Amyotrophic Lateral Sclerosis and Frontotemporal Degeneration, 2014; Early Online: 1–5

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healthcare

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ALSUntangled No. 26: Lunasin

The ALSUntangled Group

On 16 May 2014, a news story appeared on American television and online, highlighting dramatic improvements in Mike McDuff, a patient with ALS taking lunasin (1). Since then ALSUntangled has had more than 100 requests to review this. Here, on behalf of the many patients and families who requested it, we review the alleged use of lunasin for treating ALS.

What is lunasin?

Lunasin (from the Filipino word 'lunas', which means 'cure') is a 43-amino acid peptide, originally isolated from soy, also found in rye, barley and wheat (2–4). It is claimed to have a number of potential health benefits including anti-oxidant, anti-hypertensive, anti-inflammatory, anti-cancer, hypo-cholesterolemic and anti-obesity effects (3–5). However, ALSUntangled was unable to find any human trials of lunasin for any condition, either published in peer-reviewed literature (6) or underway (7). Also, at least one of the authors of articles promoting lunasin's benefits has patents on it and cofounded a company whose purpose is 'to commercialize lunasin technology' (8); this creates a potential conflict of interest which is not routinely declared in these articles.

Why might lunasin help ALS?

Lunasin has mechanisms of action that could theoretically be useful in slowing ALS progression. Lunasin can reduce free radical production by activated macrophages as well as scavenge free radicals (4,5). Abnormally activated macrophages (9,10) and elevated levels of free radicals (11) occur in PALS and have been targeted in ALS clinical trials (12–14). Lunasin can inhibit the release of pro-inflammatory cytokines such as IL-6 and TNF-α, as well as NO, PGE2 and COX-2 (4,5,15). Abnormal patterns of inflammatory cytokines have been found in the spinal fluid and blood of PALS (16–20) and have been targeted in ALS clinical trials (21). Lunasin can alter histone acetylation and in this way change patterns of gene expression and alter the risk of apoptosis (4,22,23). Histone acetylation (24) and gene expression (25,26) are altered in PALS and have been targeted in ALS clinical trials (24,27).

It should be noted, however, that while macrophage overactivation, excessive free radicals and inflammatory cytokines, and genetic dysregulation are still considered potentially important in ALS, none of the trials targeting them thus far has demonstrated a clear benefit in terms of slowing or reversing ALS in patients.

Lunasin in ALS models

ALSUntangled has been unable to find any studies of lunasin in cell or animal models of ALS.

Lunasin in PALS

M. McDuff kindly allowed us to interview him and his treating neurologist, and review his medical records. His weakness began in the arms in 2010 at the age of 58 years. By the summer of 2013 he was dependent upon his wife for dressing and feeding. His legs had weakened to where he needed to hold something to walk, and he could no longer climb stairs. His speech worsened to the point of needing to repeat to be understood and his swallowing worsened to where he could no longer sustain his weight (he lost 20 pounds) and had to have a feeding tube placed. His ALSFRS-R score in July 2013 was 21 (calculated by his recollection). His manual muscle testing (calculated by physical and occupational therapists who were following him, Table I) showed severe and diffuse arm and leg weakness. In August 2013, he began a supplement regimen from a company called Reliv (28). This included lunasin (LunaRich X Capsules, 12 capsules per day), a mixture of 'vitamins, minerals and super-powered antioxidants' called Reliv NOW (three scoops per day)

ISSN 2167-8421 print/ISSN 2167-9223 online
DOI: 10.3109/21678421.2014.959297

Table I. M. McDuff's manual muscle testing scores (R/L), as evaluated by physical and occupational therapists who followed him. Numbers refer to Medical Research Council scale (ratings from 0 to 5, where 0 means no strength and 5 is normal).

