



Redefining the Bioavailability of Curcuminoids



Curcumin C³ Reduct[®], the cascading antioxidant from Sabinsa, is standardized for minimum of 95% tetrahydrocurcuminoids. Tetrahydrocurcuminoids (THC's) are the colorless hydrogenated product derived from the yellow Curcuminoids (mainly Curcumin, Demethoxycurcumin and Bismethoxycurcumin) from the rhizomes of *Curcuma longa*.

Curcumin C³ Reduct[®]

Redefining the Bioavailability of Curcuminoids

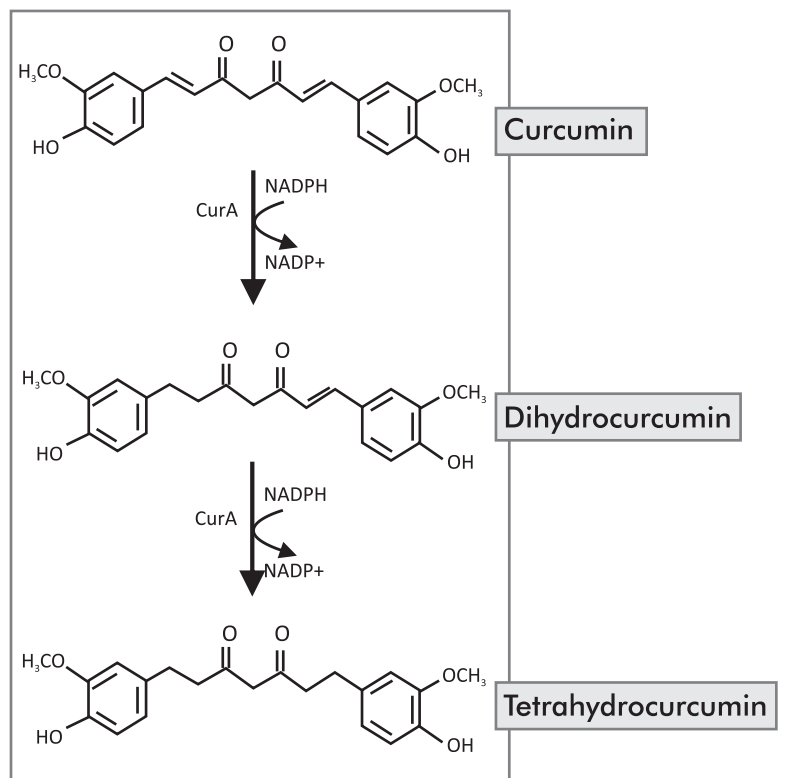
Tetrahydrocurcumin (THC), a partially reduced derivative of Curcumin found in turmeric, appears to be the major active metabolite formed when Curcumin is administered intraperitoneally (i.p.) in mice.

- ✓ Colorless compounds derived from Sabinsa's Curcumin C³ Complex[®]
- ✓ Greater absorption and bioavailability
- ✓ Better pharmacological activity
- ✓ Increased dosage efficiency

A recent and very interesting finding demonstrates that Curcumin in the human intestine is converted into THC by *E. coli* and that the resulting THC is responsible for various activities in the human body. Other *in vitro* studies show that THC is more easily absorbed from the gastrointestinal tract than curcumin itself.

Metabolic Pathway of Curcumin in the intestine

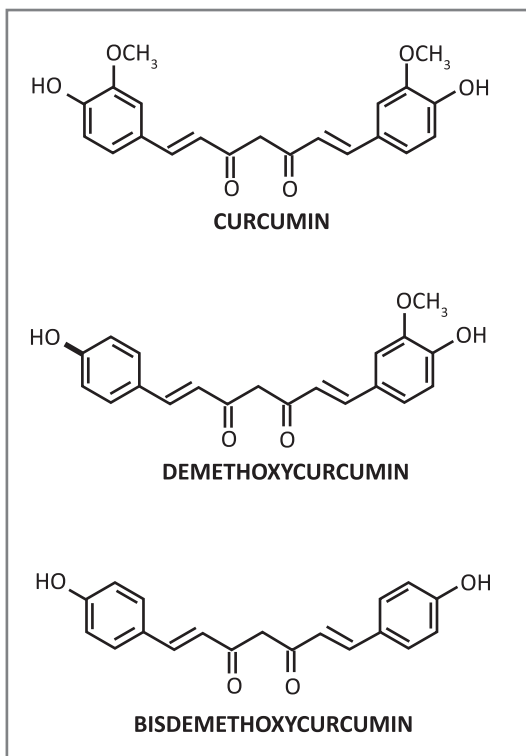
Adapted from Proceedings of National Academy of Science, April 2011



Tetrahydrocurcuminoids (THC's) include Tetrahydrocurcumin (THC), Tetrahydrodemethoxycurcumin (THDMC) and Tetrahydrobisdemethoxycurcumin (THBDMC). Curcumin and THC are the major constituents ($\geq 75\%$ of the total content) of the turmeric and reduced (hydrogenated) turmeric preparations, respectively. THC has higher physiological and pharmacological activities than its parent compound.

