CURCUMIN C3 COMPLEX®

A Versatile Phytonutrient

Safe & Superior Choice

Today, our patented C³ Complex is the most clinically studied and evaluated curcumin brand in the market place!

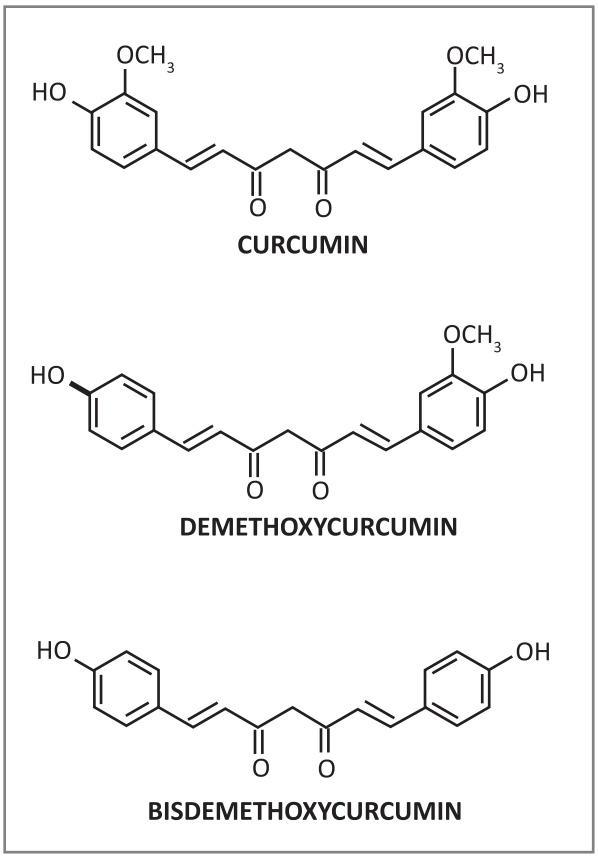
SABINSA®

Curcumin C³ Complex®

The "GOLD STANDARD" for Curcumin

Sabinsa's Curcumin C³ Complex® is obtained from the dried rhizomes of *Curcuma longa* (Turmeric) and standardized for minimum 95% Curcuminoids.

The name C³ Complex® has reference to its three main chemical compounds - Curcumin, Demethoxycurcumin (DMC) and Bisdemethoxycurcumin (BDMC) - collectively known as Curcuminoids.



Curcumin C³ Complex® is a patented and clinically evaluated "Bioprotectant" composition of three Curcuminoids of which Curcumin constitutes 75-85% of the composition.

Traditional knowledge

The rhizome of turmeric (*Curcuma longa* L.) has a rich history in India as a spice, food preservative and coloring agent and has been used for centuries in the Ayurvedic system of medicine. In Ayurvedic medicine turmeric is well-documented for treatment of various respiratory conditions (e.g., asthma, bronchial hyperactivity and various allergies), liver disorders, poor appetite, rheumatism and influenza symptoms.

Patents:

- US 5,861,415
- EP0839037

Pharmacological activity of Curcumin C³ Complex®:

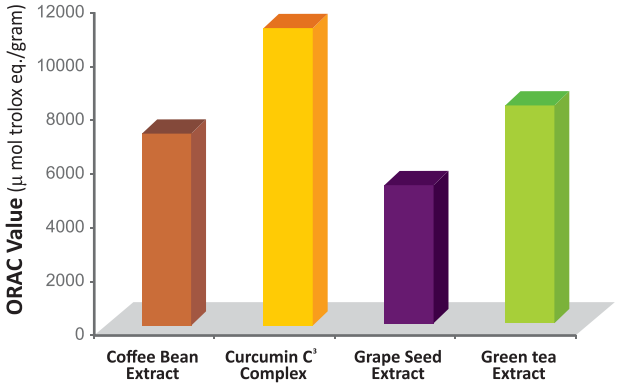
A common spice used in South Asian cooking, turmeric and more appropriately, the component curcuminoids, have been preclinically and/or clinically validated for their beneficial role in maintaining health and wellness.