	3/25/11	6/14/13	7/5/13	11/21/13	7/3/14
Shoulder Flexion	1/1		2−/2−		2−/2−
Shoulder Extension	1/1				2−/2−
Elbow Flexion	4/4		2−/2−		2−/2−
Elbow Extension	4/4		2−/2−		2−/2−
Wrist Flexion	4/4		0/0		2−/2−
Wrist Extension	4/4		0/0		2−/2−
Hip Flexion		2−/2−		2−/2−	3−/3−
Hip Extension		2−/2−		2−/2−	2/2
Knee Flexion		4−/4−		2−/2−	2+/2+
Knee Extension		4−/4−		2−/2−	4/4
Ankle Dorsiflexion		4−/4−		2−/2−	5/5
Ankle Plantar Flexion		4−/4−			2+/2+

and a mixture of 'soy protein, MCTs, creatine, CoQ10 and supercharged amino acids' called Pro-Vantage (two scoops per day). After three months, he and his wife noted improvements in his speech and swallowing. These have continued. Currently his speech and swallowing are nearly normal by their report. He has gained 20 pounds, and no longer uses his feeding tube. His legs have become stronger to where he needs to hold on less. His ALSFRS-R score in July 2014 (obtained by phone) improved to 29. His manual muscle testing is objectively better as well (Table I).

McDuff's ALS diagnosis, agreed upon by three separate neurologists, is based upon a history of painless, progressive weakness, exams showing widespread muscle atrophy and weakness with preserved sensation, EMGs showing denervation and reinnervation in multiple cervical myotomes (sparing bulbar, thoracic and lumbosacral myotomes) without sensory neuropathy or motor conduction block, and unremarkable testing for ALS mimics including cervical spine MRI, copper and MUSK antibodies. There are at least two atypical features of his case. First, he had a prior illness in the 1970s that caused sub-acute onset ptosis, dysarthria, dysphagia, neck and limb weakness. He was eventually diagnosed with myasthenia gravis, and was treated with pyridostigmine. Within two months he had improved back to normal. He never had any other treatment for myasthenia. A second atypical feature is that he has never had any upper motor neuron signs. Patients with idiopathic pure lower motor neuron disease are sometimes said to have progressive muscular atrophy (PMA) rather than ALS (29). Since the majority of such patients do have upper motor neuron dysfunction at autopsy (30), some refer to this as 'lower motor neuron predominant ALS' (31). However, pure lower motor neuron disease has a longer differential diagnosis than typical ALS, and naturally relapsing-remitting conditions such as atypical myasthenia gravis or multi-focal motor neuropathy may present in this way (32). It does not appear that the patient had antibody testing to help exclude these entities. This is especially important in light of another recently reported patient with a history of myasthenia gravis whose ALS was said to improve with a very different treatment (33); a possibility in both these cases is the spontaneous improvement known to sometimes occur with myasthenia, rather than a treatment-induced improvement in their ALS.

ALSUntangled has received a number of e-mails detailing the experiences of other PALS on lunasin. These are summarized in Table II. While several of these e-mails describe improvements, we have not been able to obtain records to independently confirm any. It is thus possible that some of these benefits may be due to a 'placebo effect' (34). There may also be a 'reporting bias' here (35); we do not know how many PALS might have tried lunasin with no benefit. Perceived positive results are typically more likely to be reported than negative ones (35).

We found one additional PALS taking lunasin on PatientsLikeMe, but they have not yet completed an evaluation of its effects (36). Google search for 'Lunasin treatment for ALS' yielded no additional cases.

Dosing, costs and side-effects

Lunasin is taken orally. It is available via several foods such as tofu and soy milk, and in purified forms (28). The optimum form or dose of lunasin for ALS is not known. Lunasin can cross the blood-brain barrier and affect the central nervous system, at least in mice (37).

Mr. McDuff used lunasin purchased from Reliv (28). This multi-level marketing company (38) sells a diverse array of products, including ones said to 'provide energy, focus and stress relief' (39), 'optimize joint performance' (40), and 'boost your immune system' (41). ALSUntangled was unable to find any trials in peer-reviewed literature to support these claims. Reliv sells seven different products containing a trademarked form of lunasin called LunaRich. LunaRich reportedly has 'an integrated shell of protease inhibitors' that 'protect the lunasin's structure after consumption' leading to 'superior bioavailability' (42). ALSUntangled was unable to find any peer-reviewed publication that proves this.

