

# Petition of Non-organically Produced Agricultural Products for Inclusion of Black Pepper Extract Powder on the § 205.606 National List

**Date Submitted :** 05/17/07

**Submitted by:**

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**Item A, Category for inclusion on the National List:**

Non-organic agricultural substances allowed in or on processed products labeled as “organic,” §205.606.

**Item B,**

**1. The substance’s chemical or material common name:**

**Black Pepper (*Piper nigrum*) Extract Powder standardized to ≥ 95% Piperine.**  
**Chemical Formula: C<sub>17</sub>H<sub>19</sub>O<sub>3</sub>N**

**CONFIDENTIAL BUISENSS INFORMATION**

**2. Manufactures Contact Information**

Information removed due to it’s confidential nature.

**3. The intended or current use of the substance:**

Used as a nutraceutical supplement with Dietary Supplements & Pharmaceuticals.

**4. Used for handling (including processing) describe mode of action:**

Black Pepper (*Piper nigrum*) Extract, containing >95% Piperine is used as a nutraceutical supplement to increase bio-availability of herbal extracts, water-soluble vitamins, fat-soluble vitamins, antioxidants, amino acids and minerals by increasing gastrointestinal absorption (bioavailability) and delivery of essential nutrients to human tissues when consumed with food and nutrients. Piperine interacts directly with the intestinal epithelial cells, increasing their ability to absorb food, nutrients and drugs<sup>1</sup>.

**4. Used for handling (including processing) describe mode of action (Continued):**

Bioavailability refers to the difference between the amount of a substance, such as a drug, nutrient, herb, or chemical, to which a person is exposed and the actual amount of substance that reaches the systemic circulation and is available at the site of action.<sup>2</sup>

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Piperine is the active principle of black pepper (*Piper nigrum*). Piperine is also the principal alkaloid of the black pepper plant which gives rise to the characteristic pungency of black pepper. The piperine content of a black pepper corn is 3-9%.<sup>3</sup>

### **5. The Source of the substance and a detailed description of it's manufacturing or processing procedures from the basic component to the final product:**

Black pepper extract is derived from the dried pepper fruit of *Piper nigrum L.* The fruit is commonly referred to as a pepper corn. The species are distributed throughout tropical and subtropical regions of the world. The Black pepper plant is a thick perennial climbing vine growing to heights of 4.5-4.7m. The plant uses adventitious roots to climb on trees or on artificial supports. The fruit clusters are formed on hanging branches that form a dense cylindrical canopy of foliage. The typical black color of the pepper corn develops only after drying. The epidermis of the dried pepper fruit is wrinkled and exhibits the characteristic odor and pungent taste normally associated with black pepper. The plant starts yielding after 3-4 years, production begins to diminish after 15 years.

After harvest the pepper corn is dried and stored for further processing. The dried black pepper corn is milled into a powder. Next the powder is steam distilled, separating the pepper oil from the deoiled fruits. The black pepper oleoresin is extracted from the deoiled fruits with ethyl alcohol and then concentrated further. The Black pepper Oleoresin is dissolved in ethyl alcohol at approx 55°C and then cooled to 10°C, filtered and precipitated into a wet solid. The precipitate is dissolved back into the ethanol, treated with alumina at 50°C and cooled to 10°C, after a final filtration the piperine crystals are formed. The piperine crystals are washed with ethyl alcohol, dried, milled and sifted into the finished Pepper Extract Powder. Testing occurs to assure that solvent residual comply with ICH (International Conference on Harmonization of Technical Requirements for Registration of Pharmaceuticals for Human Use) guidelines.

### **6. A summary of any available previous review by state or private certification programs or other organizations of the petitioned substance.**

Non-organic Black Pepper Extract Powder standardized to >95% Piperine, is currently approved for use by QAI (Quality Assurance International) in "Made With Organic" formulations. A recent review of the non-organic Black Pepper Extract Powder standardized to >95% Piperine, by QAI approved its use in products labeled "Organic" pending the following:

- 1) Inclusion of non-organic Black Pepper Extract Powder standardized to >95% Piperine to the National List as described in section § 205.606.
- 2) The use of non-organic Black Pepper Extract Powder standardized to >95% Piperine must be in compliance with section §205.302 in regard to calculation of organic ingredient percentages in product formulations.

