The MOSS NUTRITION REPORT

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Product Review

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MORE DOCUMENTATION OF THE CLINICAL EFFICACY OF MERIVA® – THE FORM OF CURCUMIN IN CURCU SELECT®

INTRODUCTION

As many, if not most of you, are undoubtedly aware, we have been seeing over the last year or so an interesting version of what I would describe as "curcumin wars" occurring in various supplement company advertisements that appear in the major clinical nutrition and alternative medicine journals. While the overall appearance of these ads varies, the main theme is always the same – absorbability. As you are probably also aware, standard, commercial curcumin is very poorly absorbed. Based on this fact, a cottage industry has developed with competing supplement companies continuing to make claims of ever more absorbable forms of curcumin. Methodologies to increase absorption range from the creation of a bioperine/curcumin complex to complexing curcumin with different lipid compounds. Equally fascinating are the various ways the companies fighting the "curcumin wars" compare their enhanced absorption curcumin complexes with the competition. Some make their respective products appear superior by comparing absorbability of their products to standard commercial curcumin. I find this marketing device almost humorous since commercial curcumin is so poorly absorbed that almost any effort to improve absorbability will look good by comparison. Still other companies producing enhanced absorption curcumin complexes seem to be engaging in an endless game of one upmanship trying to convince you that theirs is the logical product of choice due to the fact that it is the current "king of the absorption hill." Interestingly, while it is not explicitly stated, it is often obvious that the ads involved in this game of which enhanced absorption curcumin complex is "king of the absorption hill" are comparing their products to the first major enhanced absorption curcumin complex that appeared in the professional supplement marketplace, Meriva®, which is the form used in the Moss Nutrition product, **CurcuSelect®**.

Do these products containing various enhanced absorption curcumin complexes present accurate data demonstrating superior absorption compared to Meriva®? While I have not examined this data in depth, from what I can surmise, it appears that the data is accurate. Of course, this may lead you to ask, "Why does Moss Nutrition stay with Meriva® in **CurcuSelect®** if it is no longer "king of the absorption hill?"

My answer to this question is quite simple. Over the years, there have been numerous examples where the most absorbable supplement is not always the most efficacious in terms of improving health of chronically ill patients. An excellent example of this is folic acid. Even though the synthetic folic acid used in food fortification and many nutritional supplements is much better absorbed compared to food folates, the very fact that it is so well absorbed can lead to increased circulating levels of unmetabolized folic acid, a proven detriment to health. Therefore, while I take absorption levels into account when considering the form of a nutrient or supplement that will be included in the Moss Nutrition product line, overwhelmingly, the main consideration is its impact clinically.

Concerning the "curcumin wars," we continue to stay with Meriva® because, while it does not demonstrate the very best absorption level, it does demonstrate in published research a key quality that I have yet to see mentioned to any great extent by any of the companies focusing exclusively on absorption, absorption that is good enough to yield excellent clinical efficacy.

MORE EVIDENCE THAT THE MERIVA® IN CURCUSELECT DEMONSTRATES OUTSTANDING CLINICAL EFFICACY

In past product newsletters I have reviewed studies on Meriva® that demonstrated clinically significant efficacy for conditions such as osteoarthritis. The latest study that demonstrates clinical efficacy of Meriva® does so in a way that is an interesting and compelling departure from the usual condition/symptom specific study methodology. In fact, the study I am about to review demonstrates the efficacy of Meriva® in a way that we often discuss in functional medicine circles but virtually never see in published research – it discusses the efficacy of Meriva® in terms of its ability to improve organic acids test findings.

In "A pilot study of the effect of phospholipid curcumin on serum metabolomic profile in patients with non-alcoholic fatty liver disease: a randomized, double-blind, placebo-controlled trial" by Chashmniam et al (Chashmniam S et al, *Eur J Clin Nutr*, Vol. 73, pp. 1224-1235, 2019) 58 patients with non-alcoholic fatty liver disease (NAFLD) were evaluated. The patients were divided into two groups, one of which received 250 mg of Meriva® per day and the other a placebo for eight weeks. Different serum organic acid metabolites were evaluated to determine efficacy. Nine subjects dropped out so that the data from 49 of the patients were actually included in the study results.

Before discussing the results of the study, though, I would like to share some text of the study that discusses NAFLD, a condition that is becoming increasingly prevalent in chronically ill patients, often due to obesity and excessive intake of fructose containing processed foods and beverages:

"Non-alcoholic fatty liver disease (NAFLD) is a major cause of liver injury worldwide, its prevalence is elevating due to the rising epidemic of obesity. It is characterized by accumulation of lipid in the hepatocytes, which is accompanied by a wide spectrum of disorders ranging from simple steatosis to more severe non-alcoholic steatohepatitis (NASH)."

The authors go on to point out that, even though there is no approved drug for the treatment of this disease so far, evidence does suggest that curcumin may be helpful:

"…growing evidence on curcumin indicates that this component influences hepatic disorder significantly that is related to NAFLD."