At the molecular level, the curcuminoids have been shown to inhibit nuclear factor kappaB (NFkB) a transcription factor that triggers inflammatory mediators. NFkB is implicated in a variety of chronic disease conditions ranging from cardiovascular diseases to cancer. Curcuminoids offer antioxidant support, anti inflammatory support, supports a healthy immune system, and potentially prevent connective tissue break down through inhibiting destructive enzymes, with benefits in healthy aging (Aggarwal B. et al.(2006). Turmeric: The Genus Curcuma. pp 297-368).

Antioxidant: Curcumin C³ Complex® is an effective BIOPROTECTANT®.

Curcumin C³ Complex® counteract free radicals in 2 ways

- **PREVENTION** of free radical formation
- **INTERVENTION** whereby already preformed radicals are quenched by the Curcuminoids



Greater the ORAC value, better the antioxidant activity

Why Curcumin C³ Complex® stands out from the Crowd

- **Most clinically studied Curcumin Brand:**
  More than 65 scientific publications, including clinical trials, have been published on C3 Complex.
- **Most safety data:**
  Only curcumin in the market that has been reviewed and acknowledged by US FDA for GRAS status, a process which includes a comprehensive review of safety and toxicology data.
- **Most Patents-IP protection:**
  Holds patents covering composition of curcuminoids, method of manufacture, and uses.
- **Most Consistent Quality:**
  C3 Complex has the same composition of the three curcuminoids consistently in the same ratio in every batch.
- **Most Stable Supply Chain**
- **More Proven Bioavailability**
- **No One Knows Curcumin Like We Do**
- **NBJ Product Merit Award**
- **NBJ Scientific Achievement Award**

Anti-inflammatory: Saga of Inflammation

Most degenerative diseases are driven by chronic sub-clinical inflammation. The old view of the inflammation is that it represents the healing process. This is true to a certain extent; however when the inflammation becomes chronic, it becomes a disease.

Today, the study of inflammation has gone from the tissue levels deeper into the nuclear level. Cell-signaling molecules have been identified which stimulate the gene that induce the expression of the COX enzyme which in turn induce inflammation.

"NF-kB: The master regulator of Inflammation"

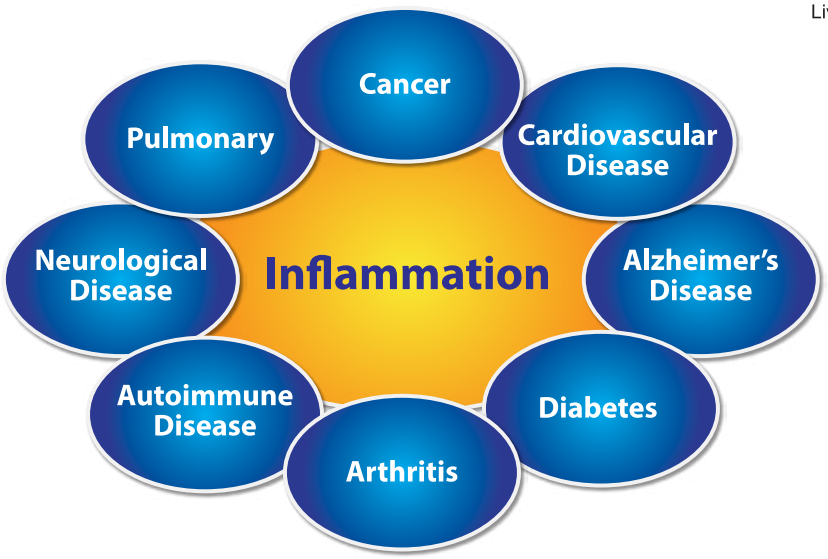
Nuclear Factor - Kappa B (NF-kappa B), as the 'master switch', is the primary means by which inflammation is 'adjusted'.