### **6. A summary of any available previous review by state or private certification programs or other organizations of the petitioned substance(Continued).**

- 3) Ability to effectively demonstrate to the accredited certifying agent that the non-organic Black Pepper Extract Powder standardized to >95% Piperine was not available in an organic form.

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## **7. Information regarding EPA, FDA, and state regulatory authority registrations including registration numbers.**

N/A

## **8. The Chemical Abstract Service (CAS) NUMBER OR OTHER PRODUCT NUMBERS OF THE substance and labels of products that contains the petitioned substance.**

N/A

## **9. The substance's physical properties and chemical mode of action including:**

### ***a) Chemical interaction with other substances, especially substances used in organic production:***

Piperine is a naturally occurring substance.

### ***b) Toxicity and environmental persistence:***

Piperine is a naturally occurring biodegradable substance.

### ***c) Environmental impacts from its use or manufacture:***

As referenced above, piperine is a naturally occurring biodegradable substance. Ethyl alcohol and Alumina are the only substances used in the manufacture of Black Pepper Powdered Extract. Alumina is considered to be non toxic, Ethyl alcohol is a common compound found in alcoholic beverages for human consumption, therefore the environmental impact is negligible.

### ***d) Effects on human health:***

Black pepper contains approximately 5-9% Piperine and is listed by the US Food and Drug Administration (FDA) as a herb generally recognized as safe (GRAS) for its intended use as a spice.

Studies have shown that piperine extract can be used in humans with no adverse effects <sup>4</sup>. In another study piperine was fed to rats based on a rate of 5-20 times the average daily intake for humans. The study revealed no affect on food intake, animal growth patterns, organ weights and produced no clinical symptoms <sup>7</sup>.

### ***e) Effects on Soil:***

Piperine is a naturally occurring biodegradable substance with no negative effects on soil are known.

## **10. Safety information about the substance including a Material Safety Data Sheet (MSDS) and a substance report from the National Institute of Environmental Health Studies.**

MSDS is attached as separate document. No other data available.

## **11. Research information about the substance which includes comprehensive substance research reviews and research bibliographies which present contrasting positions to those presented by the substance's inclusions on or removal from the National List.**

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We are unaware of any positions held in opposition to consideration of adding Black Pepper Extract Powder, standardized to > 95% piperine, to the national list.

### **12. "Petition justification Statement":**

Black Pepper Powdered Extract, standardized to  $\geq 95\%$  piperine, has demonstrated by scientific studies to significantly increase gastrointestinal absorption of a wide variety of nutrients and vitamins. For this reason Black Pepper Powdered Extract, standardized to  $\geq 95\%$  piperine is necessary to maximize nutrient bioavailability in dietary supplements.<sup>4,5,6 & 7</sup>. No other formula has been substantiated to work as effectively.

#### **Organic availability:**

Black pepper Powdered Extract standardized to > 95% piperine powdered extract is not available at this time as an organic product.

#### **Compatibility with sustainable agriculture:**

The black pepper plant remains productive up to 15 years making it potentially compatible with sustainable agriculture. The Black Pepper Extract Powder is grown without use of sewage sludge. The Camu Camu Extract Power is grown and processed free of genetically modified source material including genetically modified DNA or proteins derived from genetically modified DNA. The product and it's ingredients are not irradiated.