However, the mechanism of curcumin's action with NAFLD is unknown:

"…the exact mechanism involved in the therapeutic effects of curcumin has remained unclear."

To assist in the determination of the actions of curcumin with NAFLD the authors employed a technique that we have been using in functional medicine for years, interpreting patient specific metabolic indicators using diagnostic media such as serum. The approach of using patient specific metabolites as diagnostic tools is being described by the research community as "metabolomics":

"…it is important to investigate the effects of curcumin on biochemical pathways through holistic approaches such as 'omics' techniques. One of the 'omics' approaches is metabolomics, which is defined as the comprehensive analysis of metabolites in a biological specimen. Metabolites are considered as end products of cellular processes and these small molecules are important indicators of cellular status."

In this study, 13 metabolites were more favorably affected by curcumin compared to placebo. As those of you who have employed

organic acids testing in your practices may recognize, many of the metabolites found to be altered in the Chashmniam et al study also appear in the organic acids profiles we typically employ:

"The main altered metabolites in the serum of patients with NAFLD who were treated with curcumin were amino acids derivatives (3-methyl-2-oxovaleric acid, 3-hydroxyisobutyrate, and kynurenine), TCA cycle metabolites (succinate, citrate, and α-ketoglutarate), gut microbiota-derived metabolites (methylamine, trimethylamine, hippurate, and indoxyl sulfate), bile acids (BAs) (chenodeoxycholic acid, taurocholic acid, and lithocholic acid)."

In the next few quotes, the authors discuss the various classes of metabolites in more detail in relationship to the impact of curcumin.

Amino acid metabolites

"In the curcumin group, it has been shown that there were decreased serum levels of 3-methyl-2-oxovaleric acid and 3-hydroxyisobutyrate, which are degradation products from isoleucine and valine, respectively. These amino acids are so-called branched-chain amino acids (BCAAs). Increased levels of metabolites, which are related to BCAA catabolism during NAFLD progression have been reported previously. Lake et al suggested that this enhancement may reflect a hepatic stress response to inflammation and oxidative stress (OS), which are considered as two features of NAFLD. As these metabolites were correlated with OS and they were decreased following consuming curcumin, it was suggested that the antioxidant property of curcumin could be a plausible cause for elucidating the reduction."

Next, Chashmniam et al discuss an organic acid metabolite I have discussed frequently over the years in various newsletters and lectures, kynurenine:

"Our findings showed that consuming curcumin can decrease kynurenine levels. Investigations have revealed that kynurenine was elevated in patients with NAFLD. This metabolite was produced from degradation of tryptophan by indoleamine-pyrrole 2,3 dioxygenase (IDO) in liver cells. IDO is overexpressed in the response to inflammatory conditions, as well as there is a positive correlation between kynurenine concentrations with inflammation and OS. In accordance with our findings, it has been shown that curcumin is able to suppress the activity and expression of IDO and reduce kynurenine levels, indicating reduction of inflammation and OS."

Tricarboxylic acid (TCA) cycle

What was the impact of Meriva® on Krebs cycle metabolites? The authors state:

"We found that succinate decreased after administering curcumin. Succinate is a key substrate of the TCA cycle. In patients with NAFLD, increased levels of succinate were reported that can cause perturbations in TCA cycle that results in mitochondrial dysfunction, OS production, and cytokine release."

What about another Krebs cycle metabolite, α-ketoglutarate?

"Aragones et al. showed that α-ketoglutarate, a TCA cycle metabolite, is a biomarker of NAFLD, especially in obese ones. This metabolite was also decreased by curcumin treatment. The decrease in α-ketoglutarate of the curcumin group may indicate that liver damage was diminished."

Next consider the comments on the Krebs cycle metabolite, citrate:

"Citrate is another intermediate metabolite of the TCA cycle that elevates in patients with NAFLD. Increased levels of this metabolite may be due to high levels of free fatty acids in these patients."

What was the impact of Meriva® on citrate levels?

"Our results…showed lower levels of citrate in the curcumin group than the placebo group."

Chashmniam et al finish their discussion of aberrant TCA cycle metabolites and the impact of Meriva® in NAFLD patients with the following statement:

"As mentioned above, a decreased level of several metabolites, which are related to the TCA cycle, was observed in the curcumin group compared with the placebo group, which

suggested that the TCA cycle can be a treatment target of curcumin. In line with our findings, experiments demonstrated that the activity of mitochondrial isocitrate dehydrogenase, as the key rate-limiting step of the TCA cycle, was decreased using curcumin."

Gut microflora metabolism

What about the organic acid metabolites that relate to gut microflora metabolism? As was mentioned above, these could also be altered with NAFLD. The authors state:

"Reports…showed that gut dysbiosis, as an imbalance in intestinal microbiota, could be involved in NAFLD and NASH pathogenesis."

Furthermore:

"Increased levels of Gram-negative bacteria are associated with enhanced levels of lipopolysaccharide production, which can disrupt intracellular tight junctions and enhance gut permeability."

