AOR
Advanced Orthomolecular Research

THE TRUTH ABOUT CURCUMIN

SETTING THE RECORD STRAIGHT

THE SKINNY ON AOR'S FREE FORM CURCUMIN

THE TRUTH SERIES

THE TRUTH SERIES

As a discerning user of natural health products, you want what is best for your health. However, misinformation and deceptive marketing often makes it challenging to identify fact from fiction. The Truth Series was created by Advanced Orthomolecular Research (AOR) to share the evidence-based truth about the most controversial and confusing topics within the natural health industry. At AOR, we believe that truth and transparency are the most important values for any organization to uphold. As visionaries, we are committed to continuous innovation so that we can advance the world of natural health. As such, the Truth Series aligns with our vision of providing optimal products without compromise.

Published in Canada by: Advanced Orthomolecular Research Inc.

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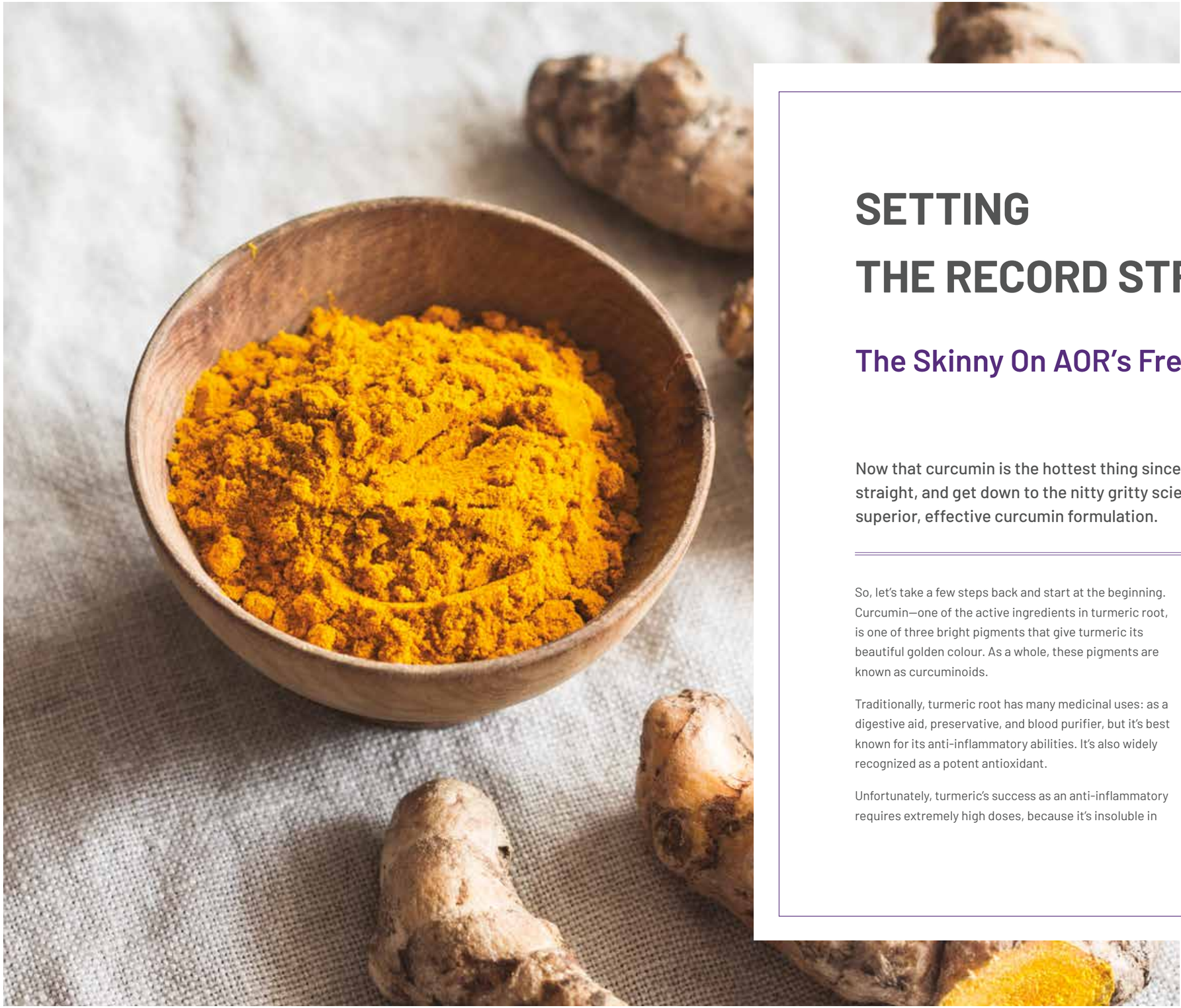


SETTING
THE RECORD STRAIGHT

The Skinny On AOR's Free Form Curcumin

Now that curcumin is the hottest thing since sliced bread, it's time to set the record straight, and get down to the nitty gritty science-based facts of what makes a truly superior, effective curcumin formulation.

So, let's take a few steps back and start at the beginning. Curcumin—one of the active ingredients in turmeric root, is one of three bright pigments that give turmeric its beautiful golden colour. As a whole, these pigments are known as curcuminoids.

Traditionally, turmeric root has many medicinal uses: as a digestive aid, preservative, and blood purifier, but it's best known for its anti-inflammatory abilities. It's also widely recognized as a potent antioxidant.

Unfortunately, turmeric's success as an anti-inflammatory requires extremely high doses, because it's insoluble in water and many fats. This means that it has a hard time dissolving, making absorption exceptionally difficult.

For example, when turmeric powder is added to water or pressed juice, you are often left with this yellow sediment at the bottom of your glass, because it has so much trouble dissolving. This results in poor bioavailability, which refers to how much of a substance is absorbed into the bloodstream.

Practitioners of Ayurveda figured this out quickly, and came up with ways to assist in absorption by slightly altering it. Turmeric was usually boiled or heated

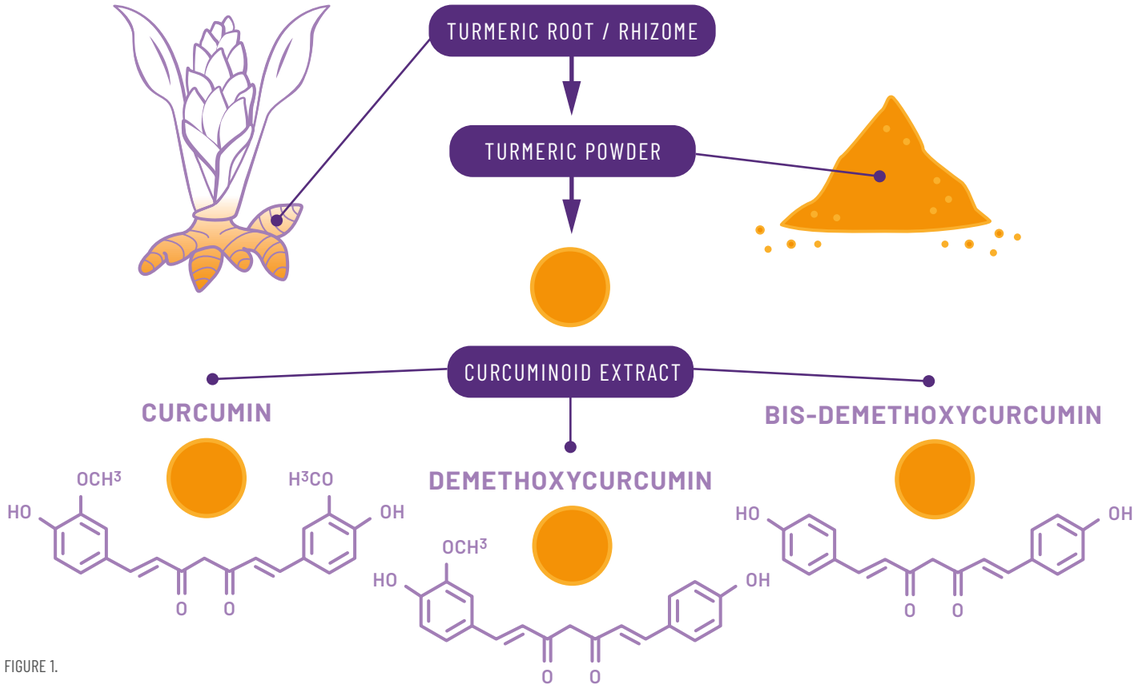


FIGURE 1.