Patents:

- ★ US6653327
- ★ US8119696
- ★ AU2006235807
- ★ EP1171144
- ★ EP1328263
- ★ NZ514884



Traditional knowledge

The rhizome of turmeric (*Curcuma longa L.*) has a rich history in India as spice, food preservative and colouring agent and has been used for centuries in the Ayurvedic system of medicine. It 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. Turmeric has been used through the ages as an "herbal aspirin" and "herbal cortisone" to relieve discomfort and inflammation associated with an extraordinary spectrum of infectious and autoimmune diseases.

Nutraceutical Applications

The remarkably superior antioxidant property of C³ Reduct[®], combined with the advantage of lack of yellow color, in addition to its diverse pharmacological activity has brought this white Curcuminoid member into sharper focus of research.

Potent Antioxidant

Studies on several *in vitro* models report that curcumin is a potent antioxidant comparable to α -tocopherol. It is possible that the metabolites of Curcumin such as THC's could mediate major antioxidant activities *in vivo*.

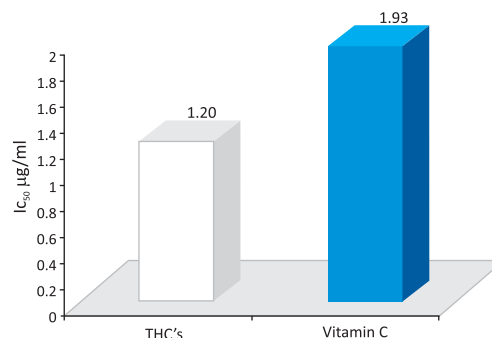
Proposed mechanisms of Antioxidant Action of THC's:

THC's counteract free radicals in 2 ways

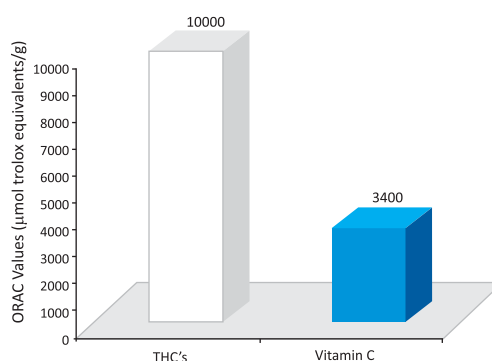
- **PREVENTION** of free radical formation
- **INTERVENTION** whereby already preformed radicals are quenched

THC's are classified as **BIOPROTECTANT[®] composition**.

In house studies reveal that the C³ Reduct[®] (THCs) was found to be more potent antioxidant than the commonly used antioxidant, Vitamin C.



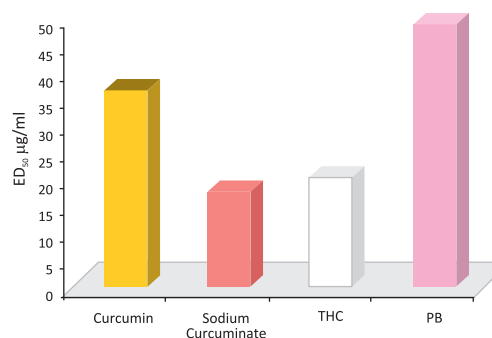
DPPH Method: Lower the IC₅₀ value, higher the antioxidant activity



ORAC Method: Greater the ORAC value, greater the antioxidant activity

Effective Anti-inflammatory

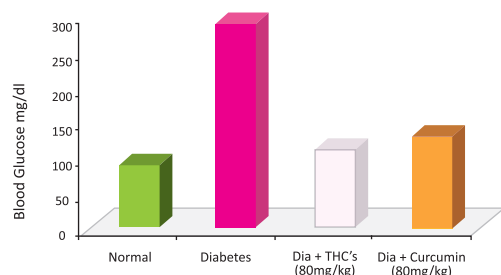
Both curcuminoids and THC showed potent anti-inflammatory effect at low doses in carrageenan-induced paw edema and cotton pellet induced granuloma pouch test in rats. THC was effective at less than half the dose of phenylbutazone (PB).