What was the impact of Meriva® on organic acids metabolites relating to disturbances in gut microflora?

"In the present study, oral administration of curcumin decreased the serum concentration of methylamine, trimethylamine, indoxyl sulfate, and hippurate. Studies showed that curcumin treatment is able to reverse some bacterial phylotypes that were altered during NAFLD. Therefore, we suppose that curcumin may alter the growth of gut microbiota in patients with NAFLD, resulting in the reduction of some endotoxins."

Bile acid (BA) metabolism

As noted by Chashmniam et al, bile acids produced by gut microflora can be altered in NAFLD patients:

"As mentioned, secondary BAs are other metabolites that were produced by gut microbiota. Several studies reported that BAs were increased in patients with NASH and NAFLD…"

What was the impact of Meriva®?

"Interestingly, we found that the levels of chenodeoxycholic acid, taurocholic acid, and lithocholic acid were reduced in curcumin treatment patients compared with placebo group. These findings can be described for at least two reasons: first, curcumin treatment can reverse some bacterial communities that were changed during NAFLD; second, reports showed that curcumin induces farnesoid X receptor (FXR) activity."

Why is the induction of FXR significant? In simple terms, it inhibits a phase 1 detoxification enzyme (CYP7A1), which is involved in BA synthesis. By inhibiting CYP7A1, BA synthesis is reduced, thereby lowering the levels of potentially pro-inflammatory BA levels in the liver.

Authors' conclusions

"Applications of un-targeted metabolomics in drug intervention studies provided a comprehensive overview through which researchers could find out the effects of the interventions and realize how the drug influences metabolic pathways. Our metabolomics results showed that curcumin intake for 8 weeks in patients with NAFLD had effects on some amino acids, TCA cycle, BAs, and gut microbiota. Overall, the anti-oxidant and anti-inflammatory properties of curcumin may be the reason for the results of this trial…"

SOME FINAL THOUGHTS

I have two final thoughts I would like to share. The first is in relation to organic acids profiles and treatment based on the results of organic acids profiles. As those of you who use organic acids testing in your practices probably know, quality research on the use of organic acids testing clinically is exceedingly difficult to find. Even more difficult is finding quality research on the use of supplementation to address abnormal findings found on organic acids profiles. For these reasons I was so glad to find the Chashmniam et al study. As you know, I am a big advocate of organic acids testing clinically and use it frequently with difficult patients. Knowing, thanks to the Chashmniam et al study, that **CurcuSelect®** can reduce elevated levels of several organic acids metabolites in seriously ill patients will

be very useful in my efforts to assist chronically ill patients with their efforts to improve quality of life. I hope the same can be said of your patients whose clinical presentation is complicated enough to warrant organic acids testing.

My second thought relates to the many enhanced absorption curcumin products that are fighting to be king of the hill from an absorptive standpoint. There is no question that Meriva®, the sunflower phospholipid form of curcumin that is the main ingredient in **CurcuSelect®**, is well absorbed. The Chashmniam et al study reviewed above confirms this, as do other studies I have discussed in this forum over the years. Furthermore, numerous anecdotal reports from you concerning the efficacy of **CurcuSelect®** make it clear to me that absorption of Meriva® is outstanding.

However, in the curcumin wars where enhanced absorption curcumin complexes continue to battle to be king of the absorption hill, is Meriva® the best? Probably not. Then why do we at Moss Nutrition stick with Meriva®? As I mentioned above, the idea that the best absorption always yields the best efficacy is, in my opinion, more representative of good marketing than good science. And, if we had to rank absorption versus efficacy, which would be most important, at least in the minds of our patients? I think we all know the answer to that question.

Thus, for me, a better question in the enhanced absorption curcumin complex curcumin wars is which delivers the best efficacy. Can I say conclusively that Meriva® is best in this regard? Honestly, I cannot. However, as far as I can tell from my examination of the published research so far, Meriva® has the best documentation of efficacy. ***That's why, until I see published research on the competing enhanced absorption curcumin complexes that proves they have better efficacy in addition to better absorption, Moss Nutrition will be staying with Meriva®.***

Products with Meriva®:

CurcuSelect® 120 VC
500 mg per serving (2 capsules)

SarcoSelect® and **SarcoSelect® DF**
250 mg per serving (1 scoop)

Select Cleanse®
250 mg per serving (1 scoop)

InflammaSelect® 120 VC, 240 VC
100 mg per serving (2 capsules)

ArthroSelect® 120 VC
75 mg per serving (4 capsules)

CV Select™ 60 VC, 120 VC
50 mg per serving (2 capsules)

HepatoDetox Select® 90 VC
50 mg per serving (3 capsules)

OculoSelect® 60 VC, 120 VC
50 mg per serving (2 capsules)

Prostate Select® 90 VC
50 mg per serving (3 capsules)

Antioxidant Select® 90 VC
25 mg per serving (2 capsules)