### **REFERENCES:**

<sup>1</sup> Johri, R.K et al. (1992). Piperine-mediated changes in the permeability of rat intestinal epithelial cells. *Biochem. Pharmacol.* 43; 1401-1407

<sup>2</sup> Shargel, L.; Yu, A.B. (1999). *Applied biopharmaceutics & pharmacokinetics* (4th ed.). New York: McGraw-Hill. ISBN 0-8385-0278-4

<sup>3</sup> General Information on Piperine Merck Index, 9<sup>th</sup> Edition (1976)

<sup>4</sup> *Planta Med.* (1998) 64(4):353-356. Influence Of Piperine On The Pharmacokinetics Of Curcumin In Animals And Human Volunteers, G. Shoba, D. Joy, T. Joseph, M. Majeed, R. Rajendran and P.S. Srinivas

### **ABSTRACT**

The medicinal properties of curcumin obtained from *Curcuma longa L.* cannot be utilized because of poor bioavailability due to its rapid metabolism in the liver and intestinal wall. In this study, the effect of combining piperine, a known inhibitor of hepatic and intestinal glucuronidation, was evaluated on the bioavailability of curcumin in rats and healthy human volunteers. When curcumin was given alone, in the dose 2 g/kg to rats, moderate serum concentrations were achieved over a period of 4 h. Concomitant administration of piperine 20 mg/kg increased the serum concentration of curcumin for a short period of 1-2 h post drug. Time to maximum was significantly increased ( $P < 0.02$ ) while elimination half life and clearance significantly decreased ( $P < 0.02$ ) and the bioavailability was increased by 154%. On the other hand in humans after a dose of 2 g curcumin alone, serum levels were either undetectable or very low. Concomitant administration of piperine 20 mg produced much higher

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concentrations from 0.25 to 1 h post drug ( $P < 0.01$  at 0.25 and 0.5 h;  $P < 0.001$  at 1 h); the increase in bioavailability was 2000%. The study shows that in the dosages used, piperine enhances the serum concentration, extent of absorption and bioavailability of curcumin in both rats and humans with no adverse effects.

<sup>5</sup> Piperine, An Alkaloid Derived From Black pepper, Increases Serum Response Of Beta-Carotene During 14-Days Of Oral Beta-Carotene Supplementation. Vladimir Badmaev, M.D., Ph.D., Muhammed Majeed, Ph.D. and Edward P. Norkus Ph.D.

### **ABSTRACT**

The effectiveness of an extract from the fruit of black pepper, consisting of a minimum of 98% pure alkaloid piperine was evaluated for its ability to improve serum response of beta-carotene during oral supplementation using a double-blind, crossover study design. Subjects were randomly selected to ingest a daily beta-carotene dose (15 mg) either with 5 mg of piperine or placebo during each of two 14-day supplementation periods. Inter-subject variability in pre-supplementation serum beta-carotene levels was minimized by limiting the selection of volunteers to healthy adult males with fasting serum beta-carotene values  $< 20$  mcg/dL. The results indicate that significantly greater increases ( $p < 0.0001$ ) in serum beta-carotene occurred during supplementation with beta carotene plus piperine ( $49.8 \pm 9.6$  mcg/dL vs.  $30.9 \pm 5.4$  mcg/dL) compared to beta-carotene plus placebo. Supplementation with beta-carotene plus piperine for 14 days produced a 60% greater increase in area under the serum beta-carotene curve (AUC) than was observed during supplementation with beta-carotene plus placebo. We suggest that the serum response during oral beta-carotene supplementation is improved through non-specific, thermogenic property(s) of piperine described in this paper as thermonutrient action.

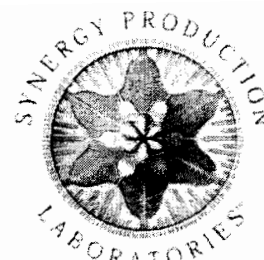
<sup>6</sup> **J. Nutr. Biochem. (2000) 11: 109-113.** Piperine Derived From Black pepper Increases The Plasma Levels Of Coenzyme Q10 Following Oral Supplementation Vladimir Badmaev, M.D., Ph.D., Muhammed Majeed, Ph.D., and Lakshmi Prakash, Ph.D.

