

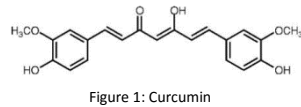
## CurcuFRESH™

### TECHNICAL SUMMARY

Curcumin from dried turmeric root is widely used, but is well known for its poor solubility and bioavailability. CurcuFRESH™ is a curcumin preparation from fresh turmeric rhizome that is never dried or extracted using solvents. The resulting curcumin remains in its native, complexed form and, when ingested, leads to dramatically higher circulating levels of beneficial, unmetabolized, free curcuminoids – up to 40 times higher than what is expected from standard curcumin extracts.

**Structure Formula:** See Figure 1.

**Biochemistry:** Curcumin: diferuloyl methane [1,7-bis (4-hydroxy-3-methoxyphenol)-1,6-heptadiene-3,5-dione]



**Allergen and Additive Disclosure:** Not manufactured with yeast, wheat, gluten, soy, corn, milk, egg, fish, shellfish or tree nut ingredients. Produced in a GMP facility that processes other ingredients containing these allergens.

**Delivery Form:** Vegetable capsules

### ROLE AS NUTRIENT/FUNCTION

Curcumin is derived from the rhizomes of turmeric (*Curcuma longa*). It is widely used as a spice and food coloring, most notably in Asian cuisine (curries). While it has been used by traditional herbalists for centuries, curcumin has been extensively researched by modern scientists and is involved in a wide array of biological processes. At a cellular level, in experimental settings, free, unconjugated rather than metabolized, glucuronidated curcumin is credited with the bulk of the regulation of the immunological responses to biological and/or oxidative stresses as well with the ability to induce apoptosis (programmed cell death).

### NATUROKINETICS®

**Liberation:** Dissolution data is not available. CurcuFRESH™ capsules pass standard disintegration test in water (< 60 min).

**Absorption:** Absorption of CurcuFRESH™ has been shown to be superior to dried turmeric curcuminoids (DTC, 95% curcuminoids). In an oral pharmacokinetic study, area under the curve (AUC) for free unconjugated curcumin following ingestion of CurcuFRESH™ was up to forty times the AUC than following administration of DTC (Figure 2, see clinical validation for more information).

**Distribution:** Curcumin has a high affinity to gastro-intestinal tissues. Once in the bloodstream, curcumin binds to serum albumin and is transported to target tissues (in descending order): intestine, spleen, liver, kidneys. Curcumin penetrates into the cytoplasm and is able to accumulate in membrane structures. Curcumin in its free, unconjugated form can also cross the blood-brain barrier.

**Metabolism:** The main metabolic pathway of curcumin biotransformation includes glucuronidation by hepatocytes, resulting in the formation of three relatively stable glucuronate-curcumin derivatives that retain only

## Supplement Facts

Serving Size 1 Veg Capsule

### Amount Per Serving

Standardized Turmeric Juice Powder (from Fresh Turmeric Rhizome Juice) ( <i>Curcuma longa</i> ) (CurcuFRESH™) (20 mg Total Curcuminoids)	500 mg*
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\* Daily Value not established.

Other ingredients: Cellulose (capsule), Rice Flour, Stearic Acid (vegetable source), Silica and Magnesium Stearate (vegetable source).

- From Fresh Turmeric Juice
- Up to 40X Better Bioavailability vs. Standard Curcumin Extracts

**SUGGESTED USAGE:** Take 1 capsule 1 to 2 times daily with food, or as directed by your healthcare practitioner.

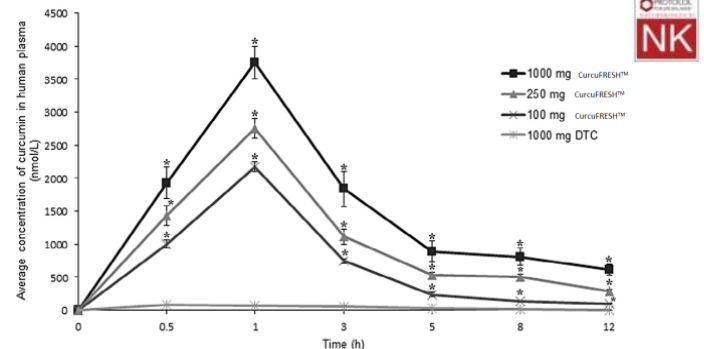


Figure 2: Average concentration of curcumin observed in human plasma after oral administration of CurcuFRESH™ containing 4.2% curcuminoids at 100, 250 and 1000 mg dose capsules. Standard curcumin with 95% purity isolated from dried turmeric rhizomes was administered at 1000 mg/kg body weight. The data are expressed as the mean ± SD (n = 15); \*p < 0.05.

some of the bioactivity of curcumin; a.) Dihydrocurcumin glucuronide, b.) Tetrahydrocurcumin glucuronide, and c.) Hexahydrocurcumin glucuronide.

**Elimination:** Unabsorbed curcumin is eliminated in feces. Absorbed curcumin is cleared from plasma within hours, and glucuronated curcumin metabolites are primarily eliminated in bile.

### CLINICAL VALIDATION

- In a single-blind pharmacokinetic study with single administration over a 12 hour period, 15 healthy volunteers (25 to 50 years old) received respectively 100 mg, 250 mg or 1,000 mg CurcuFRESH™ (obtained from the fresh juice of turmeric roots using a unique proprietary process) or 1,000 mg of commercial grade, standard, dry curcumin extract (DTC, 95.1% curcuminoids). It was possible to demonstrate a dose-dependent absorption of curcuminoids into the

bloodstream compared to DTC at equivalent doses. ( $p < 0.001$ ) The relative absorption from 100 mg CurcuFRESH™ was significantly higher ( $C_{\max}$  2,171 +/- 75 nmol/L) as compared to DTC at equivalent concentrations. CurcuFRESH™ was found to have a longer half-life, with  $T_{1/2\max}$  values of 3.1 hours and  $C_{1/2\max}$  of 616 +/- 76 nmol/L at the 1,000 mg dose. Thus, the relative absorption of curcuminoids from 1,000 mg CurcuFRESH™ was found to be about 46-fold higher, as compared to the absorption from a standard curcumin extract containing an equivalent dose of curcuminoids. (Figure 2)

## SAFETY INFORMATION

**Tolerability:** Curcumin is usually well tolerated. In some consumers it can cause mild gastrointestinal adverse effects such as nausea and diarrhea. Turmeric may cause gallbladder contractions. Use with caution in patients with gallstones or gallbladder disease.

**Contraindications:** None known.

## INTERACTIONS

**Drug Interactions:** Curcumin may interact with aspirin, clopidogrel (Plavix), dalteparin (Fragmin), enoxaparin (Lovenox), heparin, ticlopidine (Ticlid), and warfarin (Coumadin).

**Supplement Interactions:** Concomitant use of turmeric with herbs that might affect platelet aggregation could theoretically increase the risk of bleeding in some people. These herbs include angelica, clove, danshen, garlic, ginger, ginkgo, Panax ginseng, red clover, willow, and others.

**Interaction with Lab Tests:** None known.

## STORAGE

Store in a cool, dry and dark environment in original, sealed container. Protect from extended exposure to moisture, heat and direct light.