The MOSS NUTRITION REPORT

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Product Review

February 2023 #367

NEW PRODUCT IN DEVELOPMENT

ELEMENTAL SELECT – PART II:

STILL ANOTHER REASON WHY ELEMENTAL SELECT™ CONTAINS FREE-FORM AMINO ACIDS

INTRODUCTION

In part I of this series I reviewed research that supported the rationale for the use of a product such as **Elemental Select™** with patients who have poor digestive function to the point where ingestion of almost any solid food or typical meal replacement/supplement products that contain the usual protein powders (i.e., whey, pea protein, etc.) create significant symptoms. I also presented research on the specific clinical value of the free-form amino acid base in **Elemental Select™**, mainly as it relates to patient tolerability and overall efficacy. However, as suggested, in the paper "Functions and signaling pathways of amino acids in intestinal inflammation" by He et al (He F et al. *BioMed Res Int*, Vol. 2018, Article ID 9171905, 2018), in addition to the value of the amino acid blend as a whole, each of the specific amino acids in **Elemental Select™** play a major role in the optimization of gut health and function. To introduce my discussion of the value of the individual amino acids in **Elemental Select™**, please note the amino acids present in the product as listed below:

- L-Arginine
- L-Histidine
- L-Isoleucine
- L-Leucine
- L-Lysine
- L-Methionine
- L-Phenylalanine
- L-Threonine
- L-Tryptophan
- L-Valine

As you can see, the product contains all nine essential amino acids (EAAs) plus one conditionally essential amino acid (CEAA), L-Arginine. What is the value of this specific blend? As you will see, He et al provide ample evidence for the value of each of the amino acids in **Elemental Select™.**

THE UNIQUE AMINO ACID NEEDS OF THE INFLAMED GI TRACT

The first quotes I would like to feature from the He et al paper highlight the unique amino acid requirements of the inflamed gut. First, consider the following:

"The metabolic profiling of amino acids in ulcerative colitis differs from the control group, which indicates certain amino acids would be novel biomarkers for early diagnosis and treatment of patients with ulcerative colitis. For example, the levels of glutamine, glutamate, methionine, tryptophan, and histidine are significantly lower in UC patients than in the normal control group…"

Furthermore:

"…Tryptophan…exerts beneficial regulatory function in mucosal growth or maintenance and alleviation of intestinal inflammation by the 5-hydroxytryptophan (5-HT) signaling pathway, in the recovery of colitis by caspase recruitment domain family member 9, and in the function of intestinal homeostasis and anti-inflammation by

aryl hydrocarbon receptor ligands in the intestine."

Next, consider arginine:

"Arginine is a conditionally essential amino acid and has a critical function in treating intestinal inflammation by manipulation of immune responses, oxidative system, and intestinal metabolism."

The next quote I would like to feature from the He et al paper is an overview statement about why, from a metabolic perspective, certain amino acids are so beneficial concerning gut health:

"The oxidative stress and inflammatory mediators are the main etiological factors in inflammatory bowel disease; hence, amino acids are expected to alleviate it as antioxidants and anti-inflammatory agents."

The value of essential amino acids in relationship to intestinal inflammation

The next few quotes from the He et al paper specifically refer to the value of essential amino acids in reference to intestinal health. First, note the following:

"EAAs have significant effects in intestinal inflammation. It is reported that phenylalanine possesses beneficial effects in the treatment of inflammatory bowel disease by inhibiting TNF-α production and enhancing immune responses."

What about methionine?

"Methionine is able to modulate metabolism, innate immunity, and digestion of mammals and generate glutathione to neutralize oxidative stress. Methionine inhibits the increase of paracellular permeability mediated by TNF-α, which may be related to antioxidant metabolites (e.g., taurine and glutathione) to improve intestinal homeostasis. Abundant methionine is crucial for intestinal integrity and intestinal antioxidant capacity."

Next, consider lysine:

"Lysine influences the digestion of food and the expression of amino acid transporters in the intestine."

What about threonine?

"Threonine is a primary ingredient of intestinal IgA and mucins; thus, malnutrition of threonine induces inflammation and affects the immune responses through the NF-κB pathway."

The next quote refers to the value of the branched chain amino acids (Leucine, Isoleucine, and valine) as a group:

"BCAAs (e.g., leucine, valine, and isoleucine) enhance intestinal immune defense system through improving morphological integrity and immunoglobulin production in the intestine."

In closing the section on essential amino acids and gut inflammation, He et al provide the following overview statement:

"Collectively, EAAs mainly exert anti-inflammatory roles by NF-κB, CaSR, MAPK, and mTOR signaling pathway to restrain the expressions of proinflammatory cytokines."

The value of the conditionally essential amino acid, arginine, in relation to intestinal inflammation

Next He et al address the value of arginine in relation to gut inflammation. First, note the following:

"Arginine as a nutritional supplement reduces the expressions of IL-1β and IL-6, as well as delaying the onset of colitis when the colitis is not very serious, and inhibits the increase of intestinal epithelial permeability by preventing inflammatory neutrophil recruitment and oxidative stress in the DSS-induced colitis."

Furthermore:

"…arginine decreases production of IL-8 during the intestinal inflammation which may occur through increasing the production of nitric oxide via inducible nitric oxide synthase. L-arginine improves survival rate as well as antineoplastic

properties and regulates the metabolism of T cells."

Finally:

"Arginine supplementation changes intestinal microbiota, which is conducive to activate intestinal innate immune responses by NF-κB signaling pathway."