### **ABSTRACT**

An extract from the fruits of black pepper consisting of a minimum of 98% pure piperine was evaluated in a clinical study using a double-blind design. The relative bioavailability of 90 mg and 120 mg of coenzyme Q<sub>10</sub> administered in a single dose experiment or in separate experiments for 14 and 21 days with placebo or with 5 mg of piperine was determined by comparing measured changes in plasma concentration. The inter-subject variability was minimized by limiting the selection of individuals to healthy adult male volunteers with (pre-supplementation) fasting coenzyme Q<sub>10</sub> values between 0.30 and 0.60 mg/L. The results of a single dose study and the 14-day study indicate smaller, but not significant, increases in plasma concentrations of coenzyme Q<sub>10</sub> in the control group compared to the group receiving coenzyme Q<sub>10</sub> with a supplement of piperine. Supplementation of 120 mg of coenzyme Q<sub>10</sub> with piperine for 21 days produced a statistically significant ( $p=0.0348$ ), approximately 30% greater, area under the plasma curve (AUC) than observed during supplementation with coenzyme Q<sub>10</sub> plus placebo. It is postulated that the bioenhancing mechanism of piperine to increase plasma levels of supplemental coenzyme Q<sub>10</sub> is nonspecific and possibly based on its description in the literature as a thermonutrient.

<sup>7</sup> Bioperine<sup>®</sup> Nature's own thermonutrient<sup>®</sup> and natural bioavailability enhancer. Copyright<sup>©</sup> 1999 by Nutriscience Publishers, Inc. Ph.D., Muhammed Majeed, Ph.D., and Lakshmi Prakash, Ph.D. Vladimir Badmaev, M.D.

# PRODUCT SPECIFICATION



A Division of The Synergy Company™

## Synergized® Raw Materials:

**Black Pepper Powdered Extract, Standardized to ≥ 95%Piperine, Kosher**

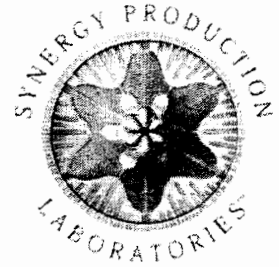
Common Name: Black Pepper Extract  
 Latin Name: *Piper Nigrum*  
 Plant part: Piper Nigrum  
 Part ID: RM10013  
 Country of origin: India

Kosher certifier: Kosher Overseers Associates of America

Shelf life: 60 months from date of manufacture, unopened in original packaging  
 Storage: Store away from moisture, light and heat; ≤70°F  
 Packaging: 5 kg net weight, double food grade poly bags, shipping carton

TEST	SPECIFICATION	METHOD
<b>ANALYTICAL</b>		
Moisture	≤2%	Gravimetric
Mesh size	95% through US 80 mesh	Sieve Analysis
Density	Between 0.55 g/ml - 0.75 g/ml	Volumetric
Solubility	Soluble in alcohol, benzene and glacial acetic acid. Insoluble in water	
<b>IDENTITY</b>		
Color	Pale yellow	Organoleptic
Flavor	Typical of black pepper	Organoleptic
Texture	Fine powder	Organoleptic
Aroma	Typical of black pepper	Organoleptic
<b>MICROBIOLOGICAL</b> Based on USP and EP Guidelines		
Standard plate count (SPC)	≤10,000 CFU/g	FDA/BAM
Coliform	≤100 CFU/g	AOAC 991.14
<i>E. coli</i>	Absent	USP
<i>Salmonella</i>	Absent	USP
<i>Staph. aureus</i>	Absent	USP
Yeast and Mold	≤1,000 CFU/g	AOAC 997.02
<b>HEAVY METAL</b> Based on NSF, EP, WHO and EPA Guidelines		
Arsenic (inorganic) (As)	≤5.0 µg/g	ICP-MS
Cadmium (Cd)	≤1.0 µg/g	ICP-MS
Lead (Pb)	≤5.0 µg/g	ICP-MS
Mercury (Hg)	≤0.2 µg/g	ICP-MS

# MATERIAL SAFETY DATA SHEET



**Identity (as on label):** Synergized® Raw Materials:  
Black Pepper Powdered Extract, Standardized to  $\geq 95\%$  Piperine

## Section I

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MANUFACTURER: L.L.C.	The Synergy Company of Utah,
ADDRESS:	2279 South Resource Blvd. Moab, UT 84532
PHONE:	435-259-4787
DATE MSDS PREPARED:	May 2, 2007
PREPARED BY:	Tim HarkWright