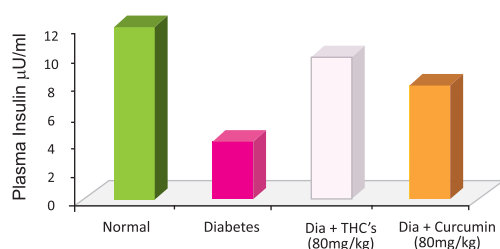
Effect of Curcumin derivatives and phenylbutazone on carrageenan-induced paw edema in rats. Lower the ED₅₀, Better the Activity.

Blood sugar management

THC's have been reported to stimulate pancreatic beta cells which play an important role in the production and secretion of insulin. Administration of THC's to diabetic animals normalizes blood glucose and causes a marked improvement of altered carbohydrate metabolic enzymes.



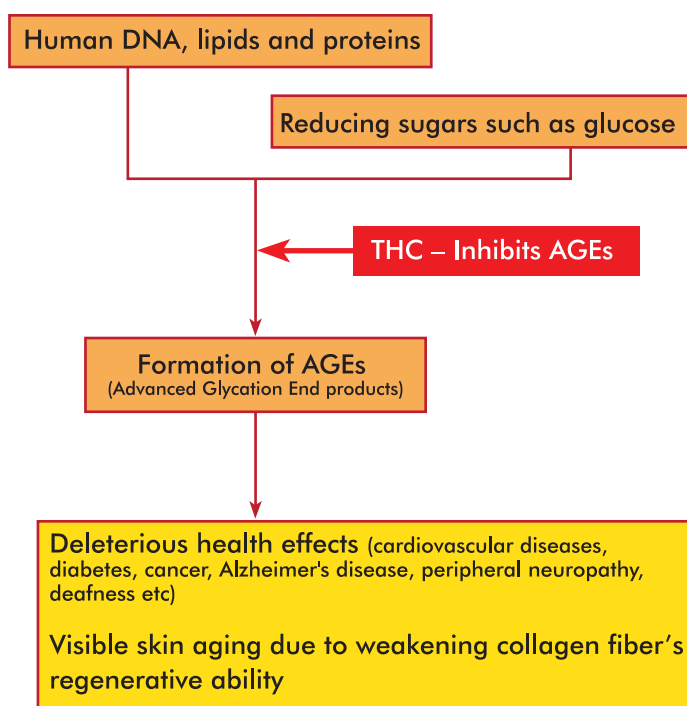
THC's better potentiate insulin secretion & decrease blood glucose level



THC's show better plasma insulin activity compared to Curcumin

Antiglycation potential

THC has shown potential as Antiglycation compound to reduce AGEs formation and cross linking of collagen.



Effect of THC's on Hydroxyproline, Total collagen, Extent of Glycation and Levels of Fluorescence Measured in Tail Tendon in Normal and experimental Rats.

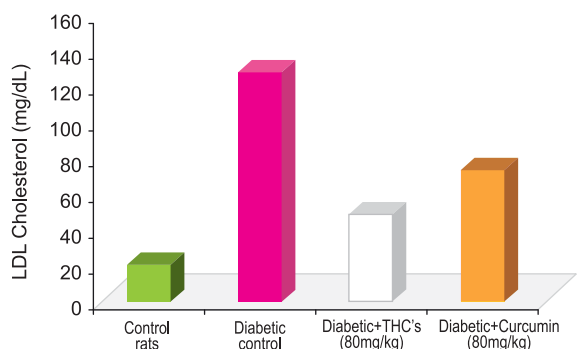
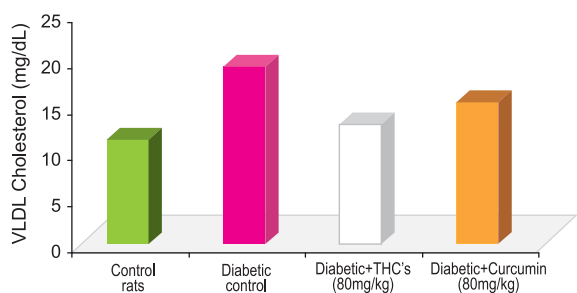
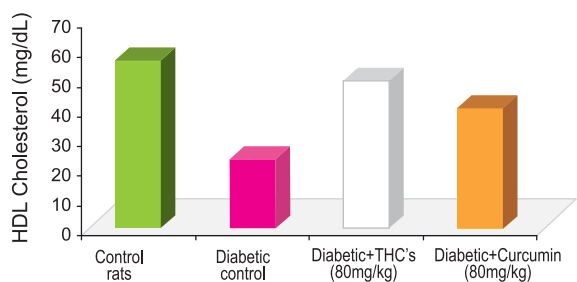
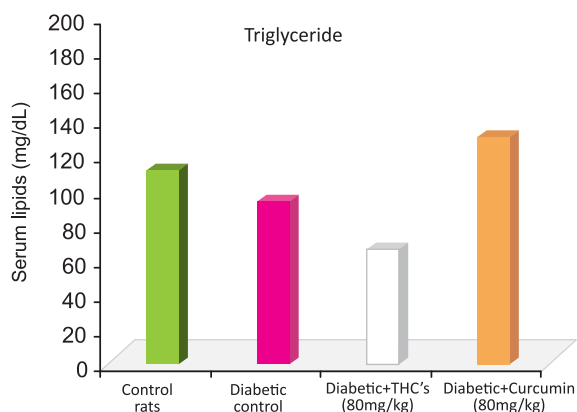
Groups	Hydroxyproline (mg/ 100 mg tissue)	Total collagen (mg/ 100 mg tissue)	Extent of glycation (µg of glucose/ mg collagen)	Fluorescence (AU / µmol hydroxyproline)
Normal	8.97 ± 0.61	65.53 ± 4.46	11.09 ± 0.76	28.23 ± 1.92
Diabetic control	15.98 ± 0.94	121.02 ± 7.14	23.19 ± 1.37	55.472 ± 3.27
Diabetic + THC's (80 mg/kg)	9.76 ± 0.71	73.46 ± 5.36	12.88 ± 0.94	32.20 ± 2.35
Diabetic + Curcumin (80 mg/kg)	10.52 ± 0.59	81.16 ± 4.61	14.90 ± 1.03	39.08 ± 2.22