Turmeric and its curcuminoids: Turmeric Rhizome (Curcuma longa L.), Turmeric powder, Curcuminoid extract. Turmeric's 3 Curcuminoids: Curcumin, Demethoxycurcumin, and Bis-demethoxycurcumin.

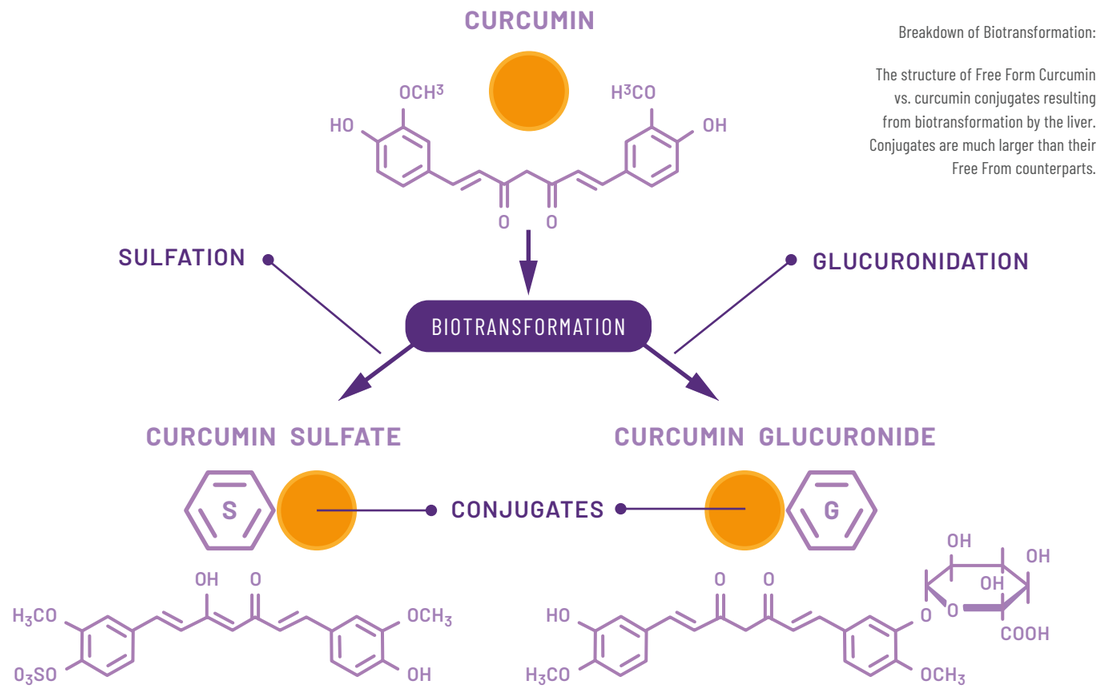


FIGURE 2.

Breakdown of Biotransformation:

The structure of Free Form Curcumin vs. curcumin conjugates resulting from biotransformation by the liver. Conjugates are much larger than their Free From counterparts.

before ingestion, or heated and suspended in a fat, such as clarified butter or milk. While these noted methods are helpful at improving the medicinal benefits of turmeric, they do little to increase the absorption of actual curcuminoids, the substances mostly responsible for its anti-inflammatory activity. This is because turmeric's curcuminoids only make up about 2-6% of the total content of the root. Furthermore, because curcuminoids are little "powerhouses"—particularly curcumin, researchers wanted to find a way to increase their concentration for maximum benefit. These factors led the industry to create more bioavailable curcumin formulas with a higher concentration of curcuminoids.

The first in a series of "altered" curcumin formulations is standardized Curcumin-95. Here, turmeric undergoes an extraction process, where the curcumin is standardized from 2% to 95%. Although this produces a stronger curcumin formulation, the buck doesn't just stop here. Granted, the higher amount of curcumin is now concentrated and therefore more potent, but the issue of absorbability/bioavailability has not been correctly addressed.

The human body is a complex organism that undergoes extremely finite processes each second. Many of these processes are governed by the liver—the metabolic centre. It is responsible for many things, most importantly detoxification. Simply put, the liver breaks down and removes substances from the body. One step in this process is known as conjugation, where specific liver enzymes essentially "tag" a substance by attaching themselves to it; readying the substance for removal from the body. Conjugation is often referred to as biotransformation because not only is the structure altered, but the substance also loses its original potency (i.e. strength in effect). Moreover, the body loves to readily conjugate curcumin and seal its fate as what we call "broken" and or "chained" curcumin. We use this analogy because it's as if the body literally takes curcumin prisoner and shackles it with a ball and chain during conjugation, ensuring that it's not free to incite a healing revolution within.

Thus, a clear understanding of this process of rapid breakdown sets the stage for what is known as Free Form Curcumin, aka unbroken, unadulterated curcumin, with AOR being the first company in Canada to bring it to market back in 2006.

Now here's the real deal—the skinny. To date, the only two curcumin formulations in the world that successfully evade rapid breakdown by the liver and produce Free Form Curcumin are **Longvida®** and **CurQfen®**. These two raw materials are the only ones with peer-reviewed clinical trials to prove this. Also, study results for numerous curcumin formulations are often skewed when it comes to naturally occurring Free Form Curcumin vs. conjugated curcumin.

WHAT KIND OF CURCUMIN DO YOU WANT COURSING THROUGH YOUR VEINS? ONE THAT IS "BROKEN AND CHAINED," OR ONE THAT IS WHOLE AND FREE TO MOVE AROUND UNINHIBITED?

In many cases, an enzyme is used to literally de-conjugate the tagged curcumin in the blood samples taken from study participants! Unfortunately, this practice generates manipulated test results, and does not accurately reflect the process curcumin undergoes within the body. This has also led certain companies to claim that the body naturally undergoes this process at a site of inflammation, resulting in all curcumin formulas producing Free Form Curcumin. Not only is this extremely unlikely, it has never been proven in humans regarding curcumin, and goes against the laws of human biochemistry. However, this is not to say that many of the curcumin formulas on the market don't work. They do, and many have excellent ingredients and well-designed studies to boot; they're just not as effective, fast acting and long lasting as their Free Form counter parts.

These formulas miss the mark with their claims to higher absorbability/bioavailability because they are producing conjugated curcumin—not Free Form Curcumin, regardless of how much better absorbed each formula is. So, although more curcumin is absorbed, it's in a form that is less active, and therefore less therapeutic, which inevitably results in a less effective product.

So, what kind of curcumin do you want coursing through your veins? One that is "broken and chained," or one that is whole and free to move around uninhibited? That said, let's explore the truth about curcumin.

THE WISDOM OF THE PAST

A History of Turmeric

Turmeric root, aka Curcuma longa L. is a Rhizome that belongs to the Zingiberaceae/Ginger Family. It has a long history dating back to 250 BCE and is used primarily as a spice in most South/Pan Asian cuisine.

