BONE & MUSCULOSKELETAL HEALTH

Curcumin 500
with Bioperine®

SUPPORTS JOINT, TISSUE, LIVER, COLON AND CELLULAR HEALTH‡

Curcumin 500 with Bioperine® provides Curcumin C3 Complex®, a studied, patented curcumin extract, with piperine (Bioperine®) to enhance curcumin bioavailability.

- Supports a healthy inflammatory response‡
- Supports joint health‡
- Supports liver function and detoxification‡
- Helps maintain colon health‡
- Provides antioxidant support‡

Curcumin is a polyphenol that maintains a healthy inflammatory response by moderating cyclooxygenase, prostaglandin and leukotriene metabolism and the production of cytokines.[1-3] Curcumin supports brain, colon, musculoskeletal and cellular health.[4-6] Curcumin also supports the body's detoxification system and helps maintain healthy hepatic function.[4‡]

The clinical efficacy of curcumin is limited by its poor oral bioavailability. Even with sufficient absorption, its extensive presystemic metabolism (glucuronidation) and efflux contribute to low or undetectable plasma levels of free curcumin in pharmacokinetic studies. The metabolites (glucuronide conjugates) do not penetrate the blood-brain barrier and are rapidly excreted. Bioperine® is a black pepper extract that contains piperine, an alkaloid that enhances curcumin bioavailability by reducing its presystemic metabolism and efflux.[7,8]

WHO IS THIS SUPPLEMENT FOR?

- Patients who failed to respond to standard curcumin or Meriva®
- Patients seeking support for joint health
- Patients wishing to be proactive about maintaining colon or brain health

‡This statement has not been evaluated by the Food & Drug Administration. This product is not intended to diagnose, treat, cure or prevent any disease.

800.753.2277 | PureEncapsulationsPro.com

MECHANISMS OF ACTION‡

Enhanced bioavailability. Bioperine® (piperine) enhances curcumin bioavailability by addressing two major underlying causes of low blood levels: (1) metabolic inactivation and (2) efflux from cells.[7-10] Piperine inhibits the activity and expression of the efflux transporter P-glycoprotein (P-gp), which sends curcumin out of cells.[9,10] Bioperine® also inhibits UDP-glucuronosyltransferase (UGT), a phase II enzyme that renders pharmacologically inactive curcumin glucuronides, which are brain-impermeable and rapidly excreted.[11]

Effects on the inflammatory response. Curcumin inhibits NFκB, a transcription factor that induces genetic expression of cytokines, including TNFα and IL-6.[2] Curcumin also inhibits the NLRP3 inflammasome.[12]

Detoxification and antioxidant enzymes. Curcumin stimulates Nrf2, a transcriptional activator of enzymes that catalyze glutathione biosynthesis and biotransformation of reactive substances and environmental xenobiotics.[13]

Brain health. A systematic review and meta-analysis of randomized controlled trials concluded that curcumin supports the production of brain-derived neurotrophic factor (BDNF).[14] BDNF plays a critical role in plasticity of the brain and supports cognitive function, learning, memory and mood. The gut-brain axis and the intestinal microbiota may contribute to curcumin's systemic and CNS effects.[15-17]

RESEARCH HIGHLIGHTS‡

- In a pharmacokinetic study in healthy human subjects, coadministration of piperine (20 mg) with 2 g curcumin increased mean curcumin bioavailability by approximately 2,000%.[7]
- In a pilot trial of 17 sedentary, moderately functioning older adults (>65 years) with C-reactive protein >1mg/dL, Curcumin C3 Complex® (1,000 mg/day) with Bioperine® (10 mg piperine) significantly increased lower-limb strength (knee extension and flexion peak torque) compared to placebo.[18]
- In a post-hoc analysis of a randomized controlled trial of 117 subjects with metabolic syndrome, Curcumin C3 Complex® (1,000 mg/day) significantly decreased serum concentrations of cytokines (TNF-α, IL-6, TGF-β and MCP-1).[5]
- In a randomized controlled trial of 35 women with high waist circumference, Curcumin C3 Complex® (500 mg/day) for 90 days significantly improved glucose homeostasis and lipid profile relative to placebo.[19]

