Considering CURCUMIN

Examining curcumin’s rapport, benefits beyond inflammation

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Viewpoint: Inflammation Buzz

Can Curcumin Develop a Rapport With Consumers?
Pete Croatto, contributing editor, explores the market for turmeric and its constituents (including curcumin), while investigating consumer recognition of curcumin.

Curcumin's Benefits Reach Beyond Inflammation
In addition to its benefits for inflammation, curcumin is making a name for itself in a number of applications including sports nutrition, brain health, beauty and more. Pete Croatto, contributing editor, reviews the latest research.

Takeaways for Your Business

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Inflammation Buzz

Like many consumers, the buzz about inflammation has grabbed my attention.

Everywhere I look (or so it seems), a magazine, TV personality, Pinterest post or other media is warning me about the effects of inflammation. Some sources, such as the famous Dr. Mehmet Oz, went as far as to label inflammation a “silent killer.” Though slightly sensational, I suppose that title isn’t untrue; chronic inflammation is, after all, linked to serious illnesses such as cancer, heart disease and dementia.

However, it may not be accurate to say inflammation is “silent.” Inflammation is linked to issues such as memory impairment, fatigue, depression and joint pain. Today’s consumers—who are increasingly proactive about health—are taking note and actively trying to manage inflammation.

Though I’m a consumer of healthy products, I also research, read, discuss and write about healthy ingredients every day (likely not the case for most consumers). That’s why I was quick to add a well-researched curcumin supplement to my daily regimen. While turmeric—from which the potent anti-inflammatory curcumin derives—is widely known (according to the article on page 14, Canadean research showed only 25 percent of consumers don’t know what turmeric is), Pete Croatto, contributing editor, asks the question: Do consumers have the same awareness regarding curcumin?

My response? Now is the time for brand owners to take charge of the buzz and start leading the conversation around the research-supported solutions such as curcumin. Beyond inflammation, research supports curcumin in areas such as brain health, sports nutrition and beauty (read more on page 5)—and those benefits need to be communicated effectively to consumers, as well. But in order to bring effective curcumin products to consumers, issues related to bioavailability and efficacy need to be addressed. This Digital Magazine addresses all aforementioned points in order to help propel your business in the curcumin space.

Happy reading,

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How Meriva® unlocks the benefits of curcuminoids

Curcumin, endowed with powerful antioxidant activity, has been shown to support joint mobility and eye health. Unfortunately, the bioavailability of the natural form is low. Which is why Indena developed Meriva®, a curcuminoid formulation that uses the exclusive, patented Phytosome system to increase bioavailability of the natural active principles. Meriva® improved the treadmill walking performance of human subjects by more than 200% in just two months.¹ Furthermore, Meriva® showed a significant improvement in individuals with eye challenges.² To discover more about how Meriva® unlocks the benefits of curcuminoids, visit indena.com today.

² Allegri P., Mastromarino A. Clinical Ophthalmology 2010, 4: 1-6

These statements have not been evaluated by the Food and Drug Administration. These products are not intended to diagnose, treat, cure, or prevent any disease. Marketers of finished products containing the ingredients described herein are responsible for determining whether the claims made for such products are lawful and in compliance with the laws of the country in which they will market the products.
Curcumin’s Benefits Reach Beyond Inflammation

INSIDER’s Take

- Curcumin has the potential to impact overall health due to its positive effects on inflammation regulation.
- In addition to its use as an anti-inflammatory, curcumin has been shown to aid metabolic syndrome management and brain health.
- Curcumin’s bioavailability and bioefficacy needs to be addressed in production formulation to ensure high-quality products.

The effectiveness of curcumin, one of the three major curcuminoids derived from turmeric, isn’t news. It boasts “over 7,500 scientific publications that validate its use, particularly as an anti-inflammatory, but more recently, with additional applications such as metabolic syndrome management and brain health,” said Shaheen Majeed, marketing director at Sabinsa Corp.

Lauren Goldberg-Samot, RD, technical sales and support, DolCas Biotech, believes curcumin should be a presence in all medicine cabinets. “Whether it’s for prevention or chronic disease, it has the potential to impact our health, and the health of everyone we care for,” she said.

This love affair, however, comes with baggage. Perhaps the heaviest parcels are curcumin’s iffy bioavailability and bioefficacy.

“Curcumin, once absorbed in the body rapidly, converts into major active conjugates known as glucuronides and sulphates, and the little active metabolite, tetrahydrocurcumin (THC),” said Sevanti Mehta, president, Unibar Corp. “Moreover, the current bioavailable formulations are loaded with excipients and have the curcuminoid content as low as from 10 percent to 20 percent. The safety of the bioavailable formulations is not well-established.”