In the normal state,

- NF-kB resides in the cytoplasm of the cell and is bound to its inhibitor -IkB (Inhibitor of k-B.)
- Injuries and inflammatory stimuli, such as free radicals, release NF-kB from its inhibitor-IkB.
- The free NF-kB, now moves into the nucleus and activates the genes responsible for expressing cyclooxygenase-2 (COX-2).
- This leads to inflammation.

NF-kB activation is a major mediator of inflammation in most diseases and inhibition of NF-kB can help prevent/delay the onset of the disease. Curcuminoids natural compounds derived from turmeric roots, inhibit NF-kB.

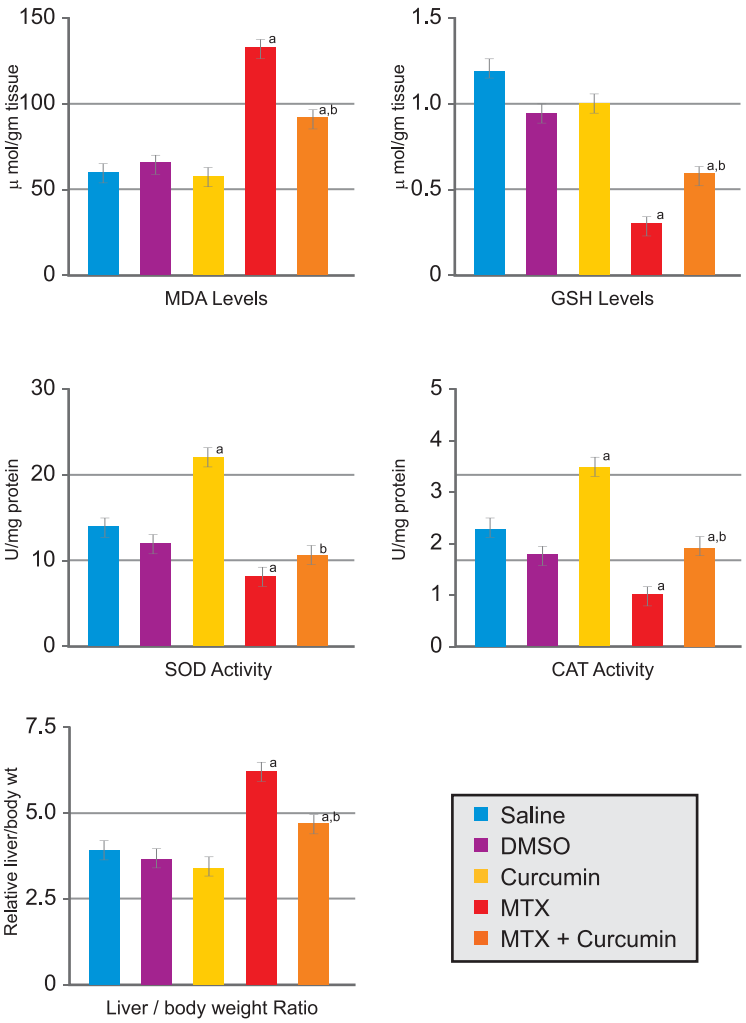
Inflammation plays a major role in development of most disease



Hepatoprotective Potential

In a study, Curcumin treatment for 5 consecutive days following MTX (Methotrexate - folic acid antagonist used as a cytotoxic chemotherapeutic agent) significantly decreased the serum activities of ALT (Alanine Aminotransferase) and AST (Aspartate Aminotransferase) by –21% and –14% compared to MTX treated.

Also administration of curcumin after MTX significantly decreased MDA level by –24%, restored the GSH level by 87% , increased the activities of the SOD and CAT by 57% and 90%, and reduced the relative liver weight by –24% (Hemeida RA. et al. (2008). *J Egypt Natl Canc Inst.*;20(2):141-8).