Side-effects from lunasin appear rare, but have been reported including swelling, lightheadedness, rash and stomach aches (43). One website cautions patients with soy allergies against taking lunasin (44), although the Reliv website says this is safe (45).

LunaRich X at a dose of 12 capsules per day costs $240 per month (46). If taken with the

Table II. Other cases of PALS reporting improvements on lunasin. These were obtained via e-mails. RN (Reliv Now), LX (Lunarich X), PV (Provantage). See text for details.

Age/ Gender	Lunasin Dosing	Lunasin Duration (weeks)	Improvement Reported	Records To Confirm Diagnosis	Atypical Features	Records To Confirm Improvements
48/M	RN 3–4 scoops BID; LX 4 caps BID	6	Speech, swallowing, arm and leg strength, breathing	Y	Y (Pure Upper Motor Neuron Disease)	N
30/M	RN 3 scoops QD; LX 12 caps QD; PV 3 scoops QD	4	Improved handwriting, decreased twitching and cramps, easer to maintain weight	Y	N	N
76/M	RN 2–3 scoops QD; LX 6–7 caps QD	9	Stopped progressing; more alert	N	?	N
70/M	RN 1 scoop BID; LX 3 caps TID;	7	Improved energy, decreased spasms	N	?	N
59/F	RN 4.5 scoops QD, LX 12 caps QD; PV 9 Tablespoons QD	11	Improved hand, arm, torso strength; improved stiffness	N	?	N
64/M	Classic 2 scoops QD, LRX 12 caps QD	11	Improved walking and energy	N	?	N
43/M	LRX 9 caps QD	4	None	N	?	N
63/F	LRX 9 caps QD	8	Improved speech, limb strength, fluidity and energy	N	Pure Upper Motor Neuron	N
66/M	?	4	None	N	?	N
74/M	RN ½ scoops QD; LRX 2 caps QD; PV 1.2 scoop QD.	8	None	N	?	N
?/M	RN 3 scoops QD; LRX 12 caps QD; PV 3 scoops QD	8	Improved speech	N	?	N
49/F	?	8	Improved breathing, twitching	N	?	N
74/?	?	8	Improved walking	N	Pure lower motor neuron disease	N
51/M	?	8	None	N	?	N
55/M	?	8	Improved swallowing, leg strength, energy	N	?	N
?/M	?	8	Improved sleep	N	?	N
?/F	?	8				
?/F	RN 1 scoop QD; LRX 5 capsules QD, PV 1 scoop QD, others	11	Improved arm and leg strength	N	?	N

additional Reliv products Reliv Now (three scoops per day) and Provantage (two scoops per day), as many PALS are doing (Table II), the cost increases to $691 per month (46). We found no data to support the addition of these other products.

Conclusions

Lunasin has interesting mechanisms of action that might be useful in treating ALS, and it appears reasonably safe although some forms of it are expensive. While some PALS have reported improvements on lunasin, we have thus far found only one in which we were able to independently validate these improvements. This patient had atypical features for ALS including a history of myasthenia gravis, which can produce weakness that improves spontaneously.

At this time there is not enough evidence to recommend that PALS take lunasin. A reasonable next step would be a small pilot trial of lunasin with validated ALS diagnoses and outcome measures.

Acknowledgements

ALSUntangled is sponsored by the Motor Neurone Disease Association.

The ALSUntangled Group currently consists of the following members: Richard Bedlack, 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, Jeff Dietz, 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, Hubert Kwiecinski, 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, 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, Michael Weiss, John Kissel, Jonathan Goldstein, Jeffrey Rothstein, Dan Pastula, Gleb Levitsky, Mieko Ogino, Jeffrey Rosenfeld, Efrat Carmi, Merit Cudkowicz, Christina Fournier, Paul Barkhaus, Eric Valor, Brett Morrison, Lorne Zinman, Craig Oster.

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.

Declaration of interest: The authors report no conflicts of interest. The authors alone are responsible for the content and writing of the paper.

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