It possesses a rich, deep, bright orange/golden colour due to its high content of pigments known as curcuminoids. These beautiful pigments are known as fluorochromes, meaning they are fluorescent! This explains why turmeric has been used as dye, a colouring agent in paint, and why it stains so easily. These pigments are truly unique and very special, seeing they are mostly responsible for turmeric's therapeutic activity.

There are three active curcuminoids present in turmeric: curcumin, demethoxycurcumin (DMC), and bis-demethoxycurcumin (BDMC), with curcumin being the most concentrated. It comprises approximately 2/3 of total curcuminoids, while the other two comprise the remaining 1/3 (Nardo et al., 2011).

In Sanskrit, turmeric root has many names associated with it such as, "auspicious or lucky," "to give a fair complexion" and "killer of poison" denoting how revered this substance is.

It has been used in Ayurveda—India's Traditional Medical System for 4000 years and like its gorgeous colour, is literally worth its weight in gold!

Traditionally, turmeric is used for both prevention and treatment of disease. Its traditional uses include: treating inflammation, managing pain, treatment of skin ailments like acne and skin cancer; digestive issues, such as colic; distention, and liver/gallbladder complaints. In Ayurveda, it is used to strengthen overall Prana or Life Force, regulate menstruation, purify blood, treat respiratory conditions and rheumatism; and dissolve gallstones.

Both Ayurveda and TCM consider turmeric as a highly supportive digestive bitter.

Turmeric is the most clinically studied natural substance in the world. With over 4000 publications to date, its proven therapeutic benefits are vast. Studies have confirmed that curcumin has potent anti-oxidant, anti-microbial, anti-inflammatory, and anti-tumour properties (Ireson et al., 2001; Sandhur et al., 2007).

IN SANSKRIT, TURMERIC ROOT HAS MANY NAMES ASSOCIATED WITH IT SUCH AS, "AUSPICIOUS OR LUCKY," "TO GIVE A FAIR COMPLEXION" AND "KILLER OF POISON."

MULTIPLE AREAS THAT CURCUMIN HAS BEEN STUDIED

Cancer

Cardiovascular Disease

Infection

Inflammation

Lifestyle Factors

Neurological Disease

Furthermore, studies suggest that curcumin acts on multiple tissues in many diseases, including: cancer, diabetes, cardiovascular disease, neurological diseases, and rheumatoid arthritis (Gupta et al., 2012).

Curcumin's issues of absorbability and bioavailability have led to an array of products with varying technologies that address these two factors. Unfortunately, while their aim is good, they still miss the mark. Although bioavailability and absorbability are important factors in evaluating the effectiveness of curcumin, the key lies in its ability to remain free.

When curcumin is formulated to not only solve issues of bioavailability and absorbability, but address rapid breakdown within the body, the result is Free Form Curcumin. Because curcumin retains its free "unbroken" form, it is taken up directly through the bloodstream where it is stable, concentrated and able to cross the blood brain barrier.

The liver is the major organ responsible for metabolizing or breaking down substances. When something is ingested, it is normally absorbed into the bloodstream through the hepatic portal vein. The first stop for this "portal blood" is the liver. Here, these substances have phase II enzyme groups known as glucuronide or sulphate added to them. This process is known as conjugation or biotransformation (hepatic first pass metabolism) and makes a substance extremely soluble. These newly formed metabolites are then carried to our kidneys and bowel and ready for excretion.

When curcumin is able to avoid this rapid breakdown, it retains its activity. Furthermore, a true understanding of Free Form Curcumin clarifies how bioavailability and absorbability are only one side of a very complex coin when it comes to curcumin. When the whole picture is in view, we are able to gain clarity into the present state of curcumin within our industry. What you might believe is a high quality, effective product, might not be, and products with superior formulation are often highly misunderstood. However, once the process of biotransformation is better understood, it becomes clear that all of curcumin's benefits significantly increase when it retains its Free Form. Thus, resulting in a highly potent, bio active product.

CURCUMIN — A RESEARCH-BACKED BOTANICAL POWERHOUSE

In more recent years, the anti-carcinogenic activity of curcumin both in prevention and treatment has been studied in colon, bone marrow, breast (Liu et al., 2013), prostate, and lung cancer (Sharma et al., 2001; Gomez-Bougie et al., 2015; Tieten et al., 2010; Tsai et al., 2015). While curcumin has been established as safe and nontoxic at high doses in humans (Krishnakumar et al., 2015), how curcumin has such a diverse range of medicinal effects is less understood.

GETTING CURCUMIN INTO THE BODY

Understanding Bioavailability

It is now clear that poor bioavailability limits curcumin's use. With respect to the whole food approach in particular, large quantities of turmeric powder can be consumed and may not result in beneficial concentrations of curcumin in the blood.

Trials have shown that low levels of curcumin are present in the blood samples of participants administered high doses of curcumin (Anand et al., 2007). Some estimates suggest that only about 2% of curcumin taken orally is transported via the blood to the tissues. Furthermore, Pan and colleagues showed that 99% of curcumin in the bloodstream is conjugated curcumin (Pan et al., 1999). Studies have shown that conjugated curcumin has significantly lower bioactivity as compared to Free Form Curcumin and is readily excreted by the kidneys (Ireson et al., 2001; Pal et al., 2014; Shoji et al., 2014; Choudhary et al., 2015). Moreover, conjugated curcumin is also bulkier since it has a glucuronide or sulphate group attached, so less able to cross the lining of blood vessels and the blood brain barrier (BBB) (Krishnakumar et al., 2015).

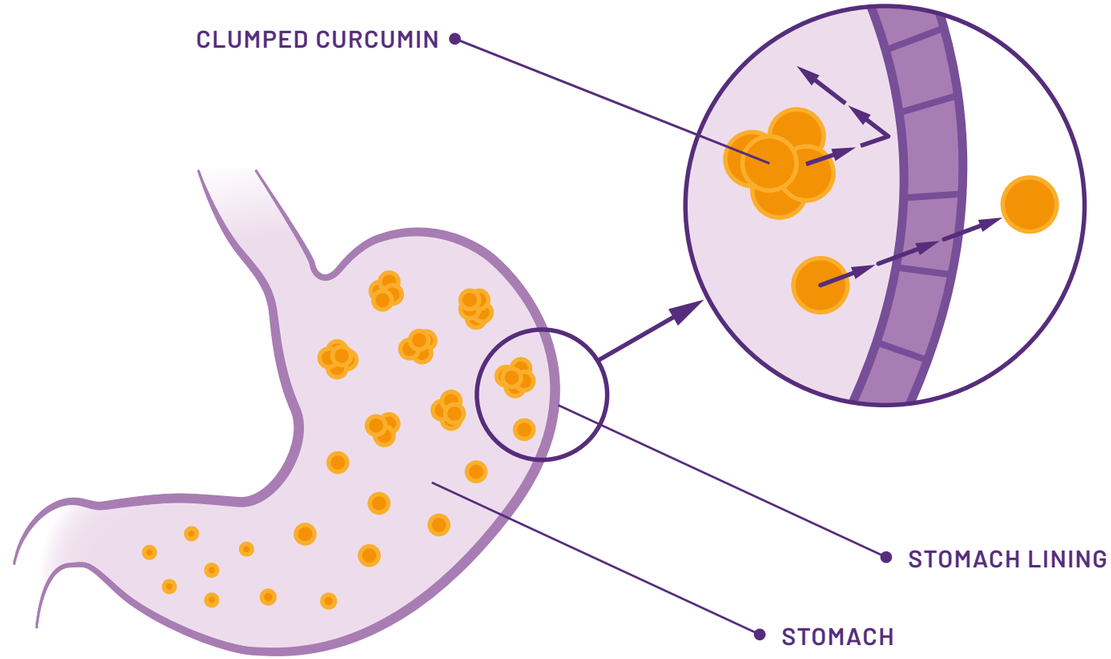


FIGURE 3.

