zinc Sulfate, Ammonium Sulfate, Citric Acid, Silver Citrate, Farnesol, Phenyl Dimethicone, Copper Sulfate, Sodium Hydroxide' (3).	'Purified Water (Aqua), Mineral Oil, Propylene Glycol, Isopropyl Palmitate, Vegatable Glycerin, Stearyl Alcohol, Cetyl Alcohol, Dimethicone, Steareth-21, Steareth-2, Grapeseed Extract (Vitis Vinifera), Co-Q10 Enzyme (Ubiquinone), Tocopheryl Acetate (Vitamin E Acetate), Glutathione, Xanthan Gum, Panthenol (Pro-Vitamin B5), Superoxidase Dismutase, Maganesium Aluminum Silicate, Tetrasodium EDTA, Citric Acid, Saccharomyces Lysate Extract, Phopholipids, Lecithin, Sodium Milkamidopropyl PG-Dimonium Chloride Phosphate, Methyparaben, Propylparaben, Diazolidinyl Urea. Active Ingredient Two: Copper Sulfate, Zinc Sulfate, Ammonium Sulfate, Sulfuric Acid, Sodium Hydroxide' (6).	"The CC Formula uses zinc and copper in a 7:2 ratio (11)" "Water, Cetearyl Alcohol, Dicetyl Phosphate, Shea Butter, Dimethyl Isosorbide, Caprylic/Capric Triglyceride, Ceteth-10 Phosphate, Cetyl Alcohol, Sodium Hyaluronate, Zinc Sulfate, Ammonium Sulfate, Farnesol, Phenyl Dimethicone, Copper Sulfate, Citric Acid, Sodium Hydroxide, Silver Citrate (11)."	'The BAM-FX formula contains zinc and copper in a 7:2 ratio, in a patented formulation of Bio-Available Minerals for easy uptake by the plant. . ..BAM-FX contains a balanced ratio of ionic Zinc and Copper, a small percentage of which are surrounded by Ammonia Ligands together with Sulfate' (18).
Proposed mechanism	'Mutated or non-typical cells do not follow the Krebs cycle with only about 18 steps and absorb all foods (particularly sugars). These cells will also absorb minerals such as Zinc and Copper; however, the high concentrations (as included in our formulation) are toxic to these mutated, non-performing cells, causing them to die. The surrounding healthy tissues, following the Krebs cycle, take up the amounts of Zinc and Copper needed to function more efficiently and excrete the excess minerals. Following the Krebs 32 steps, versus the 18 steps that diseased cells follow, saves and replenishes minerals in normal healthy tissue while killing the mutated cells'(3).	'Abnormal cells do not follow the Krebs cycle and absorb all foods (particularly sugars). The abnormal cells take up excessive amounts of minerals such as Zinc and Copper (which is in our formulation) in amounts that are toxic to the abnormal cells causing them to die. The surrounding healthy tissues following the Krebs cycle take up the amounts needed to function and excrete the excess minerals' (7).	'Diseased and/or mutated cells (such as cancer cells) do not follow the Krebs cycle. Rather they follow an alternative metabolic cycle with only about 18 steps and absorb all foods (particularly sugars). The diseased cells will also take up excessive amounts of minerals such as Zinc and Copper (in our formulation) in amounts that are toxic to them, causing the diseased cells to die. The surrounding healthy tissues (following the Krebs cycle's 32 steps) take up only the amounts of Zinc and Copper needed to function and excrete the excess minerals. Following the Krebs 32 steps versus the 18 steps that cancer and other diseases follow saves normal healthy tissue while killing the diseased cells' (12).	'The Krebs cycle describes the metabolic pathways of the higher plants and animals where the parallel use of available fuels, oxygen, water, and other essentials follow the same basic metabolism of the sugars, fats and proteins. . .The metabolic system is a well documented and familiar process. The protection provided by at least thirty-two steps in the process provides a system that protects oxygen-driven plants and animals. . .Any excess ionic elements will be discarded unless supplied at extremely high rates. Lower order organisms are not as complex regarding the metabolic pathway as the higher order organisms. The cycle followed by lower order diseases such as bacteria, fungi and

(continued)