Unibar’s CurQnetic is a proprietary enhanced bioavailable curcumin (80 percent curcumin) manufactured by Synthite—the largest manufacturer of oleo resins in India and the largest processor of curcumin in the world—from the rhizomes of Curcuma longa.

“Formulators should ask about the percentage of curcumin contained in each ingredient, as most rely on 75 percent to 85 percent of excipients and carriers to improve absorption,” Goldberg-Samot observed. Synthetic versions continue to fool formulators seduced by price and unaware of curcuminoids’ benefits, Majeed said. The safety parameters are considerable, said Krishnakumar Im, Ph.D., general manager, R&D, Akay Flavours & Aromatics Pvt. Ltd.: heavy metals, microbials, mycotoxins, illegal dyes, PAHs, pesticides and so on.
Larger doses of curcumin do not equate to increased bioavailability, Majeed added. How curcumin is “absorbed and used by the body” matters. “The fact of the matter is that curcuminoids transform in the body to tetrahydrocurcuminoids and many other metabolites,” he explained, “which is what should be looked for when verifying absorption.”

Most curcumin, and turmeric, said David Garner, CEO, Molecular Health Technologies, is excreted from the body within four to six hours. “Formulators should be careful in just looking at rapid uptake or C-Max levels of active curcuminoids, as transport ingredients such as piperine—a form of black pepper extract—can increase the uptake,” he said. “Unfortunately, that peak falls off almost as dramatically as the rise.”

Curcumin’s ability to permeate the blood-brain barrier comes with a giant caveat, Im said: few formulations provide “stable, free curcuminoids” in plasma long enough for it to penetrate the barrier. Food and beverage inclusion is far from guaranteed. “Flavor, aroma, color, water insolubility and stability are very often limitations,” he added. Its yellow color, noted Cosimo Palumbo, sales area manager, North America, Indena S.p.A., makes curcumin hard to pull off in topical applications—unless you want to look like a deli sandwich.

Yet, buzz is surrounding curcumin as companies meet the challenges of this talented, but tempestuous, antioxidant.

A few examples: Indena’s curcumin formulation Meriva reaches plasmatic and tissue levels connected to clinical outcomes in 24 published clinical trials. OmniActive Health Technologies’ CurcuWIN has “46-times greater relative absorption than standard curcumin and significantly greater absorption than other enhanced forms,” said Lynda M. Doyle, senior vice president, global marketing, OmniActive. “Even after 12 hours, retention of CurcuWIN was significantly higher than all other forms tested.” Akay, a curcumin manufacturer, offers a blood-brain barrier permeable curcumin formulation, CurQfen.

Garner pointed out that Molecular Health Technologies’ liquid curcumin NovaSQL has an advantage: “The liquid-gel absorption is exponentially more bioavailable and absorbable than any powdered extract.” Aside from its voluminous research, Sabinsa’s Curcumin C3 Complex can be incorporated into various dosage forms, including capsules, gummies and beverages. Goldberg-Samot described DolCas’s BCM-95 as “the only bioavailable curcumin extract without fillers, additives, excipients or bio-enhancers.”

Curcumin’s role as an anti-inflammatory makes these efforts worthwhile.

“The importance of chronic low-grade inflammation in the pathology of numerous age-related conditions is now clear,” Palumbo said. “The unresolved inflammatory response is likely to be involved from the early stages of cardiometabolic disorders. Establishing and quantifying reliable, precise curcumin-inflammasome-cardiometabolic health associations is reliant on the current availability of a standardized and efficiently delivered curcumin ‘ingredient.’”
Palumbo is referring to Indena’s Meriva, but more companies offer curcumin ingredients aimed at addressing inflammation. “The demand for curcumin in nutraceutical/preventive medicine is heading toward anti-inflammation, which is the root cause for all disease,” said John Nechupadom, managing director, Plant Lipids Inc. Aurea Biolabs, its nutraceutical-based company, offers curcuminoids inside a complete natural turmeric matrix.