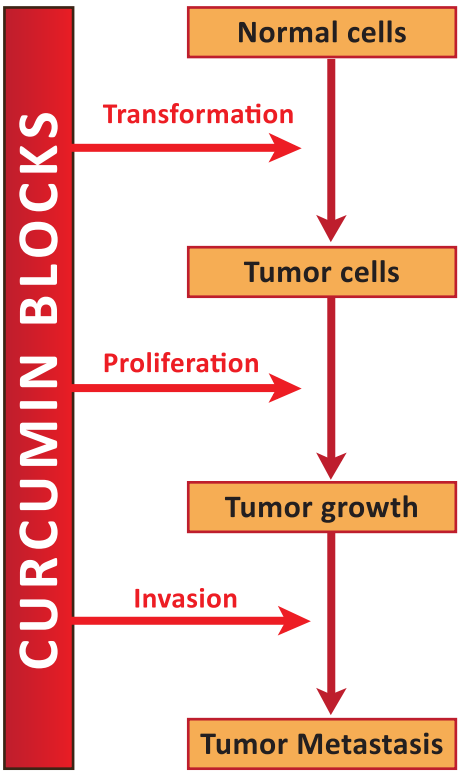


a. Significantly different from control saline at p<0.05.

b. Significantly different from MTX at p<0.05

Anticancer:

Curcuminoids act by inhibiting several processes that contribute to the survival, proliferation, invasion and metastasis of tumor cells (Kuttan G. et al. (2007). *Adv Exp Med Biol.*;595:173-84).

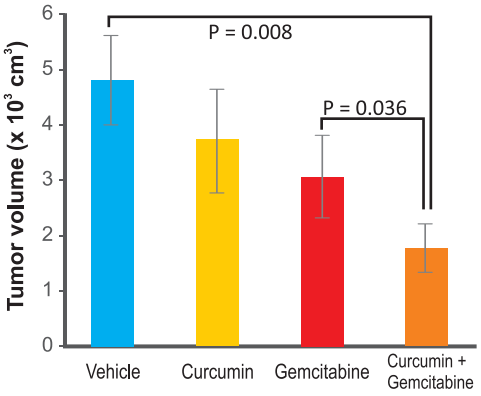


Curcuminoids act by interfering with signaling mechanisms (critical for tumor growth), regulation of apoptosis (cell death), and tumor angiogenesis (new blood vessel formation which feeds tumors).

Significant amounts of research, both pre-clinical and clinical studies have been conducted using Sabinsa's Curcumin C^3 Complex® in the management of various forms of cancer.

Pancreatic Cancer

In vitro, studies have shown that curcumin inhibited the proliferation of pancreatic cancer cells and potentiated the apoptosis induced by gemcitabine.



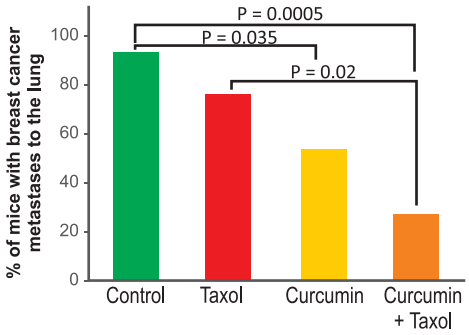
In vivo, pancreatic cancer tumors treated with a combination of curcumin and gemcitabine showed significant reductions in tumor volume compared to controls (Kunnumakkara AB. et al. (2007). *Cancer Res.*;67(8):3853-61.).

Phase I clinical trials have shown that curcuminoids are safe at doses up to 8 g/day (Cheng AL. et al. (2001). *Anticancer Res*:2895-900.).

Phase II clinical trials indicated that orally administered curcuminoids have biological activity with advanced pancreatic cancer (Dhillon N. et al. (2008). *Clin Cancer Res.*;14(14):4491–4499.).

