

Gaining treatment synergy by combining high-dose biotin and NAD+ for neurodegenerative disease.

Ross Grant, Ph.D./ CEO, Australasian Research Institute

Preliminary results of ongoing studies with high dose pharmaceutical grade biotin (up to 300 mg/day) to target demyelination appear promising. An Australian research team has next asked the question:

Would the addition of NAD+ work synergistically with the high dose biotin to repair the myelin sheath?

There is good rationale for potential synergy when NAD+ (nicotinamide adenine dinucleotide) is added to the high dose biotin.

“While the exact cause(s) of demyelination remains unknown, several key links are understood, all of which reduce the normal myelination process.”

- *Oxidative stress (i.e. free radical damage),*
- *Inflammation*
- *Reduction in fatty acid production*

Fatty Acid Synthesis

“High dose biotin seems to be driving the fatty acid synthesis, and with fatty acid synthesis there is signaling that goes on with the ACC (Acetyl CoA Carboxylase). ACC is a biotin-dependent enzyme that functions to regulate the metabolism of fatty acids which inhibit beta oxidation of fatty acids within the mitochondria. Therefore, an increase in ACC may drive the carbohydrate backbones toward fatty acid synthesis.”

Biotin as a Co-factor

“In addition, biotin is also a cofactor for three other enzymes that can help increase ATP production:

- *Propionyl-CoA carboxylase (PCC),*
- *3-methylcrotonyl-CoA carboxylase (MCC) and*
- *Pyruvate carboxylase (PC) which helps convert substrates such as amino acids & pyruvate to intermediates that feed into the TCA cycle for ATP (energy) production.”*

Mitochondrial Efficiency

The combined effect in MS sufferers is a potential increase in fatty acid production (useful for re-myelination) and improved mitochondrial energy (ATP) production. However the generation of ATP from the TCA cycle requires NAD+ as an electron carrier.



Ross Grant, PhD
Sydney Medical School/
Adventist Hospital

“NAD+ is required for a number of functions at the cellular level,” Grant continued “but perhaps the most important thing NAD+ can do is transport electrons in the form of reducing equivalents to the mitochondrial respiratory chain for ATP (energy) production. So we have to have enough NAD+ to be able to pick up the electrons to transfer where they need to go.”

Complications of Oxidative Stress

“However if free radical (i.e. oxidative stress) levels are high, as occurs in conditions like MS, then NAD+ levels will decrease as NAD+ is also needed to help repair nuclear (DNA) damage. So oxidative stress damages DNA which reduces NAD+ which subsequently lowers energy (ATP) production.”

Synergy of Biotin and NAD+

“Increasing biotin may therefore help drive enzyme activity that stimulates fatty acid synthesis and increase TCA intermediates that can ultimately be turned into energy (ATP), but only if there is enough NAD+ available to transfer electrons. Clearly then, increasing both Biotin and NAD+ in MS sufferers has the potential to provide synergistic benefit when supplemented at appropriate levels.”

“NAD+ should potentiate the effect of biotin by increasing the available ATP, which means that ACC which is the enzyme that is responsible for fatty acid synthesis and is necessary for maintaining the myelin sheath, should work better. Biotin is a cofactor for those enzymes so it means you will have plenty of biotin around which is able to then provide the right kind of stimulus for producing the required fatty acids for the maintenance of the myelin sheath and for myelin repair. Biotin is also necessary for some of the energy production itself, so our greater story here is that by adding NAD+ in an appropriate amount, both ingredients should work synergistically together for patients seeking to restore their myelin sheath.”

“NAD+ on its own is going to have positive effects on both energy metabolism and cellular DNA repair which will hopefully improve cell viability of the oligodendrocytes helping to drive the fatty acid synthesis required for re-myelination, which is exactly what you want. So pairing NAD+ with Biotin is likely to be very beneficial because biotin is going to be the cofactor which is necessary to drive effective fatty acid synthesis while NAD+ both improves energy production and DNA repair.”

SOURCE:

Ross Grant, PhD is a clinical Associate Professor at the University of Sydney Medical School and the CEO of the Australasian Research Institute, Sydney Adventist Hospital. He is a biochemical pharmacologist with a PhD in Neurochemistry/Neuropharmacology whose research is focused on NAD+, specifically the role of oxidative stress and NAD+ metabolism. Dr. Grant is the world's foremost expert and author in the field of NAD+ research and has over fifty articles published in peer-reviewed scientific journals. Dr. Grant serves as a member of Avior Nutritionals Scientific Advisory Board.