Angiotensin-converting enzyme 2 (ACE2) and its relationship with intestinal inflammation and amino acid malnutrition

As you undoubtedly recall, COVID-19, almost overnight, transformed one of the least recognized, most obscure enzymes in human physiology into a metabolic, physiologic buzzword that became an essential part of our COVID-19 vocabulary. What was that enzyme? Of course, it was angiotensin converting enzyme 2 (ACE2). Why did it become inextricably tied to the COVID-19 lexicon? The ACE2 receptor acts as a "gateway" of sorts for the SARS-CoV-2 virus to enter from, primarily, the respiratory system into the internal milieu. Of course, the bad news did not end there. Once the ACE2 receptor allows the virus to gain entrance, the virus systematically starts to destroy the enzyme. Because ACE2 possesses important vasodilating and anti-inflammatory properties, the ACE2 destruction, in turn, leads to many of the signs and symptoms we not only associate with COVID-19 but long-COVID.

Interestingly, He et al discuss at the end of their paper an entirely different role of ACE2 as it relates to not only intestinal inflammation but the relationship between amino acid nutriture and intestinal inflammation. What is even more interesting, though, is this paper was published in 2018, almost two years before the onset of the COVID epidemic. Therefore, this discussion by He et al is both unique and refreshing in that it addresses ACE2 without any explicit or implicit bias driven by COVID-19.

The first quote on the subject I would like to feature discusses how the relationship between amino acid malnutrition and intestinal inflammation is mediated by ACE2:

"A series of evidence suggests that malnutrition is related to intestinal inflammation. A study indicates that amino acid malnutrition is always related to intestinal inflammation via angiotensin-converting enzyme 2 (ACE2), which plays significant roles in amino acid homeostasis, innate immune responses, and intestinal microbiota. ACE2 is an important enzyme of the renin-angiotensin system (angiotensin 1-7), which is expressed in various organs including the small intestine, and has a crucial function in controlling intestinal inflammation as a stabilizer of neutral amino acid transporters."

In addition:

"ACE2 regulates innate immune response and intestinal microbiota, which illuminates intestinal inflammation under conditions of severe malnutrition. Mice with ACE2 knockout and ACE2 mutation show the decline in the uptake of tryptophan, leading to the decrease of expression of antimicrobial peptides and the change of intestinal microbiota, resulting in the high sensitivity to intestinal inflammation, which is restored by tryptophan supplementation."

As I hope you can see, the many reports of intestinal destruction of ACE2 by the SARS-CoV-2 virus that I highlighted in the **Some thoughts on Coronavirus** newsletter series have obvious parallels to the impact of ACE2 elimination in mice that was reported in the above quote. In turn, as also suggested in the above quote, it might be reasonable to hypothesize that amino acid supplementation that includes tryptophan, which is a component of **Elemental Select**, would be helpful for the severe intestinal inflammation that is being noted, more and more, in both COVID-19 and long-COVID/PACS patients.

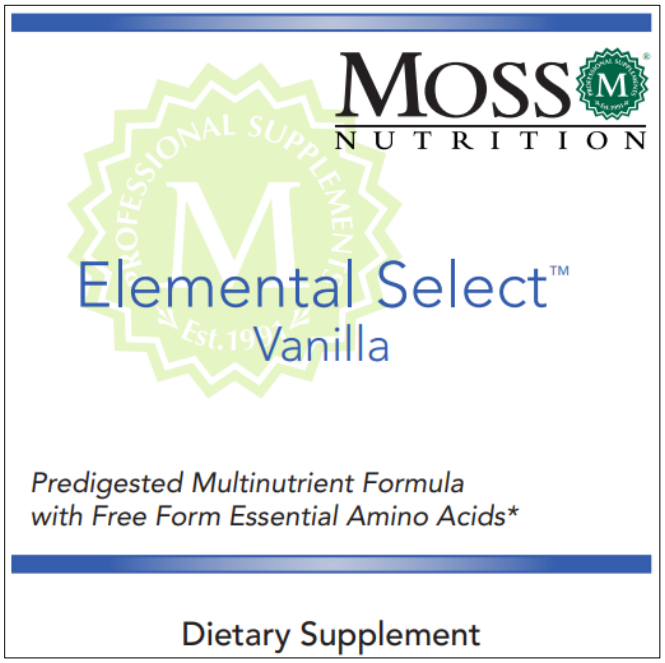
To finish this discussion of the He et al paper, I would like to feature the authors' concluding summary statement:

"In conclusion, the functions of amino acids in intestinal inflammation are mainly associated with improving the intestinal barrier, attenuating intestinal injury, suppressing oxidative stress, and inhibiting the expressions of proinflammatory cytokines."

SOME FINAL THOUGHTS ON THE HE ET AL PAPER

As I mentioned in part I of this series, our initial thinking about the use of amino acids as well as most of the other constituents in **Elemental Select™** related to both ease of absorption and the minimization of GI distress, which, as was also discussed in part I, is well supported by published research. Therefore, it is certainly gratifying to note that He et al make it clear that the amino acid formulation in **Elemental Select™** will not only act to optimize systemic health but the primary issue with inflammatory bowel disease – healing and repair of the intestinal tract.

In part III of this series, I will review still more research that demonstrates **Elemental Select™** should be considered as a product of choice for those inflammatory bowel disease patients who have a history of intolerance to the usual diets and supplemental interventions.



A portion of the Elemental Select™ label.