Table I. Continued

				virus follow a less complicated process that allows disease to multiply at an almost exponential rate based on available resources in an anaerobic cycle that has far fewer steps. Plant cells that are weakened by mineral deficiencies are attacked by disease, insects and other predators. Fortifying plants by providing mineral supplements in the form of ionic metals allows for simple diffusion and immediate 'first aid' for plants stressed by specific mineral deficiencies and may save a specimen plant or even an entire crop' (19).
Reported difference between this product and other mineral compounds	'Our formula contains a patent pending technology which makes its key ingredients much more bioavailable than others. This is very important as we feel that we can deliver key minerals directly into non-typical cells which adversely impact the health of humans, animals and plants' (3).	'Our formula contains a patent-pending technology which makes its key ingredients much more bioavailable than others. This is very important as we feel that we can deliver key minerals directly into non-typical, abnormal cells which adversely impact the health of humans, animals and plants' (6).	This formula contains a patent-pending technology which makes its key ingredients much more bioavailable than others. The manufacturer believes that this will deliver minerals directly into non-typical cells which adversely impact the health of humans, other animals, and plants' (11).	'a patented formulation of Bio-Available Minerals for easy uptake by the plant' (18).
Common patient testimonials (condition)	Robert P (cancer, 4) Jenny H (ALS, 4) C Wells (cancer, 4) Bonnie B (cancer,4)	Robert P (cancer, 8) C Wells (cancer, 9)	Robert P (cancer, 13) Jenny H (ALS, 14) C Wells (cancer, 15) Bonnie Butler (cancer, 16)	Not applicable
Published human clinical trials in any condition	None	None	None	Not applicable
Price	$300 for 2.1 ounces (5)	$339 for 1.7 ounces (10)	$299 for 3.38 ounces (17)	Not available

Table II. TOE grades for Accilion in ALS.

	Grade	Explanation
Mechanism	F	Mechanism proposed by AMC does not seem plausible in PALS
Pre-clinical	U	No studies of Accilion in pre-clinical ALS models
Cases	C	One case with validated ALS diagnosis and improvements
Trials	U	No clinical trials of Accilion in PALS
Risks	C	At least 10% of exposed patients experienced harms (no hospitalizations or deaths)

system. Most PALS do not have a definable mutation in their cells that would make them targetable by this compound (23). We are aware of no data in PALS demonstrating that any particular cell type has this shortened Krebs cycle.

Altered copper homeostasis has been proposed as part of ALS pathogenesis (24), although it remains unclear whether, how or in which direction it should be manipulated. Some animal studies suggested that lowering copper levels with chelators might be useful (24), but a small human trial of a copper chelator showed no benefit (25). A very recent animal study suggested that supplementing a specific form of copper (CuATSM) was beneficial (26), though 'killing mutated cells' has not been suggested as a mechanism for these beneficial effects. While a small human trial of CuATSM will start soon, we are aware of no mechanism whereby the copper in Accilion skin cream could find its way into motor neurons in the central nervous system, least of all in just the right amount to influence disease progression. Based on all this, ALSUntangled assigns a TOE 'Mechanism' grade of F (Table II).

Pre-clinical data

We found no studies of Accilion in any pre-clinical ALS models. ALSUntangled assigns a TOE 'Mechanism' grade of U based on this information (Table II).

Clinical data

Cases

The AMC website has a video of a person named Jenny H who is reported to have ALS and to have had improved motor function on Accilion (4). With her permission (27), medical records were forwarded to us to validate this report (28). We confirmed that she did have a slowly progressive upper and lower motor neuron disease involving bulbar, cervical and lumbar segments. It is not clear what ALS mimic testing she had, but multiple neurologists including a recognized ALS expert (29) agreed with this diagnosis. Approximately seven years into her disease, she started using Accilion. Within one month, she and her family noted increased voluntary movements in her arms and legs. Comparing her neurologist's notes from just before treatment to what is seen later on the video, there does appear to be modest objective improvement in her distal upper and lower extremity strength (going from less than antigravity to barely antigravity). Her chiropractor also documented improvements in "surface paraspinal electromyographic scanning"; however, it is not clear that this is a useful outcome measure in ALS (30). No other ALS outcome measures were consistently obtained throughout her course. A lengthy testimonial ascribed to Jenny H also appears on the CC formula website with the title "Testimonial - ALS - Lou Gehrig's Disease My Improvement is Indisputably Due to My Use of the CC Formula" (14). Jenny H denies using CC formula or other similar mineral creams, and states that the use of her video to promote any product other than Accilion is "being done without my knowledge or permission" (27).