The curcumin conundrum: Because curcumin is insoluble in water, it has a hard time dissolving in the stomach. Furthermore, due to its acidic pH, curcumin begins to clump and is largely unable to pass through the stomach lining into the bloodstream (Kharat et al., 2017).

FACTORS FOR POOR CURCUMIN BIOAVAILABILITY ARE:

INSOLUBILITY / INSTABILITY:
Turmeric is highly insoluble and has a very hard time dissolving in water, much like sand. Its curcuminoids are hydrophobic and lipophilic (i.e. water hating, fat loving), and as a result, have a high tendency to clump and then crystallize as the pH gradient shifts through the digestive process. This significantly inhibits absorption into the gut and bloodstream.

RAPID BREAKDOWN:
Unfortunately, what does manage to escape this ill-fated process, is readily broken down by the liver through biotransformation.

RAPID ELIMINATION / SHORT HALF-LIFE:
The rapid elimination of curcuminoids through the bowel further reduces curcumin's bioavailability since its half-life is less than two hours, with little curcumin previously absorbed into the bloodstream (Sharma et al., 2001). Half-life refers to the time at which half the amount (50%) of an ingested substance will have been eliminated.

UNDERSTANDING DIFFERENT TYPES OF “ENHANCED” CURCUMIN

Curcumin Just Can’t Seem To Get A Break.

This has led researchers worldwide to try and effectively remedy the profound conundrum curcumin faces as a therapeutic, multi targeted medicine. How could Nature bestow one little spice with such propensity for healing, yet have it almost be completely unable to achieve its biochemical goal once ingested? It’s ever perplexing to say the least and takes us to the ins and outs of modern curcumin delivery methods and formulation.

Modern delivery methods include: micronization and nanoparticles; micelles, enhancing agents, and fibre complexes.

MICRONIZED NANOPARTICLES:

This is a when a particle is significantly reduced in size, and is defined as less than 100 nanometers in diameter, or 0.1 micrometers. There is also a process known as sub-micronization, where although particle size is significantly reduced, it is still larger than a nanoparticle. In the case of curcumin, size reduction aids with absorption into the bloodstream.

MICELLES:

These little “fat” spheres are generally made of phosphatidylcholine aka lecithin. These coated curcumin particles have increased stability within digestive juices, and are able to absorb into the bloodstream more easily. Curcumin micelles can either have standard curcumin particles or nanosized ones.

ENHANCING AGENTS:

There are a variety of enhancing agents used in modern formulations to address the issue of poor absorption and rapid breakdown such as: piperine, turmeric essential oil, Tween-80, and galactomannan.

PIPERINE

Piperine is the most common and widely documented enhancing agent used because it inhibits the biotransformation of curcumin by the liver. Neat little trick, right? Although this sounds like a “magic bullet” cure to the curcumin conundrum, it looks better on paper, than in actual application. Because piperine inhibits the phase II liver enzymes (necessary gatekeepers), the liver’s ability to do its job correctly is significantly diminished. So although one would have “free form” curcumin coursing through their veins, the body is now vulnerable to unwanted invaders, such as toxins, pesticides, and carcinogens. Thus, a truly intelligent formulation would find a way to evade this rapid breakdown, without disarming the body’s defences and endangering it as a whole.

TURMERIC ESSENTIAL OIL

Turmeric Essential Oil, like all essential oils, is classed as a volatile oil. Because of its solubility issues, it is made by a solvent extraction process. Furthermore, they are termed volatile for a reason, seeing they are extremely potent and generally only regarded as safe when ingested in tiny amounts. Usually only 1-2 drops are suggested short term, not large doses for extended periods. Because the vast majority involved in botanical medicine tend to be cautious with volatile oil consumption, one can’t help but wonder if there isn’t a risk at higher doses, long term. The research is conflicting as well, seeing some of it regards turmeric essential oil as safe, while other data notes high toxicity (Funk et al., 2006, 2010; Joshi et al., 2003). Until there is enough well-established data in humans confirming safety at high doses, long term, the use of this enhancing agent is questionable.

TWEEN 80

Tween 80, also known as Polysorbate 80, is another questionable enhancing agent used in modern formulation. It is a detergent classed as a surfactant/emulsifier and commonly used in processed foods, cosmetics, pharmaceuticals, etc. Although known to be well tolerated up to 100 mg per day, it is banned in Japan, while Taiwan and Korea have set limits to less than 2%. Interestingly, there has also been some research correlating Tween-80 with the aggravation of autoimmune diseases, such as colitis. It was also shown to potentiate obesity and metabolic syndrome (Chassaing et al., 2015). Do you find it ironic that an agent designed to enhance an anti-inflammatory might be the possible cause of pro-inflammatory conditions?

GALACTOMANNAN

Galactomannan aka Fenugreek (Trigonella foenum-graecum L.), is the latest breakthrough in effective curcumin delivery, stability and absorption. Due to the fact it is a water soluble dietary fibre, yet highly branched and gum like, it is able to offer superior protection to ensure absorption into the bloodstream.