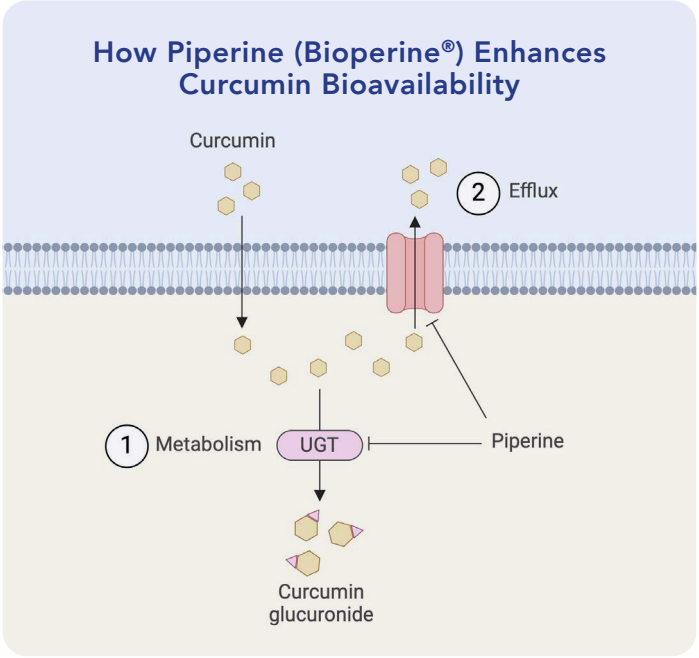

Figure 1. *Poor oral bioavailability of curcumin is largely attributed to (1) rapid metabolism and (2) efflux back into the intestine following absorption. Curcumin is extensively metabolized by conjugated, which is catalyzed by UDP-glucuronosyltransferase (UGT) in the intestinal wall and liver, rendering inert and readily excreted metabolites (curcumin glucuronide). Curcumin also undergoes efflux (removal from the cell via a transporter). Piperine modulates both processes to enhance curcumin bioavailability.*[7-11]

HOW IS THIS PRODUCT DIFFERENT FROM MERIVA®?

- **Composition.** This product contains a unique extract (Curcumin C3 Complex®) that has been the subject of scientific investigations and clinical trials at several hospitals and universities. Curcumin C3 Complex® is a patented mixture of 3 curcuminoids (curcumin, demethoxycurcumin and bisdemethoxycurcumin), all of which contribute to the bioactivity of turmeric (*Curcuma longa*) rhizome.
- **Mechanism of bioavailability enhancement.** Absorption is not the only challenge with curcumin. In contrast to a phytosome (Meriva®) which enhances curcumin absorption across intestinal cell membranes, Bioperine® works by slowing its metabolism and efflux (reverse uptake) from the cells, factors that prevent curcumin from reaching significant plasma concentrations.

- **Risk of drug interactions.** Since piperine may also slow the metabolism and modify the bioavailability of certain drugs, this product is not ideal for everyone.

While there are currently no published studies comparing the pharmacokinetics of these delivery methods, Curcumin 500 w/ Bioperine® may be a good choice for individuals who failed to respond to Meriva® or standard curcumin.

	Curcumin C3 Complex® and Bioperine®	CurcumaSorb (Meriva®)
Curcuminoids per capsule	475 mg	45 mg
Number of capsules to reach clinically efficacious dose	1-3 capsules per day	2-6 capsules per day
Primary areas of clinical research	Cellular health Inflammatory markers	Joint discomfort Musculoskeletal health
Bioavailability enhancement technology	Addition of Bioperine® (piperine)	Phytosome (phospholipid-based vesicle)
Mechanism of bioavailavility enhancement	Inhibition of UGT and P-glycoprotein	Improved diffusion across membranes
Potential drug interactions	May interact with propranolol, atorvastatin, phenytoin, temoxifen, raloxifene and theophylline	Unlikely to ineract with medications

POTENTIAL INTERACTIONS

Piperine may interact with propranolol, atorvastatin, phenytoin, tamoxifen, raloxifene and theophylline. To check whether a medication may have clinically significant interactions with [nutrients and] ingredients based on doses commonly used in dietary supplements, visit our Drug-Nutrient Interaction Checker and consider a formula without piperine (such as CurcumaSorb) if needed.