## Section II - Hazardous Ingredients/Identity Information

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IDENTITY/COMMON NAME:	Black Pepper Extract Powder
CHEMICAL NAME:	1- Piperoylpiperidine
CHEMICAL FAMILY:	Food chemical
HAZARD CLASS:	Not regulated
HAZARDOUS COMPONENTS:	None
HEALTH HAZARD:	Nuisance dust

## Section III - Physical/Chemical Characteristics

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BOILING POINT:	Not established
SPECIFIC GRAVITY (H <sub>2</sub> O=1):	Not established
VAPOR PRESSURE (MM HG):	Not established
MELTING POINT:	Not established
SOLUBILITY IN WATER:	Insoluble
EVAPORATION RATE:	Not established
APPEARANCE:	Powder
ODOR:	Typical of black pepper

## Section IV - Fire and Explosion Hazard Data

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FLASH POINT:	Not established
FLAMMABLE LIMITS:	Not established
EXTINGUISHING MEDIA:	Water spray, dry chemical, carbon dioxide or foam as appropriate for surrounding fire and materials
SPECIAL FIRE FIGHTING PROCEDURES:	None
UNUSUAL FIRE AND EXPLOSION HAZARDS:	None

## Section V - Reactivity Data

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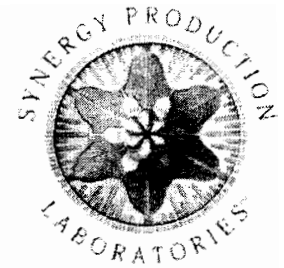
STABILITY:	Stable dry powder
CONDITIONS TO AVOID:	None
INCOMPATIBILITY:	Strong oxidizers (materials to avoid)
HAZARDOUS POLYMERIZATION:	Will not occur
HAZARDOUS DECOMPOSITION OR BY-PRODUCTS:	None known

## Section VI - Health Hazard Data

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ROUTES OF ENTRY:	Inhalation, skin, ingestion
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# MATERIAL SAFETY DATA SHEET



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Black Pepper Powdered Extract, Standardized to  $\geq 95\%$  Piperine

HEALTH HAZARDS:	Nuisance dust;
CARCINOGENICITY:	None known
NTP:	Not applicable
IARC MONOGRAPHS:	None
SIGNS AND SYMPTOMS OF EXPOSURE:	None known
OSHA REG.:	None
MEDICAL CONDITIONS GENERALLY AGGRAVATED BY EXPOSURE:	Nuisance dust; respiratory irritation possible if inhaled
EMERGENCY AND FIRST-AID PROCEDURES:	
EYES:	May cause irritation, Irrigate thoroughly with water
SKIN:	May cause irritation, Wash off thoroughly with soap and Water.
INGESTION:	Flush out moth with water. Induce vomiting (ipecac is recommended) to prevent further absorption. Obtain medical attention.
INHALATION:	May cause irritation of respiratory tract. Remove to fresh air. If irritation persists, obtain medical attention

## ***Section VII - Precautions for Safe Handling and Use***

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STEPS TO TAKE IN CASE MATERIAL IS RELEASED OR SPILLED:	Wear appropriate respirator and chemically compatible gloves. Vacuum or sweep up spillage. Avoid dust. Place spillage in appropriate container for waste disposal. Wash contaminated clothing before reuse. Ventilate area and spill site.
WASTE DISPOSAL METHOD:	Non-hazardous- Dispose of waste in accordance with all applicable Federal, State and Local laws.
PRECAUTIONS TO BE TAKEN IN HANDLING AND STORING:	To insure product integrity, store in poly bags or tight container as supplied. In This material should be handled and stored per label and other instructions.

## ***Section VIII - Control Measures***

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RESPIRATORY PROTECTION:	Dust mask or respirator mask
VENTILATION:	Use local ventilation
PROTECTIVE GLOVES:	Required
EYE:	Goggles or safety glasses required
OTHER:	Appropriate laboratory and/or working apparel