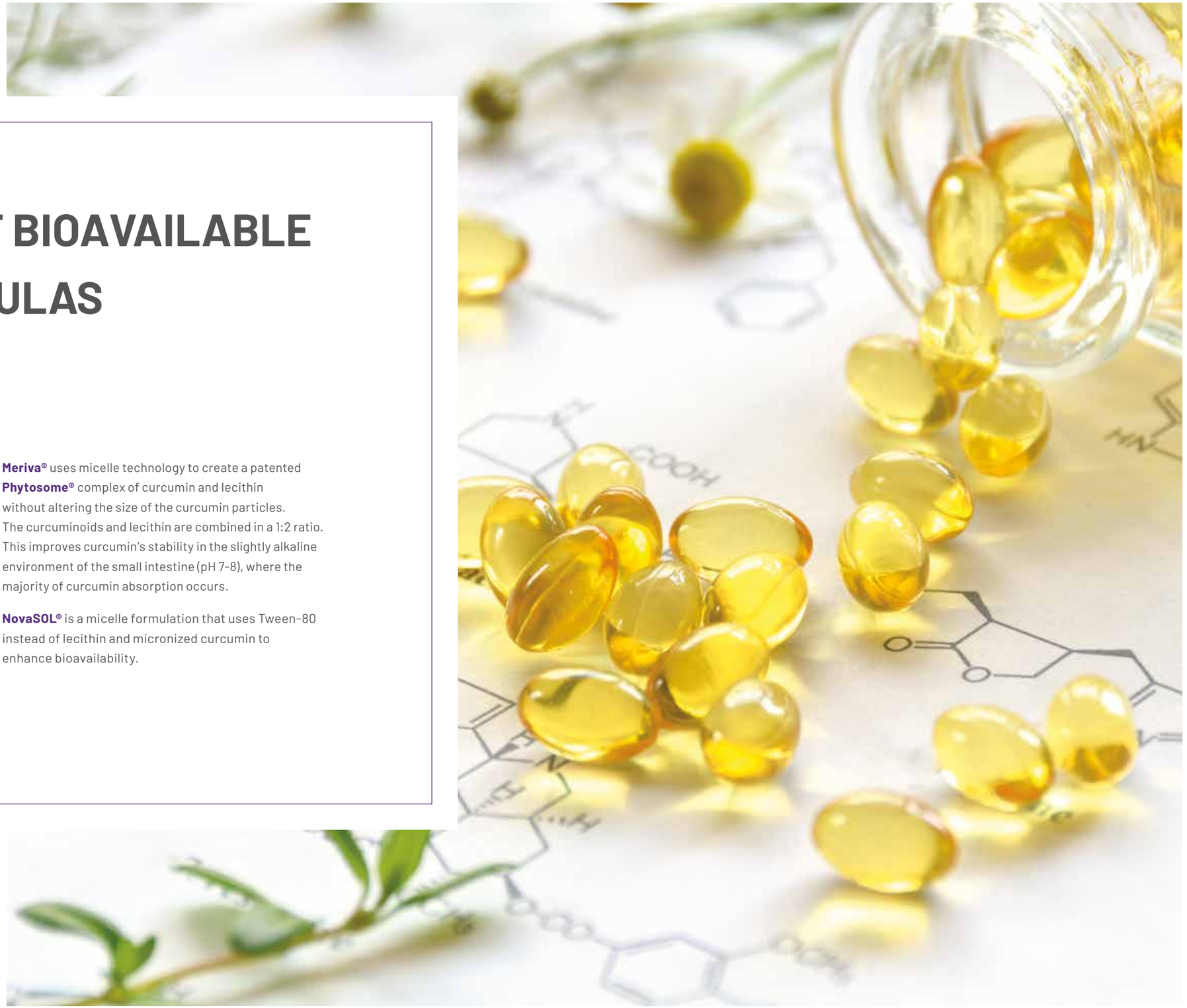
AN OVERVIEW OF BIOAVAILABLE CURCUMIN FORMULAS

Theracurmin™ is a nanosized curcumin formula made from a mixture of micronized curcumin and gum ghatti solution. Theracurmin's particle size is reduced via a wet mill grinding process and then dispersed using a high-pressure blending technique. This creates a colloidal suspension that is highly water soluble.

BCM-95® is a patented curcumin formula that combines curcumin and volatile agents in turmeric essential oil to increase bioavailability. The formula is also comprised of lecithin and medium chain triglycerides to further assist in this process. Turmeric essential oil constitutes approximately 9% of the formulation.

Meriva® uses micelle technology to create a patented **Phytosome®** complex of curcumin and lecithin without altering the size of the curcumin particles. The curcuminoids and lecithin are combined in a 1:2 ratio. This improves curcumin's stability in the slightly alkaline environment of the small intestine (pH 7-8), where the majority of curcumin absorption occurs.

NovaSOL® is a micelle formulation that uses Tween-80 instead of lecithin and micronized curcumin to enhance bioavailability.



Although all the delivery methods discussed above do effectively address issues of absorbability/bioavailability, and have studies to prove this, they still can't successfully evade rapid break down. They absolutely do not yield Free Form Curcumin—only conjugated curcumin, regardless of whatever marketing pitches are given.

Again, there is no clinical data to support this claim for the aforementioned formulas, and data results are often manipulated to show falsified "free form" values. This is done by using an enzyme known as Beta-glucuronidase. This processes de-conjugates the curcumin metabolites by removing the glucuronide or sulphate chain from study blood samples before analysis. Talk about sneaky! Furthermore, the claim that all curcumin is Free Form Curcumin is also in the vein of fake news. The hypothesis that Beta-glucuronidase is excreted at sites of inflammation and can therefore de-conjugate curcumin at the site is just not sound. This idea goes against the laws of human biochemistry and has never been proven with curcumin in humans. For the sake of argument, however, let's just say this were true. If so, then how would Beta-glucuronidase know to only to liberate curcumin and not other hazardous substances that have been tagged for removal? If this process was actually natural in humans, then would it not render the entire detoxification processes obsolete? If someone ingested a known carcinogen which was then logically conjugated for safe removal, and then de-conjugated again, would it not create a rogue carcinogen?

Moreover, would it not then just freely reign and immediately induce disease? Lastly, if all of this were indeed true, the "Free Form" created would have lost almost all of its therapeutic activity, seeing conjugated curcumin is much less bioactive than true Free Form (Shoji et al., 2014). Without having a legitimate leg to stand on, this nonsensical assumption seems like more for the sake of a fake argument, than anything else.

To date, there are only two formulas that yield true Free Form Curcumin: **Longvida®** and **CurQfen®**, and both have accurate studies to prove this. So what on earth makes these two so very special in comparison to the rest?

Longvida® is based on Solid Lipid Curcumin Particle (SLCP™) Technology. This consists of a unique combination of highly purified lipids that coat the micronized curcumin particles. This is different from a micelle, as there are lipids other than just lecithin involved. This combination of minute particles is organized in such a way as to increase bioavailability and absorption, and remarkably avoid rapid break down. This unique formulation allows for each SLCP™ to be taken up through the lymph system as opposed to being absorbed directly into primary circulation and broken down by the liver; therefore, successfully evading rapid breakdown.

TO DATE, THERE ARE ONLY TWO FORMULAS THAT YIELD TRUE FREE FORM CURCUMIN.

As mentioned, the liver—our master organ, governs most functions in the body and is responsible for the primary metabolism of substances. This process is known as first pass metabolism. However, depending on the molecular structure of a substance, a secondary, intermediate process known as enterocyte first pass metabolism comes into effect. When a substance has a high molecular weight and is comprised of very specific lipids, such as fatty acids and phospholipids, it is taken up through the enterocytes (nutrient absorption cells) that line the small intestine. It is then carried into the lymph system, which is how it is able to successfully evade rapid breakdown. Unlike the portal blood, the intestinal lymph empties directly into the primary circulation without first passing through the liver. Once in the lymph, it is transported directly to the heart. The heart will then pump this newly "enriched blood" to sites of therapeutic activity such as the brain, lungs, tissues, etc. before it returns to the liver where it will eventually undergo metabolism. **Longvida®** was the first formulation to successfully achieve this world-wide.

Now, fast forward to 2015 where a ground breaking formula came to life, embodying the next step in Free Form Curcumin delivery.

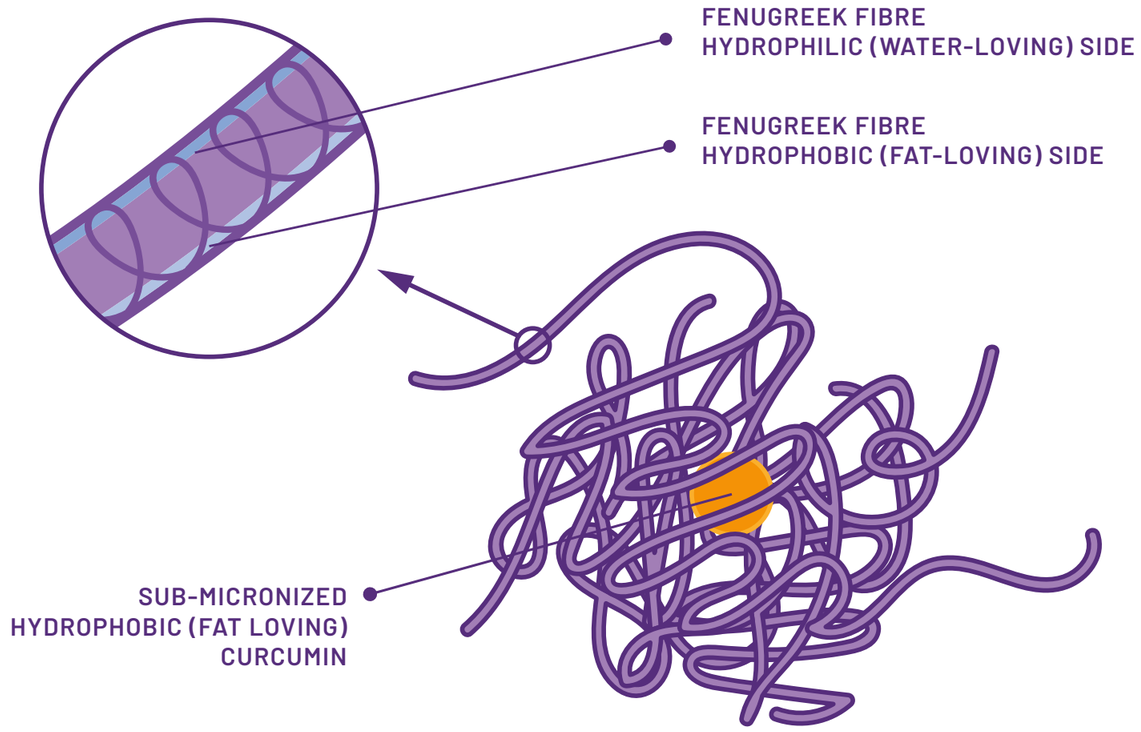


FIGURE 4.