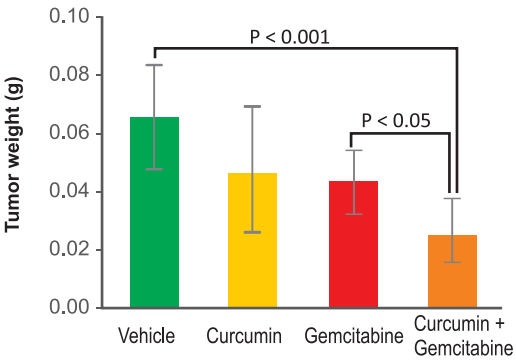
Breast Cancer

In a xenograft model Curcumin prevents breast cancer metastasis possibly through suppression of NF-κB and NF-κB regulated gene products (Aggarwal BB. et al. (2005). *Clin Cancer Res*.11(20):7490-8.).



Bladder Cancer

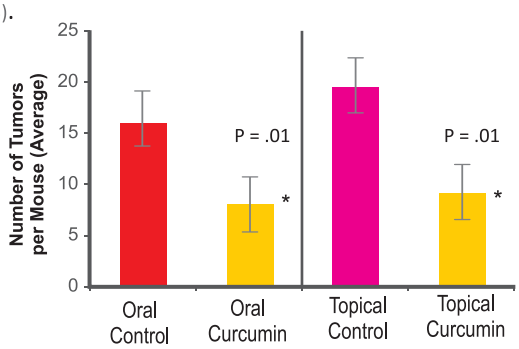
Curcumin alone exhibits significant antitumor effects against human bladder cancer and it further potentiates the effects of gemictabine, possibly through the modulation of NF-κB signaling pathway (Tharakan. et al. (2010). *Biochem Pharmacol*. 79(2): 218–228).



Skin Cancer

First study to demonstrate curcumin's inhibition of UVB radiation induced skin cancer *in vivo*.

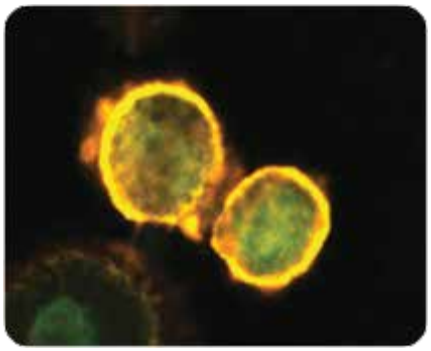
Curcumin appears to inhibit skin cancer formation and prolong time to tumor onset when administered by either an oral or topical route (Phillips. et al. (2013). Otolaryngol Head Neck Surg.. 148(5); 797-803).



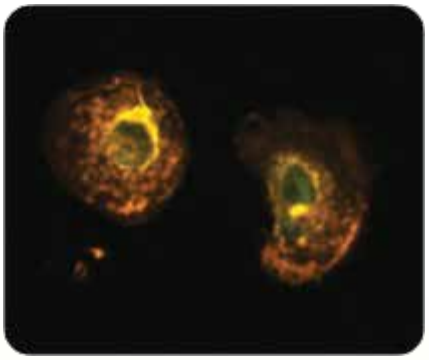
Oral and topical curcumin inhibit tumor multiplicity. Significantly fewer tumors were formed in the oral (P=.01) and topical (P=.01) curcumin groups, compared with respective controls

Alzheimer's Study:

Group of researchers from UCLA treated macrophages of six Alzheimer disease (AD) patients with curcuminoids *in vitro* and measured anti-amyloid β (Aβ) uptake using fluorescence and confocal microscopy. After treatment Aβ uptake by macrophages of three of the six AD patients was significantly increased.