Values are given as mean ± SD from six rats in each group; AU- Arbitrary Units; THC's- Tetrahydrocurcuminoids

Cholesterol control

Based on *in vivo* studies, C³ Reduct® (THCs) was found to be effective against the lipoprotein abnormalities developed in Diabetic condition (Pari and Murugan, 2007). Oral application of THCs showed lowering of Total Cholesterol, LDL (Bad Cholesterol) and VLDL cholesterol as well as increase in HDL (Good Cholesterol).

Influence of THCs and Curcumin on the levels of Total cholesterol, HDL, LDL and VLDL cholesterol in control and experimental rats



Liver Protection

THCs hepatoprotective activity was analyzed against hepatotoxicity induced by Chloroquine, Erythromycin estolate and Streptozotocin in rats. THCs significantly decreased activities of the key metabolic enzymes such as AST (Aspartate transaminase), ALT (Alanine transaminase), ALP (Alkaline phosphatase) and Bilirubin.

Onco Management

Both Curcumin and THC have shown to produce both anti-proliferation and anti-angiogenesis effect with THC showing better activity owing to its higher anti-oxidant activity. In a particular study on HepG2 cells, it was found that THC expressed its anti-angiogenesis without any cytotoxic activities to HepG2 cells itself even at the highest doses. The anti-angiogenic properties of CUR and THC represent a common potential mechanism for their anti-cancer actions.

Established Human Safety

Sabinsa conducted a single centered, open labelled clinical trial in humans for establishing safety of oral supplementation of C³ Reduct®. The study involved 20 healthy human volunteers who were given 300mg of C³ Reduct® (THCs) once daily for 28 days and analysed for 15 vital parameters. C³ Reduct (THCs) was established to be safe.



Curcumin
C³ Reduct®

Patented and clinically safe
95% tetrahydrocurcuminoids.

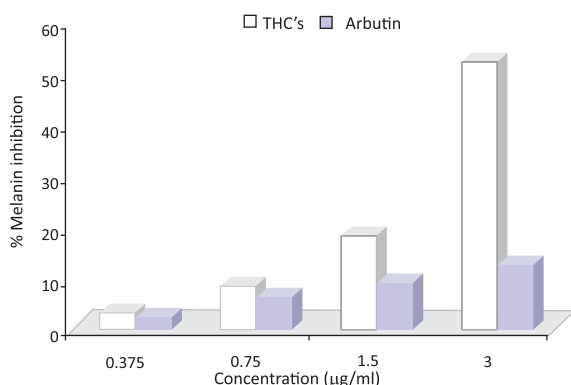
- ✓ Color-free Extract
- ✓ Greater Absorption
- ✓ Most Active Metabolite
- ✓ Lower Dosage Required
- ✓ Better Antioxidant Activity
- ✓ Non-Staining / Photo-Stable

Cosmetic Applications

C³ Reduct® was found to be effective as skin lightening actives with multifunctional topical benefits and no sensitization side effects.