CurQfen® at a glance: A fenugreek-curcumin fibre complex with its highly branched "arms" that hide and protect the curcumin deep within.

CurQfen® is comprised of fenugreek-curcumin fibre complexes. These little whole food wonders, not only tremendously enhance absorption and bioavailability, they also successfully evade rapid breakdown. Fenugreek is a highly branched, gum like fibre that is extremely sticky. Therefore, it allows a high concentration of sub-micronized curcumin to bind deep within the fibre. Here, it remains safe from digestive juices and can be readily absorbed by the gut and then into the bloodstream. Because the nature and structure of these complexes are so unique, they allow for rapid, yet sustained release into the bloodstream. This is due to the tightly wound, sticky nature of the water soluble fenugreek fibre, which adheres to the gut lining like a glue. This glue creates a slow, sustained release effect, because fibre naturally takes longer to break down in the digestive tract. Now you might be wondering how exactly does it absorbs rapidly, if the glue creates a long lasting effect?

The answer is in how it evades rapid breakdown. Because the complexes are so tightly wound, and the fenugreek so highly branched, curcumin particles are able to literally hide deep within the complex. This is also a result of the strong bonding between the fenugreek and curcumin. Furthermore, the fibre has a hydrophobic (fat-loving) side that faces inward which is strongly bound to the hydrophobic curcumin particles. Conversely, the fenugreek fibre also has a hydrophilic (water-loving) side that faces outward in the direction of the water molecules, making the complex more water soluble. Thus, it is this tightly weaved tapestry that acts like a Trojan horse, as it carries its precious curcumin cargo

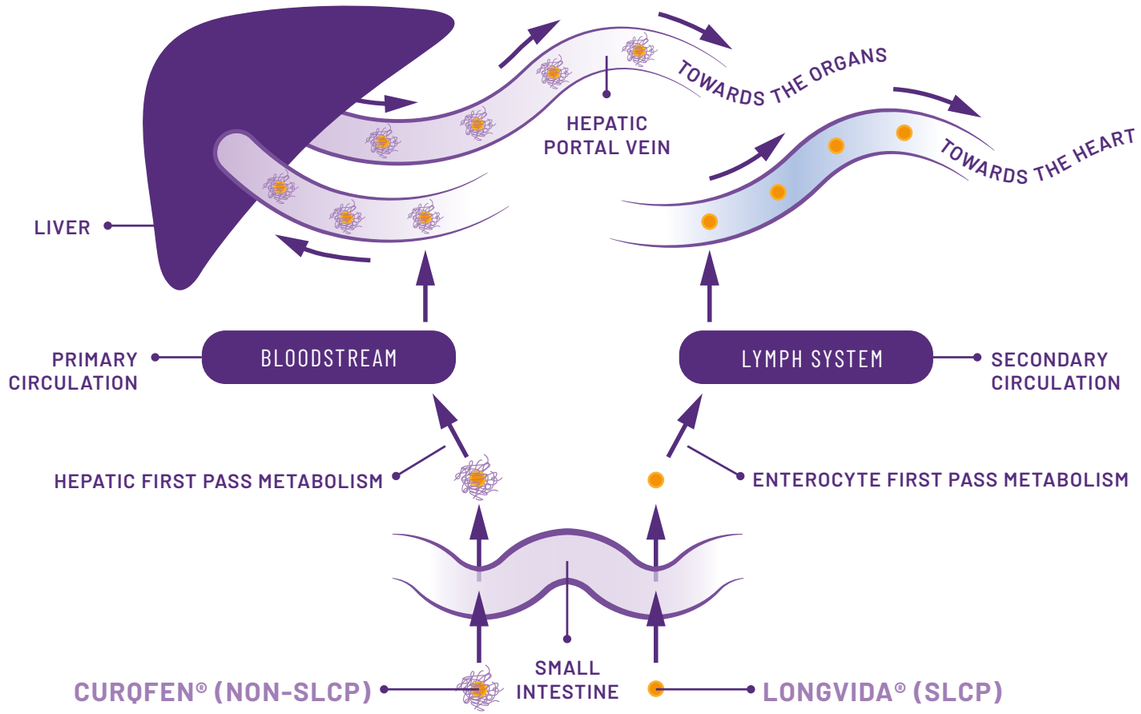


FIGURE 5.

Evading rapid breakdown: Methods of preserving Curcumin's "Free Form".

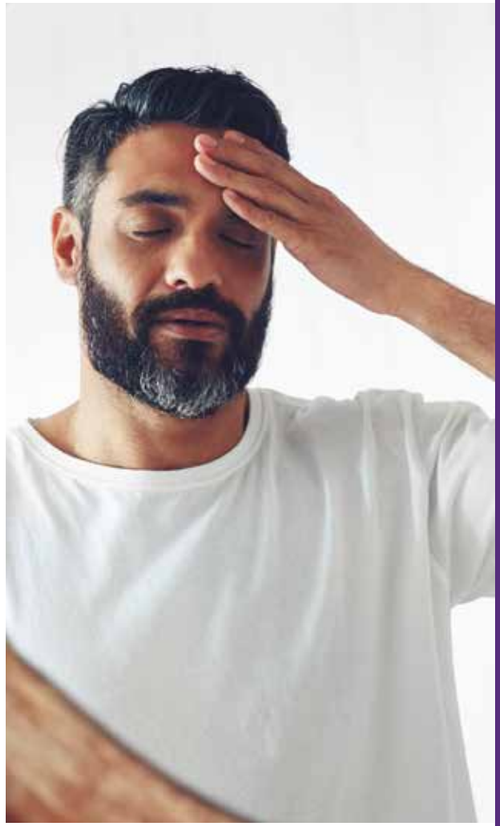
Left: CurQfen® is taken up through primary circulation. Due to its structure, it effectively shields the curcumin from phase II liver enzymes.

Right: Longvida® is taken up through the enterocyte into secondary circulation, i.e. lymph. It's carried to the heart and then the organs, effectively retaining its Free Form. Because standard curcumin doesn't have the fenugreek shield, it goes through the liver; wherein, most of it is conjugated and excreted.

right to and through liver, ensuring they remain undetected during first pass metabolism!

Pretty neat, right? Apart from fenugreek's incredible ability to protect curcumin, the very fact it is a highly soluble, well tolerated, gentle fibre opens the doors to the potential healing of a vast array of inflammatory bowel disorders.

Unlike **Longvida®** which bypasses phase II enzymes by escaping to the lymph system, this simple, food-based delivery method tricks the liver's guard dogs as it passes by! In turn, this ensures the effective delivery of Free Form Curcumin to all tissues. Believe it or not, **CurQfen®** actually goes one step further with evidence proving bioaccessibility. In 2016, Kumar and colleagues were able to prove that curcumin not only gets into the bloodstream in its Free Form, it is able to penetrate and saturate various organs and tissues within the body. This is the first study of its kind on the tissue distribution kinetics of Free Form Curcumin, showing actual uptake of **CurQfen®** by target tissues. Moreover, due to the fact it is a truly synergistic formula, studies have demonstrated positive effects with anxiety, energy levels and depression due to the presence of fenugreek (Kumar et al., 2016; Sudheeran et al., 2016). Lastly, several health benefits are also attributed to fenugreek, including maintaining healthy blood glucose and reducing elevated blood lipid levels (Sharma and Raghuram, 1990; Al-Habori and Raman 1998; Neelakantan et al., 2014).