AMC sent us the contact information of two clinicians who used Accilion in other patients with ALS (21). Only one of these responded to our requests for information, reporting that he had used Accilion in two PALS (31). One of these had slower progression of ALS symptoms by patient report. This was not quantified with any objective outcome measures. The other PALS had no change (31). No PatientsLikeMe members reported taking Accilion. Google search identified no additional PALS reporting use of Accilion. Based on all this, ALSUntangled assigns a TOE 'Cases' grade of C (Table II).

Trials

We found no published trials of Accilion in PALS. Based on this, ALSUntangled assigns a TOE 'Trials' grade of U (Table II).

Risks, dosing and costs

We found no large case series in which Accilion safety monitoring was done in any systematic way. The AMC website states 'use of this formula may produce one or more of the following 'expected' reactions: redness or discolored skin, skin crusting resulting in temporary scabbing, flaking and/or peeling of the skin, small black and/or red 'pinpoint' spots on the treated or other areas (some with white halos around them), stinging, itching and/or scabbing of the skin, skin nodules of various sizes and colors, extreme or mild fatigue (depending upon seriousness of condition, age and strength of the

immune system), bowel and/or urine incontinence, white cloudy material in urine and/or stools, itchy foot bottoms, unusual body and/or stool/urine odors, a metallic taste in the mouth, flu like symptoms and sensitivity to direct sunlight. Other reactions may include manageable to severe pain' (3). The expected frequency of these is not listed. The clinician we corresponded with had used Accilion in four patients (two with ALS and two with cancer), and noted skin irritation in one that resolved with varying the application site (31). We found no evidence of hospitalizations or deaths associated with Accilion. Based on all this, ALSUntangled assigns a TOE 'Risks' grade of C (Table II).

Accilion is currently being sold on one website at a cost of $300 per bottle (5). The seller-recommended dosing is as follows: 'As a minimum treatment, apply once. For maximum treatment, apply three times each day initially and two times each week thereafter. A non-allergenic bandage may be used to concentrate the treatment. If the area is washed, reapply it for maximum benefit. Do not use a metal applicator or allow metal to contact the skin cream" (5).

Conclusions

In our opinion, Accilion does not have a mechanism that is plausible for the treatment of ALS. There is one patient with a confirmed diagnosis of slowly progressive ALS who had modest objective improvements in motor function while using Accilion. However, improvements such as these have been described before, even in patients taking a placebo (32). We believe improvements in PALS are important to study, but they may have multiple explanations and thus are not proof of treatment efficacy (32). At this time we do not recommend the use of Accilion for ALS.

Declaration of interest: ALSUntangled is sponsored by the ALS Association and the Motor Neurone Disease Association.