UNTREATED



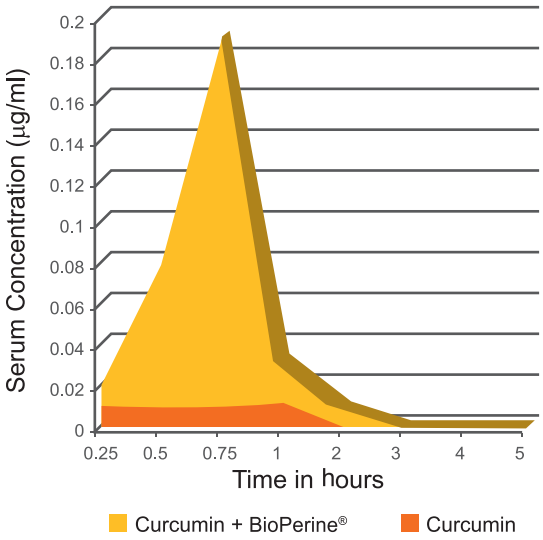
CURCUMINOIDS TREATED

Phagocytosis of Aβ by AD macrophages is increased by curcuminoid treatment Confocal microscopy, **FITC-Aβ (green)**, **phalloidin-FITC (red)**, **colocalization (yellow)**.

Confocal microscopy of AD macrophages responsive to curcuminoids showed surface binding in untreated macrophages but co-localization with phalloidin in an intracellular compartment after treatment (Zhang L. et al. (2006). *J. Alzheimers Dis.* 10(1):1-7)).

Bioavailability of Curcumin with BioPerine®

A clinical study done at St. John's Medical College, Bangalore, India and published in Planta Medica provided clinical evidence of piperine's role in increasing the bioavailability of Curcumin, and has become one of the most downloaded papers of that journal.



The bioavailability of Curcumin (2000mg) co-administered with BioPerine® (20mg) was enhanced than the oral bioavailability of Curcumin alone in humans at doses that were devoid of adverse side effects (Majeed M. et al. (1998). *Planta Med.*;64(4):353-356).

Sabinsa assisted the United States Pharmacopeial Convention (USP)

Sabinsa assisted the United States Pharmacopeial Convention (USP) in preparing the monographs on curcuminoids and turmeric, and in developing validated analytical methods.

Additionally Sabinsa Corporation supplied reference standards for the individual curcuminoids to the USP. These monographs are published in the Pharmacopeial Forum 33(6), Nov-Dec 2007.

Research on Curcumin C³ Complex®

More than 65 studies in conditions ranging from Arthritis, Inflammation to various forms of Cancer and Alzheimer's disease have used Sabinsa's Curcumin C³ Complex® alone or in combination with BioPerine® to enhance bioavailability (as an investigational new drug after FDA review). More than twenty five clinical trials have used C³ Complex® as the active substance for the studies.

The following list of publications includes several human clinical trials using Curcumin C³ Complex®.

Bioavailability Study with BioPerine®

- Planta Med. 1998; 64(4): 353-6.

Anti-Alzheimer Studies

- J. Alzheimers Dis. 2006; 10(1):1-7.
- J.Biol.Chem. 2005; 280(7): 5892-5901.
- Alzheimers Res. Ther. 2012; 4(5): EPUB .
- Brain Res. 2011; 1-18.
- J. Alzheimers Dis. 2011; 23(1); 61-77.
- Neuroscience. 2010; 169, 1296-1306.
- Pharmacol. Biochem. Behav. 2009; 91(4):554-9.
- Synapse. 2011; 65(7):572-582.

Anti-Arthritis Study

- Int. J. of Pharm and Life Sci.; 2012; 3(2): 1413-1423.

Anti-Cancer Studies include Pancreatic, Colon, Bladder, Skin, Lung, Breast & Head and Neck Cancer