“Research shows that curcumin is a highly pleiotropic molecule capable of interacting with numerous molecular targets involved in inflammation,” Palumbo explained. “Curcumin modulates the inflammatory response by suppression of NF-kB (nuclear factor kappa-light-chain-enhancer of activated B cells) activation, down-regulating the activity of enzymes (cyclooxygenase-2 [COX-2], arachidonate 5-lipoxygenase [5-LOX], and inducible nitric oxide synthase [iNOS]) by inhibition of the production of the inflammatory cytokines tumor necrosis factor alpha (TNF-α), interleukins (IL-1,-2,-6,-8 and -12), monocyte chemoattractant protein (MCP) and migration inhibitory proteins.” Or as Carol Cheow, founder and general manager, Cactus Botanics, put it: “Research shows that curcumin has anti-inflammatory effects on all acute, sub-acute and chronic inflammation.”

“The result is a cascade of promising studies featuring curcumin’s influence throughout the body, which is a boon for product manufacturers. Marketing inflammation, Majeed said, is risky. However, “since condition-specific products are extremely popular with today’s consumers, brand owners can utilize structure/function language to convey the benefits to consumers legally.”

**Brain Health**

“Pre-clinical studies indicate that curcumin has a neuroprotective effect,” Mehta said. “Chronic administration of curcumin significantly reversed levels of 3, 4-dihydroxyphenylacetic acid, noradrenaline, serotonin and 5-hydroxyindoleacetic acid in the hippocampus region of male albino rats. Also, curcumin normalizes the levels of dopamine, noradrenaline and 5-hydroxyindoleacetic acid in the frontal cortex of rats.”

Palumbo highlighted two more studies: the first from *The International Journal of Ophthalmology and Clinical Research* in 2014; the last from *Biochimica et Biophysica Acta* in 2015.

In the first, Umur Kayabasi from Istanbul’s World Eye Hospital provided “the first objective evidence that curcumin labels amyloid beta (Aβ) plaques in the retina of...
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pre-Alzheimer’s disease (AD) patients [which substantiates] the use of curcumin in chronic degenerative mental conditions.” In the second study, curcumin was shown to enhance docosahexaenoic acid (DHA) synthesis. “These animal data will have important implications for human health in the prevention of cognitive and mood disease,” Palumbo explained, “Because DHA deficiency is linked to several disorders, such as anxiety-like behavior, AD and depressive disorders.”

**Sports Nutrition**

Palumbo said a 2007 study in *The American Journal of Physiology - Regulatory, Integrative and Comparative Physiology* is “one of the first demonstrations of curcumin’s effects on inflammation and performance recovery following eccentric exercise-induced muscle damage.⁶

“This is a well-done preclinical model conducted in a specialized American center, and the positive results have been recently translated in humans by Drobnic,” he said, referring to a 2014 study. “The trial was a randomized, placebo-controlled study. Even if the sample size is low and the administration very short, interesting objectives (statistically significant) and subjective parameters were recorded after the use of curcumin phytosome.”

On the proprietary side, “Theracurmin has a randomized, double-blind placebo controlled crossover study in healthy subjects showing a significant improvement in strength recovery over four days compared to the placebo,” said Alice D. Hirschel, Ph.D., commercial development specialist, Innophos Nutrition. “Theracurmin also has a study with a similar design showing significant improvements in blood flow during exercise, supporting critical nutrient delivery.” Both of these studies are unpublished.

**Beauty**

For years, Majeed said, turmeric—the source of curcumin—has long been popular in beauty care routines.

“Turmeric has been traditionally used in creams and lotions, promoted for smooth and radiant skin,” he said. “It is also well-recognized for its antimicrobial property and finds use in anti-acne formulations. Curcuminoids help prevent connective tissue breakdown through inhibition of destructive enzymes and thus finds application in anti-aging, sun care and ultraviolet (UV)-protectant formulations.”

Palumbo said clinical research published in *BioMed Research International* demonstrated that “oral curcumin is effective as an adjuvant therapy for the treatment of psoriasis vulgaris, a common chronic inflammatory disorder of the skin and nails.”⁸ As for another beauty care element, Steve Siegel, vice president, Ecuadorian Rainforest LLC, pointed to a study published this year suggesting curcumin could be a useful ingredient for oral hygiene.⁹

“When it comes to research, I would definitely encourage formulators and consumers to focus on clinical studies that look at the effects of curcuminoids and turmerones together,” Goldberg-Samot said. “BCM-95 [from
DolCas Biotech] is a combination of both, and many clinical trials show that efficacy improves with turmerones. Turmerones, in general, have anti-inflammatory, anti-microbial and anti-cancer effects that synergistically work with the anti-inflammatory/antioxidant effect of all three curcuminoids.”

Goldberg-Samot said she believes curcumin could be used as an “adjunct” to chemotherapy and radiation therapy. Her focus on curcuminoids and turmerones is a reminder to formulators to exercise caution when evaluating branded curcumin ingredients and deciding which option to elevate.