References

1. URL:http://www.alsuntangled.com/open.php. Accessed: 2016-06-12. (Archived by WebCite® at http://www.webcitation.org/6iDYPP0VT)
2. URL:http://advancedmineralcompounds.com. Accessed: 2016-06-12. (Archived by WebCite® at http://www.webcitation.org/6iDYd2Tgv)
3. URL:http://advancedmineralcompounds.com/wp-content/uploads/2013/09/AMC-FAQ-141216.pdf. Accessed: 2016-06-12. (Archived by WebCite® at http://www.webcitation.org/6iDYhooU4)
4. URL:http://advancedmineralcompounds.com/testimonials-2/. Accessed: 2016-06-29. (Archived by WebCite® at http://www.webcitation.org/6id9xKvvd)
5. URL:http://5t1g.com/product/accilion/. Accessed: 2016-07-06. (Archived by WebCite® at http://www.webcitation.org/6ingqoy2h)
6. URL:http://biominix.com/product-faqs/. Accessed: 2016-06-24. (Archived by WebCite® at http://www.webcitation.org/6iWACXbEV)
7. URL:http://biominix.com/science-of-biominix/. Accessed: 2016-06-24. (Archived by WebCite® at http://www.webcitation.org/6iWAMROBO)
8. URL:http://biominix.com/success-stories/. Accessed: 2016-06-29. (Archived by WebCite® at http://www.webcitation.org/6idCcf2Jf)
9. URL:https://www.youtube.com/watch?v=cynyiF2GW78. Accessed: 2016-07-18. (Archived by WebCite® at http://www.webcitation.org/6j6BIeD7U)
10. URL:http://biominix.com/shop-biominix-products/. Accessed: 2016-06-29. (Archived by WebCite® at http://www.webcitation.org/6idCl6aGv)
11. URL:http://www.cancer-cell-treatment.com/images/PDF-Files/bioavailable-ionic-minerals-for-disease-mitigation-july-3-2014.pdf. Accessed: 2016-06-24. (Archived by WebCite® at http://www.webcitation.org/6iWASxyVj)
12. URL:http://www.cancer-cell-treatment.com/the-cc-treatment/treating-diseases-using-the-cc-formula. Accessed: 2016-06-24. (Archived by WebCite® at http://www.webcitation.org/6iWAdBqxQ)
13. URL:http://www.cancer-cell-treatment.com/prostate-cancer/cancer-cell-treatment-for-prostate-cancer. Accessed: 2016-06-29. (Archived by WebCite® at http://www.webcitation.org/6idDyrsk1)
14. URL:http://www.cancer-cell-treatment.com/als/testimonial-als-lou-gehrig-s-disease-my-improvement-is-indisputably-due-to-my-use-of-the-cc-formula. Accessed: 2016-06-29. (Archived by WebCite® at http://www.webcitation.org/6idE8p1VL)
15. URL:http://www.cancer-cell-treatment.com/prostate-cancer/am-i-going-to-die-of-cancer-by-christmas. Accessed: 2016-07-18. (Archived by WebCite® at http://www.webcitation.org/6j6Blhcg7)
16. URL:http://www.cancer-cell-treatment.com/ovarian-cancer/my-battle-with-ovarian-cancer. Accessed: 2016-07-18. (Archived by WebCite® at http://www.webcitation.org/6j6Bs6lU5)
17. Emails between ALSUntanled and Kevin Rude of Medical Treatment Management who answered our request for information on the product website, June 24, 2016.
18. URL:http://www.bamagsolutions.com/bam-fx-technology. Accessed: 2016-07-18. (Archived by WebCite® at http://www.webcitation.org/6j6HY1XTn)
19. URL:http://patft.uspto.gov/netacgi/nph-Parser?Sect1=PTO2&Sect2=HITOFF&p=1&u=%2Fnetahtml%2FPTO%2Fsearch-bool.html&r=1&f=G&l=50&co1=AND&d=PTXT&s1=BAM-FX&OS=BAM-FX&RS=BAM-FX. Accessed: 2016-06-24. (Archived by WebCite® at http://www.webcitation.org/6iWAlSfFL)
20. URL:http://advancedmineralcompounds.com/about-us/jw-kennedy/. Accessed: 2016-06-29. (Archived by WebCite® at http://www.webcitation.org/6idRxpSaM)
21. Emails between ALSUntangled and Mike Noder of AMC, March–July 2016.
22. Boillee S, Vandevelde C, Cleveland D. ALS: a disease of motor neurons and their non-neuronal neighbors. Neuron. 2006;5:39–59.
23. Boylan K. Familial amyotrophic lateral sclerosis. Neurol Clin. 2015;33:807–30.
24. Tokuda E, Furukawa Y. Copper homeostasis as a therapeutic target in amyotrophic lateral sclerosis with SOD1 mutations. Int J Mol Sci. 2016;17:636.
25. Bousser M, Malier M. Penicillamine in amyotrophic lateral sclerosis. Lancet. 1979;313:168.

26. Williams J, Trias E, Beilby P, Lopez N, Labut E, Bradford S, et al. Copper delivery to the CNS bu CuATSM effectively treats motor neuron disease in SODG-93A mice coexpressing the copper chaperone for SOD. Neurobiol Dis. 2016;89:1–9.
27. Emails and telephone call between ALSUntangled and Jenny H and her caregiver, June and July 2016.
28. Emails between ALSUntangled and David Cebert, October 2013.
29. URL:https://neurosciences.ucsd.edu/faculty/Pages/john-ravits.aspx. Accessed: 2016-06-12. (Archived by WebCite® at http://www.webcitation.org/6iDYqAjFw)
30. Pullman S, Goodin D, Marquinez A, Tabbal S, Rubin M. Clinical utility of surface EMG. Neurology. 2000;55:171–7.
31. Emails between ALSUntangled and Yoshi Rahm, May 2016.
32. Bedlack RS, Vaughan T, Wicks P, Heywood J, Sinani E, Selsov R, et al. How common are ALS plateaus and reversals? Neurology. 2016;86:808–12.