Support the body's natural detoxification system and inflammatory response with Curcumin 500 w/ Bioperine®.‡

Supplement Facts

1 capsule, 1-3 times daily, between meals.

Each (size 00) vegetarian capsule contains:

Turmeric (*Curcuma longa*) extract (root) (standardized to contain 95% curcuminoids)	500 mg
Bioperine® black pepper (*Piper nigrum*) extract (fruit) (standardized to contain 95% piperine)	5.3 mg

Other ingredients: hypoallergenic plant fiber (cellulose), vegetarian capsule (cellulose, water), ascorbyl palmitate

Curcumin C3 Complex® is a registered trademark and patented product of Sabinsa Corporation.

Bioperine® is a registered trademark and patented product of Sabinsa Corporation.

Bone & Musculoskeletal Health

NON GMO · V · VEG

Curcumin 500 with Bioperine®	Quantity	Order Code
	120	CUB51
	60	CUB56

Visit PureEncapsulationsPro.com/quality for more information on our GMO Policy.

Certified Gluten-Free by the Gluten-Free Certification Organization, gluten.org

REFERENCES

1. Rao CV. *Adv Exp Med Biol.* 2007;595:213-26.
2. Zamanian MY, Alsaab HO, Golmohammadi M, et al. *Cell Biochem Funct.* 2024 Jun;42(4):e4030.
3. Panahi Y, Rahimnia AR, Sharafi M, et al. *Phytother Res.* 2014 Nov;28(11):1625-31.
4. Farzaei MH, Zobeiri M, Parvizi F, et al. *Nutrients.* 2018 Jul 1;10(7):855.
5. Panahi Y, Hosseini MS, Khalili N, et al. *Biomed Pharmacother.* 2016 Aug;82:578-82.
6. Ghasemi F, Bagheri H, Barreto GE, et al. *Neurotox Res.* 2019 Jul;36(1):12-26.
7. Shoba G, Joy D, Joseph T, et al. *Planta Med.* 1998 May;64(4):353-6.
8. Athukuri BL, Neerati P. *J Pharm Pharm Sci.* 2017;20:28-37.
9. Najar IA, Sharma SC, Singh GD, et al. *Chem Biol Interact.* 2011 Apr 25;190(2-3):84-90.
10. Han Y, Chin Tan TM, et al. *Toxicol Appl Pharmacol.* 2008 Aug 1;230(3):283-9.
11. Reen RK, Jamwal DS, Taneja SC, et al. *Biochem Pharmacol.* 1993 Jul 20;46(2):229-38.
12. Hasanzadeh S, Read MI, Bland AR, et al. *Pharmacol Res.* 2020 Sep;159:104921.
13. Ghafouri-Fard S, Shoorei H, Bahroudi Z, et al. *Biomolecules.* 2022 Jan 5;12(1):82.
14. Sarraf P, Parohan M, Javanbakht MH, et al. *Nutr Res.* 2019 Sep;69:1-8.
15. Di Meo F, Margarucci S, Galderisi U, et al. *Nutrients.* 2019 Oct 11;11(10):2426.
16. Enayati A, Soghi A, Butler AE, et al. *J Neurogastroenterol Motil.* 2023 Oct 30;29(4):409-418.
17. Scazzocchio B, Minghetti L, D'Archivio M. *Nutrients.* 2020 Aug 19;12(9):2499.
18. Mankowski RT, Sibille KT, Leeuwenburgh C, et al. *J Frailty Aging* 12, 143–149 (2023).
19. de Sousa Guardiano Reis PC, Alves AGP, et al. *Arch Endocrinol Metab.* 2022 Nov 17;66(6):800-807.

PEOP-CURC0125

The Drug-Nutrient Interaction Checker is supported by a license from PEPID, LLC.

‡This statement has not been evaluated by the Food & Drug Administration. This product is not intended to diagnose, treat, cure or prevent any disease.