It’s important to read the studies carefully. “All of our clinical studies have examined key inflammatory biomarkers, which is why it is so important for formulators to know about these biomarkers and how they interact,” said Sonya Cropper, vice president of marketing and innovation, Verdure Sciences. “It is not just one measure; it is a measure of the combined benefits of each of the biomarkers. For example, (two studies led by researchers) DiSilvestro and McFarlin have shown impressive results in inflammatory biomarkers.10,11 At the same time, McFarlin examined recovery after exercise-induced muscle damage, which inherently lends itself to a ‘sports nutrition’ category. Furthermore, both of the aforementioned studies used a single 400 mg daily dose of Longvida (from Verdure Sciences).”

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— Lauren Goldberg-Samot, R.D., technical sales and support, DolCas Biotech

Im urged product manufacturers to understand the research behind curcumin—and what lies ahead.

“Current understanding is that free unconjugated curcuminoids possess better bioactivity and permeability for cell uptake and furnish beneficial pharmacological effects,” Im said. “Considering this factor, a tremendous amount of academic research is going on to develop nanoparticles suitable for injections. Unfortunately, not many food-grade formulations capable of oral delivery to achieve the goal of free curcuminoids absorption are commercially available. So, the manufacturers should identify suitable formulations capable of providing the bioactive forms of curcuminoids in high levels. Industry has not taken this important latest information in the seriousness it deserves. Substantial education efforts regarding the important determinants that decide the activity of curcuminoids more than just number of folds bioavailability, is thus crucial.”
Ingredient companies need to look beyond bioavailability, Goldberg-Samot said. “Formulators should request research that shows the curcumin ingredient can be effective for joint pain, cognitive health, prostate health, inflammation and as an adjunct therapy,” she said.

Palumbo offered a list of questions that manufacturers should ask, covering three categories. First, is consistency regarding the ingredient’s quality attributes: “Does the supplier provide a clear composition of its formulation? What is the standardization of the extract?” Then, the studies have to be examined: “Is the bioavailability issue with curcumin solved? Is the pharmacokinetic study published in a peer-reviewed journal?” Finally, comes proprietary data: “Is efficacy available on the specific formulation or is it just borrowed science?”

“Manufacturers should continue to invest and engage with their ingredient suppliers, especially when it comes to education,” Cropper said. Majeed offered the following warning: “Not all curcumin products are created equal. The differences are profound, literally from the ground up. From their sourcing to their manufacturing, certain processes will produce the best curcuminoids for consumption and health benefits.”

And, of course, using an effective amount of curcumin helps.

“Clinical substantiation is key when looking at technical ingredients, especially regarding clinical dosing,” Cropper said. “For instance, many ingredients have substantiations for larger doses over 1,000 to 3,000 mg per dose. However, formulators will create a finished product using a subtherapeutic dose.” Or, she added, formulators jump at a lower price point for curcumin, use more and end up paying the same (if not more) as a vetted, beneficial ingredient.

“We invested substantial time and money of our R&D [research and development] to develop various forms of curcumin suitable for meeting the varying demands of new product design, dreams and challenges,” Im said. “We are also happy to work with the marketers or formulators to develop specific and exclusive forms.”

Wait for it …

“Now,” Im added, “marketers should lead the way by designing and formulating unique forms suitable for various age groups—say pediatrics to geriatrics.”

Translation: We’ve stepped up our game, finished product manufacturers. It’s your turn to make some news.
References


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Can Curcumin Develop a Rapport with Consumers?

by Pete Croatto

The optimism over curcumin has spread to consumers. Kind of.

Turmeric sales over the last year are impressive. According to SPINS LLC, an information provider for the natural and specialty products industry, turmeric and its constituents saw sales explode by up to 90 percent across the food and beverage category in the natural and multiple outlet channels: around US$5.2 million and $5.8 million, respectively.

Growth was also robust when it came to turmeric vitamins, supplements, herbs and homeopathics:

- Multiple outlets saw sales of close to $20 million, a leap of more than $10 million
- In the natural channel, sales increased from $31.2 million to $42.7 million

Both sets of statistics were based on sales for the 52 weeks ending May 15, 2016. Sales of turmeric, in this instance, also refer to its constituents, including curcumin, said Kimberly Kawa, senior nutrition researcher, SPINS.

“Turmeric is still a trendy ingredient with mainstream appeal,” Kawa said. “I’m always coming across new research on turmeric and constituents. Noticing the use of turmeric gaining more traction as part of a whole food diet, like incorporating in smoothies, golden milk, on veggies, popcorn topping, scrambled eggs, soups/curries and so on—the possibilities are endless. It’s even turning up in body care products, in addition to DIY (do it yourself) oral care applications.”