- Mol. Pharmacol. 2007; 72(1): 29-39.
- Carcinogenesis.2012; 33(8): 1608-1615.
- Cancer Prev. Res. 2012. 5(2): 205-215.
- Clin. Cancer Res. 2004; 10(20):6847-54.
- Cancer Epidemiol Biomarkers Prev. 2005; 14(1):120-5.
- Clin. Cancer Res. 2008; 14(7); 2128-2136.
- Int. J. Cancer 2009; 125(9), 2187–2197.
- Cancer Prev. Res. 2011; 4(3); 354–364.
- Cancer Prev. Res. 2012; 6(2); 119-28.
- Clin. Cancer Res. 2007; 13(11): 3423-30.
- Biochem. Pharmacol. 2010; 79 (2): 218–228.
- Mol. Cancer Ther. 2007; 6(3):1022-30.
- Breast Cancer Res. Treat. 2010;122(3):777-85.
- Clin.Cancer Res. 2005; 11(20); 7490-8.
- Cancer Res. 2007; 67(8); 3853-61.
- Clin. Cancer Res. 2008 ; 14(14):4491-4499.
- Nutr. Cancer 2010; 62(8), 1137–1141.
- Cancer Chemother. Pharmacol. 2011; 68(1): 157-64.
- Cancer Prev. Res. 2010; 3(12): 1586-1595.
- Otolaryngol Head Neck Surg. 2011; 145(1); 58-63.
- Otolaryngol Head Neck Surg. 2013; 148(5); 797-803.
- J. Skin Cancer; 2012 ; doi: 10.1155/2012/147863.
- Eur. J. Cancer Prev. 2012; 21(5): 407-412.
- Mol. Cancer Ther. 2009; 8(4): 959-970.
- Journal of Hematological Malignancies. 2013; Vol. 3, No.2.
- Clin. Caner Res; 2009. 15(18): 5917- 5922.
- Am. J. Hematol. 2012; 87(5): 455-460.

Oral Mucositis

- Altern. Ther. Health Med. 2013;19(3): 21-4.

Antidiabetic Studies

- Endocrinology 2008; 149(7): 3549-3558.
- BMC Complement. Altern. Med. 2010; 10:67.
- Biochem. Biophys. Res. Commun.2009;388(2):377-82.

Hepatoprotective Potential

- Gut 2010; 59(4): 521-530.
- Br. J. Cancer 2004; 90(5):1011-5.

Cachexia (Muscle Wasting)

- Br. J. Nutr. 2009; 102:967-975.

Dyslipidemic Effect in Obese Patients

- Phytother. Res. 2013; 27 : 374-379.

Radiation Dermatitis

- Radiat. Res.2013 June 7. [Epub ahead of print]

Oral Lichen Planus Studies

- Phytomedicine. 2007; 14: 437-446.
- Phytomedicine 2012; 19(5): 418-423.
- J. Am. Acad. Dermatol. 2012; 66(5); 752-760.

Anti inflammatory Studies (Chronic Pruritus)

- Br. J. Nutr. 2012; 108(7); 1272-9 Epub 2011 Nov 18.
- Ann. Clin.. Biochem 2012; 49:580 -588.

Physical Studies

- Food Chemistry. 2008; 108:419-424.
- Langmuir. 2010; 26(11):7679-7681.
- J. Agric. Food Chem. 2011; 59(17): 9120-9126.
- J. Agric. Food Chem. 2012; 60(21): 5373-5379.
- J. Nanobiotechnology, 2012; 10:38.

Dosage form and Suggested use level

Curcumin C^3 Complex® can be used in the form of capsules or tablets.

Suggested use level:
250 to 500mg three times a day.

Brand Name	Curcumin C^3 Complex®
Common Name	Turmeric extract
Description	Orange yellow Powder
Bulk Density	Tapped Bulk Density – Between 0.50g/ml and 0.90g/ml Loose Bulk Density – Between 0.30g/ml and 0.50g/ ml
Particle Size	20 mesh - Not less than 95% w/w 80 mesh - Not less than 75% w/w
Melting Point	Between 172°C - 178°C
Solubility	Soluble in acetone
Assay	
Content of total Curcuminoids by HPLC	Not less than 95.0% w/w and not more than 102.0% w/w on dry basis
Shelf life	5 years
Storage Condition	Store at room temperature
Certification	
Product certifications	Kosher Certified, Halal Certified, GMO Free, FSSC, TSE-BSE Free, Nanotechnology Free
Manufacturing certifications	ISO, GMP, FDA audited, FSSAI

Our Innovation Is Your Answer
since 1988
Discover • Patent • Repeat

SABINSA®

* These statements have not been evaluated by the Food and Drug administration. This product is not intended to diagnose, treat, cure or prevent any disease.

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