STUDIES HAVE DEMONSTRATED POSITIVE EFFECTS WITH ANXIETY, ENERGY LEVELS AND DEPRESSION DUE TO THE PRESENCE OF FENUGREEK

(KUMAR ET AL., 2016; SUDHEERAN ET AL., 2016)

SAFETY CONCERNS

Unfortunately, there are certain curcumin formulations being sold that have safety issues regarding the selection of raw materials and efficacy of study design.

One capsule of **NovaSOL®** contains over six times the amount of Tween-80 normally found in our diet. Again, Tween-80 is known to be well-tolerated up to 100 mg per day, but the health issues with consumption of larger quantities on a regular basis are unknown.

SIDE EFFECTS

Most curcumin products have excellent safety profiles, however, Schiborr (2014) reported side-effects from the use of **NovaSOL®** within a group of 23 human participants including:

1. ***Mild nausea (seven females, three males)***
2. ***Vomiting (one female)***
3. ***Mild fatigue (one female)***
4. ***Mild headache (one female)***
5. ***Mild stomach ache (one female)***
6. ***Incidental regurgitation (one female)***

Unfortunately, **NovaSOL's®** use of Tween-80 may be the cause of these side effects, since there is no human biosafety data with **NovaSOL's®** serving size of Tween-80. Furthermore, studies using **BCM-95®** have also reported a higher incidence of side effects including raised liver enzymes, blood thinning effects and worsening of GI symptoms in one study (Chandran and Goel, 2012).

DELVING INTO THE SCIENCE

Breaking Down Clinical Research

Now that we have fully explored the nitty gritty bits of Free Form Curcumin, it is time to delve a bit deeper to a place where many do not like to go—The Research.

Although interfacing with clinical data can even make our heads spin at times, it's important to have an understanding of what actually makes a good, viable study. Indeed, this is not very exciting per se, but will allow you to see through any skewed marketing tactics and make a truly informed decision.

MEASUREMENTS:

Unfortunately, many publications report the bioavailability of curcuminin without actually distinguishing between Free Form Curcumin, curcumin metabolites, and total curcuminoids (curcumin, DMC, BDMC).

This will inevitably skew what was actually measured in sample blood, versus what is reported in the corresponding publication. Don't forget about our little friend Beta-glucuronidase either, seeing the use of this enzyme further skews results generating false values for Free Form Curcumin. For the sake of accuracy, simple honesty, and the varying potency of each form, it is critical that all of the forms are clearly distinguished and measured correctly. These details can be confirmed in the materials and methods section of a study.

THE IMPORTANCE OF SPECIFIC SCIENTIFIC CONTROLLED VARIABLES IS CRITICAL TO A WELL-DESIGNED STUDY.

Here is a loose outline of what a "curcumin" study looks likes to help you imagine the process:

1. A set dose of a curcumin is administered to human subjects once a day.
2. Blood samples are collected before curcumin is administered at very specific intervals over the course of 24 hours.
3. The concentrations of curcuminoids are measured in order to plot a concentration time curve.

Results include the following:

- Cmax (Concentration maximum) is when a drug reaches its peak concentration in the blood after administration. This is depicted by the highest point on a graph.
- Tmax (Time maximum) is the time a substance takes to reach maximum concentration.
- AUC (Area Under the Curve) is the overall amount of a therapeutic agent in the bloodstream after a dose. The AUC is dependent on the dose and the rate of elimination from the body.

Some other important keys to a well-designed study are: human subjects, the number of subjects, and appropriate controlled variables.

The human league should be the only league when it comes to study subjects. Although there is merit in animal studies, humans are not rats, mice, or any other kind of animal. We have entirely different anatomy, physiology, and biochemistry. Thus, data from a different species cannot accurately show what happens within humans in all cases. This is why healthy human volunteers are used in bioavailability studies to increase accuracy by removing factors such as disease, medication, smoking and other lifestyle influences.

When it comes to sample size, the more the merrier. Although some studies with smaller samples are still very well-designed and executed, it is even better when more subjects are involved.

Larger sample sizes offer higher accuracy, seeing the result is demonstrated many more times. This is a standard that all studies should strive for.

The importance of specific scientific controlled variables is critical to a well-designed study. Unbiased studies incorporate positive and negative controls, including placebos, randomization, blind and double-blind experiments.

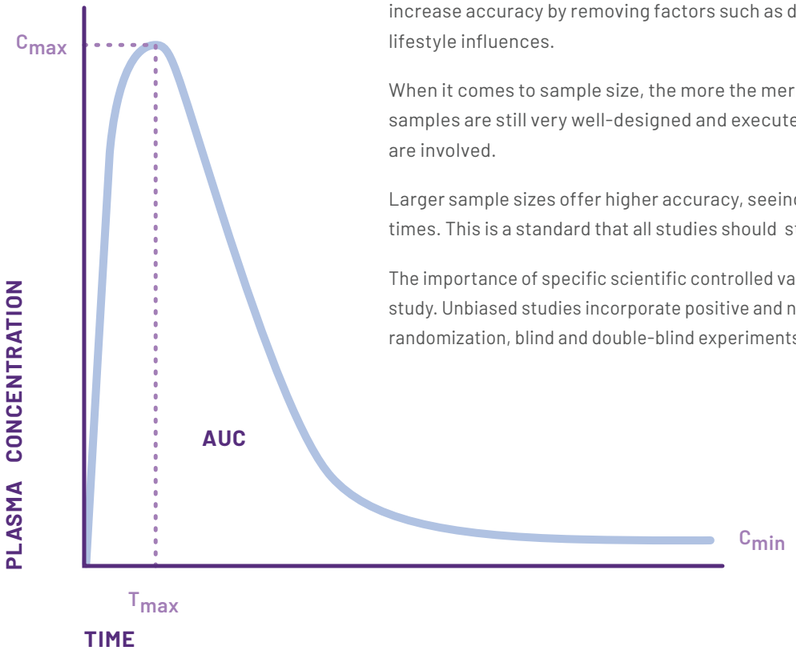


FIGURE 6.

All in the Curve: Area under the plasma concentration-time curve, which depicts the exposure of the body to administered curcumin.

Making Sense of Curcumin Bioavailability Claims

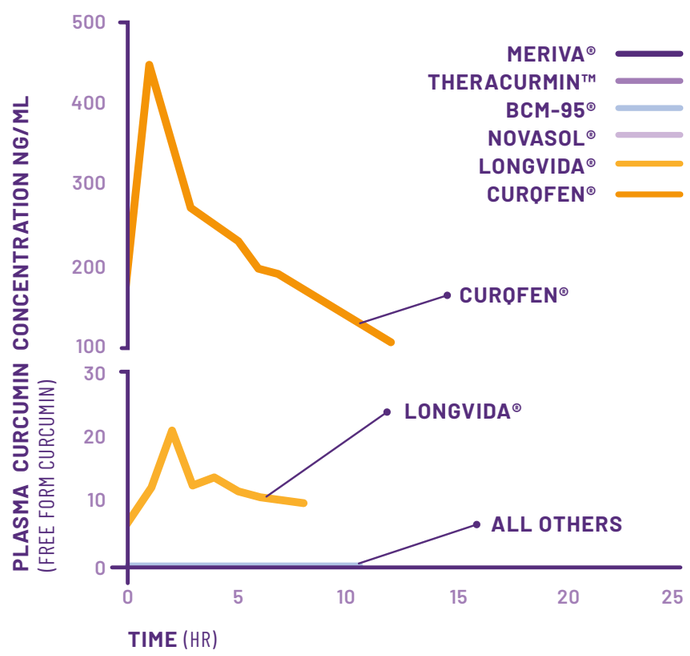
This is where things can get a little technical. Instead of hiding behind altered data and complex arguments, let's clarify the research associated to some of the popular curcumin forms on the market. As mentioned, every curcumin on the market has a bioavailability study that companies base their absorption claims on, i.e. 100x more bioavailable.