Skin lightening / brightening

Hyperpigmentation, the darkening of skin is due to uncontrolled melanogenesis in the melanocytes of skin. Hence, inhibition of melanin production helps in lightening the skin tone. On comparison with Arbutin, it was observed that THC had a higher melanin inhibitory potential with an IC₅₀ of 3.0±0.5 µg/ml.



Dermal protection

Reactive oxygen species generated in the body due to stress conditions like UV exposure, pollution, ageing etc affect melanocytes of the skin. THC has an IC₅₀ of 1.5µg/ml which implies that concentrations as low as 1.5 µg/ml can reduce generation of reactive oxygen species (ROS) in Swiss 3T3 mouse fibroblast cell line by 50%. THC is effective in scavenging the stable free radical Diphenylpicryl hydrazyl (DPPH) with an IC₅₀ of 0.8 µg/ml.

Anti-aging

Inhibition of lipid peroxidation of melanocyte membranes augments depigmentation process. THC was found to be more effective than coffee bean extract for lipid peroxidation having an IC₅₀ of 27.8 µg/ml.

UV protection

THC has high ORAC value of 10,786 ± 490 µ mol trolox equivalents/gram. THC is effective in inhibiting the peroxy radicals that are generated due to harmful UV radiations.

Acute Oral Toxicity LD₅₀	: > 5000mg/kg body weight
Acute Dermal Toxicity LD₅₀	: > 2000 mg/kg body weight
Primary skin irritation Test	: Did not cause irritation
Mucous Membrane irritation Test	: Did not cause irritation
AMES Test	: Non-mutagenic

Sabinsa offers the following grades of THCs

Product	Standardization	Application
C ³ Reduct® ODN	95% Tetrahydrocurcuminoids	Nutraceutical
C ³ Reduct® ODS	95% Tetrahydrocurcuminoids	Nutraceutical
Tetrahydrocurcuminoids CG	95% Tetrahydrocurcuminoids	Cosmeceutical

Dosage form and Suggested use level

Nutraceutical Application

C³ Reduct® can be used in the form of capsules, tablets or incorporated in functional foods.

It can also be incorporated into various beverages.

Due to its non staining nature it can also be used in oral hygiene products such as toothpaste, dental creams or washes

Suggested use levels of THC's:

200 to 400 mg in two divided doses.

Cosmetic Application

THC CG can be used for topical application conveniently in the form of creams, sprays, serums, gels and lotions.

THC CG be used at levels of 0.2% to 1.0% w/w in topical formulations.

Can be used in:

- Anti-aging Creams & Lotions
- Skin-lightening and brightening Creams & Lotions
- Sun Care & After Sun Care Creams & Lotions
- Skin care serums

Brand Name	Curcumin C ³ Reduct®
Common Name	Tetrahydrocurcuminoids
Description	Creamy white crystalline powder
Solubility	Soluble in alcohol, acetone and glacial acetic acid
Bulk Density	Tapped Bulk Density – 0.4 to 0.7 g / ml Loose Bulk Density – 0.3 to 0.6 g / ml
Particle Size	20 mesh – NLT 100% w/w 40 mesh – NLT 80% w/w 80 mesh – NLT 70% w/w
Melting Point	90° to 100°C
Shelf life	5 years
Assay	
Content of total	Not less than 95.0% w/w
Tetrahydrocurcuminoids by HPLC	Not more than 102.0% w/w on dry basis
Certification	
Product certifications	Kosher Certified, Halal Certified, GMO Free, FSSC, TSE, BSE Free
Manufacturing certifications	ISO 22000:2005, GMP, FDA audited, FSSAI



Pharmacologically Superior - Truly Bioavailable Curcumin - Greater Solubility - Better pH Stability
More Formulation Choices - Color Free Extract - 100,000 Times More Potent Than Metformin
250 Times More Potent Than Curcumin



(daily recommended dosage of 3 x 500mg)
Curcumin



(daily recommended dosage of 1 x 400mg)
Curcumin C³ Reduct®

REDUCTIO AD ABSURDUM



Overcoming challenges are nothing new for us, it's the way we face those challenges that define us. With Curcumin C³ Reduct®, scientists at Sabinsa overcame several challenges with curcumin including poor bioavailability, staining orange color, high dosage, and pH stability by unlocking its true potential in the form of its major metabolites - Tetrahydrocurcuminoids. Standardized to 95% Tetrahydrocurcuminoids, Curcumin C³ Reduct® will reduce to absurdity any and all challenges.

Patents: US 6653327, AU2006235807, EP 1171144, EP 1328263, NZ 514884

an ingredient of 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.