In Canadean’s 2015 ingredient survey, only 25 percent of American consumers didn’t know what turmeric is, noted Tom Vierhile, the company’s innovation insights director. Do consumers have the same awareness regarding curcumin?

“Based on what is happening in new products, consumers are more likely to be familiar with turmeric than curcumin,” Vierhile said. “But there are some categories where curcumin awareness may be higher, like joint pain relief products. Given the chronic nature of joint pain, consumers that suffer from it may be more motivated to...
seek novel solutions to the problem than they would seek out the ingredient in more general applications. The difficulty with evaluating something like curcumin is that there seems to be a laundry list of reputed benefits for curcumin, including the ability to cure cancer or ease depression, but it isn’t clear if any of these reputed claims have been substantiated.”

Sonya Cropper, vice president of marketing and innovation at Verdure Sciences, sees the demand for curcumin going “up, up and away” as consumers become more educated. However, product manufacturers and formulators must “really dig into the research and bring it to market in an easily understood way—be the advocates for your end consumer.”

“The demand for curcumin products is big enough that having a single product offering in a line isn’t enough, and we’re seeing more manufacturers include curcumin into multiples categories, including multivitamin and children formulas,” said Lynda M. Doyle, senior vice president, global marketing, at OmniActive Health Technologies. “This trend also parallels the increased demand for enhanced curcumin products to address issues of solubility, bioavailability and efficacy using smaller dosages.”

Pete Croatto has been writing about the natural products industry since 2003; from 2011 to 2015 he was the community manager of INSIDER’s Supplement Perspectives. He currently resides in Ithaca, New York, where he is a full-time freelance writer.
Takeaways for Your Business

Curcumin, one of the three major curcuminoids derived from turmeric, offers health benefits supported by more than 7,500 scientific publications, according to Shaheen Majeed, marketing director at Sabinsa Corp. While much of curcumin’s supporting research focuses on its anti-inflammatory effects, Majeed noted newer research is looking at its benefits related to applications such as metabolic syndrome management and brain health.

Pre-clinical studies indicate curcumin has a neuroprotective effect (Adv Exp Med Biol. 2007;595:197–212), and normalizes the levels of dopamine, noradrenaline and 5-hydroxyindoleacetic acid in the frontal cortex of rats (Brain Res. 2016;1642:219-25). Further, it was shown to enhance docosahexaenoic acid (DHA) synthesis (Biochimica et Biophysica Acta. 2015;1852(5):951-961)—beneficial for mood and cognitive disease—and has been supported for use in chronic degenerative mental conditions (Int J Ophthalmol Clin Res. 2014;1:1).

Its anti-inflammatory effects have proven beneficial to athletes (Am J Physiol Regul Integr Comp Physiol. 2007;292(6):R2168-73), and in certain beauty applications.

Though scientific validation is important, developers can’t neglect two primary concerns when considering curcumin—bioavailability and bioefficacy.

Sevanti Mehta, president, Unibar Corp., explained: “Curcumin, once absorbed in the body rapidly, converts into major active conjugates known as glucuronides and sulphates, and the little active metabolite, tetrahydrocurcumin (THC). Moreover, the current bioavailable formulations are loaded with excipients and have the curcuminoid content as low as from 10 percent to 20 percent. The safety of the bioavailable formulations is not well-established.”

Larger doses of curcumin do not equate to increased bioavailability, Majeed warned.

How curcumin is “absorbed and used by the body” matters.

Though there are ways to improve uptake of curcumin within the body, there’s more to consider than rapid uptake, cautioned David Garner, CEO, Molecular Health Technologies. “Formulators should be careful in just looking at rapid uptake or C-Max levels of active curcuminoids, as transport ingredients such as piperine—a form of black pepper extract—can increase the uptake,” he said. “Unfortunately, that peak falls off almost as dramatically as the rise.”

The market for turmeric and its constituents is experiencing considerable growth. During the 52 weeks ending May 15, 2016, sales exploded by up to 90 percent across the food and beverage category in the natural and multiple outlet channels: around US$5.2 million and $5.8 million, respectively, according to SPINS LLC. Further, according to Canadean’s 2015 ingredient survey, only 25 percent of American consumers didn’t know what turmeric is, noted Tom Vierhile, the company’s innovation insights director. But developers must consider the question: Do consumers have the same awareness regarding curcumin?
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