Before comparing any two products, there are a few points to take into consideration. In general, studies investigating bioavailability of curcumin have focused on exploring the fold increase in comparison to standard Curcumin-95, which we know has very poor bioavailability. AUC (area under the curve) is considered the best method to use in any comparison. While comparing to a standard is a good reference point, the AUC method is dose dependent; therefore, it is not possible to conclude with any accuracy what the effect of an increase or decrease in dose will have on the AUC.

Again, many publications report the bioavailability of curcuminin without actually distinguishing between Free Form Curcumin, curcumin metabolites, and total curcuminoids (curcumin, DMC, BDMC). However, in Schiborr et al., (2014), each individual curcuminoid (curcumin, DMC, BDMC) was investigated separately. Using this same methodology, Kumar et al., (2016), highlight that CurQfen is 270x higher than standard curcumin.

FIGURE 7.

A plotted graph:
Comparison of Free Form Curcumin plasma concentrations of various curcumin formulations. Using accurate experimental methodology, the above data shows the concentration-time-point curve for major curcumin formulas, measuring the levels of Free Form Curcumin. A comparison of the area under the curve (AUC) for CurQfen® and Longvida® reveals that CurQfen® is 6.7x more bioavailable than Longvida® at equivalent doses. Because correct adjustments are used, levels of Free Form Curcumin for other formulations are difficult to detect.



THE NEXT STEP IN CURCUMIN EVOLUTION

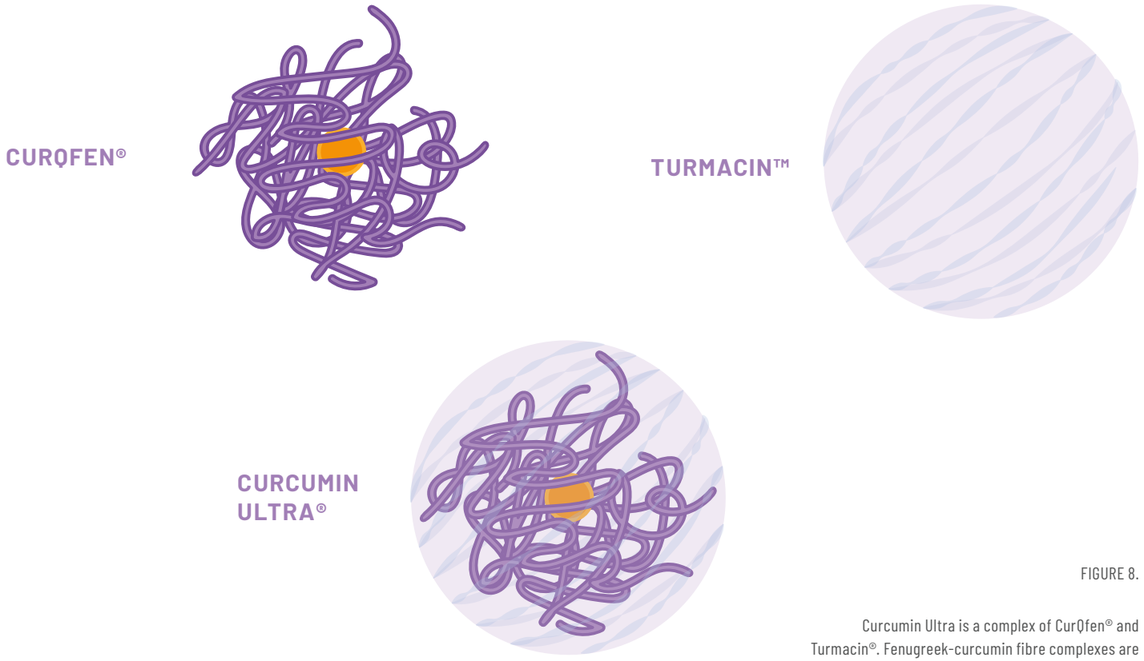


FIGURE 8.

Curcumin Ultra is a complex of CurQfen® and Turmacin®. Fenugreek-curcumin fibre complexes are combined with Turmeric polysaccharides to make Curcumin Ultra®.

With integrity informing every decision, we never settle for mediocrity by ensuring complacency never takes hold. Because if it were to do just that, evolution would cease, and cutting-edge breakthroughs towards better medicine may never come to be. It is with this fierce dedication to continuous, diligent innovations, we always pave the way forward, rather than simply imitate by following others.

Because curcumin has literally hit a glass ceiling in terms of truly innovative delivery methods, AOR was inspired to challenge this and make something unique. This brings us to the next step in curcumin evolution, **Curcumin Ultra®**.

Comprised of two truly innovative raw materials: **CurQfen®**, and **Turmacin®, Curcumin Ultra®** offers the benefits of a more whole food, truly botanical formula, while showing a significant increase in bioavailability. This is due to the addition of **Turmacin®**, which is comprised of highly water soluble sugar chains known as polysaccharides. AOR prioritizes Free Form Curcumin only; thus, reporting 48x more bioavailability in its marketing material.

Kumar et al., (2016), also compared the ratio of Free Form Curcumin to conjugated curcumin. Here, they reported 75% Free Form Curcumin and 25% conjugated curcumin in the plasma 5 hours after administration of **CurQfen®** (1000 mg). This exceedingly high concentration of Free Form Curcumin suggests that the fenugreek-curcumin complex effectively protects curcumin from rapid breakdown; thus, resulting in a fast acting, yet long lasting, highly potent effect.

While the conundrum of curcumin's various solubility issues has been made clear, we have to take a step back and remember that the South Asian population have been using turmeric for thousands of years with effect. Indeed, not a therapeutic, drug like effect per se, but effective nonetheless. Perhaps this has more to do with accessing the synergistic constituents of the whole root, as opposed to just curcuminoids, and isolated curcumin in many cases?

Traditionally, turmeric root is boiled in water and/or milk before ingestion. With the former method, it is highly unlikely it extracts any curcuminoids, seeing they are hydrophobic. Rather, this water extraction method liberates water soluble components from turmeric, i.e. polysaccharides. Conversely, the latter method most likely yields minimal amounts of curcuminoids, with a possible increase if clarified butter is added—remember "fat loving"?

The use of **Turmacin®** in osteoarthritic patients has shown promising results. In a randomized, single-blind, placebo controlled trial, the effects of **Turmacin®** (1000 mg/day) were compared to glucosamine sulfate (1500 mg/day), a combination of **Turmacin®** and glucosamine (1500 mg/day), and placebo (800 mg/day) over a 42-day period. Osteoarthritis patients showed the greatest symptom improvement. This was measured by physical performance, questionnaires and clinician assessment when given **Turmacin®** over time. Turmacin® was well-tolerated at high doses (Madhu et al., 2013).

As you can see, there is benefit to incorporating traditional methods, while still adhering to an orthomolecular, targeted, therapeutic approach. **Curcumin Ultra®** combines synergistic aspects of turmeric and a full spectrum of curcuminoids, while still providing the highest Free Form Curcumin available on the market.

Now that we have finally set the record straight, it is clear how truly complex curcumin is biologically speaking, and as the subject of research. However, now that we have taken this journey, we hope that everyone can make a truly informed decision when choosing a modern curcumin formulation. What do you want coursing through your veins? The choice is yours.

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