The Wonder Molecule Called Phycocyanin

July 2011

Praneel Datla
Parry Nutraceuticals, Division of EID Parry (India) Ltd, Chennai, India.
e-mail: datlapraneel@parry.murugappa.com • www.parrynutraceuticals.com

Key words: *Phycocyanin,* ***Parry Organic Spirulina, Organic Spirulina, Spirulina, Parry, Free-Radical Scavenging,Immune System, Immunity***

valensa™

Parry Nutraceuticals

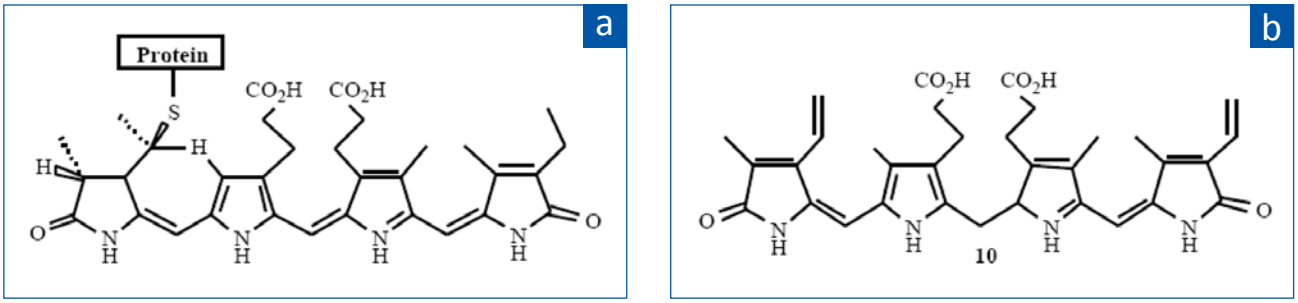
United States Office: Valensa International, 2751 Nutra Lane, Eustis, Florida 32726
(877) 876-8872 • e-mail: sales@valensa.com • www.valensa.com

Introduction

Phycocyanin is one of the major pigment constituents of Spirulina, a microalgae used in many countries as dietary supplement whose nutritional and therapeutic values have been very well documented. Spirulina is known to have nutritional advantages of high-quality protein content and other components such as vitamins; minerals, and essential fatty acids including γ -linolenic acid, and β-carotene

Phycocyanin occurs as the major phycobiliprotein in many Cyanobacteria and as a secondary phycobiliprotein in some red algae. The pigment has a single visible absorption maximum between 615 and 620 nm and a fluorescence emission maximum at ~650 nm. Its molecular weight is between 70,000 and 110,000 Daltons. The pigment is composed of two subunits, α and β, which occur in equal numbers, but the exact number of α and β pairs which make up the molecule may vary among the species. Both α and β subunits contain only the PCB chromophore. In addition to absorbing light directly, this intensely blue pigment accepts quanta from phycoerythrin by fluorescent energy transfer in organisms in which PE is present. The red fluorescence of C-PC is transferred to allophycocyanin. [1]

The chemical structure of the bilin chromophores in Pc is very similar to bilirubin, a heme breakdown product. Bilirubin is considered to be a physiologically important antioxidant against reactive species. It inhibits oxidative modification of plasma proteins and aromatic amino acid residues. Scavenging of oxygen radicals by bilirubin has been shown to protect serum albumin as well as other biological targets.



Chemical structure of phycocyanin bilin chromophore (open-chain tetrapyrrol) (a) and bilirubin (b). Adapted from Romay et. al

Free Radical-Scavenging Activity of Phycocyanin

From this analysis it was concluded that micromolar concentrations of Pc are able to reduce the steady state concentration of the peroxyl radicals by one half, indicating a high antioxidant activity for this compound. It also demonstrated the involvement of the bilin chromophore in the radical scavenging activity of Pc by studying the reactivity of the protein with peroxyl radicals derived from AAPH thermolysis [2]. Invitro studies have shown 10µM had significant effect.

Effect of Phycocyanin on Lipid Peroxidation

Lipid peroxidation mediated by ROS is believed to be an important cause of destruction and damage to cell membranes, because a simple initiating event can result in the conversion of hundreds of fatty acids side chain into lipid peroxides, which alters the structural integrity and biochemical functions of membranes. It has been shown that Pc significantly inhibits the lipid peroxidation at a concentration of 500µM in rat microsomes. Pc also reduced CCl4-induced lipid peroxidation invivo.

Hepatoprotective Effect of Phycocyanin

Researchers have shown that intraperitoneal administration of Pc (50-200 mg/kg body wt) 3 h prior to CCl4 treatment resulted in significantly lower production of malondialdehyde than was found in rats receiving only CCl4. It is known that in CCl4 intoxication, free radicals arising from its biotransformation induce lipid peroxidation. Phycocyanin may reduce the cytochrome P450 mediated reaction.

Anti-inflammatory Effect of Phycocyanin

The major role of Phycocyanin is its anti-inflammatory activity. It has been shown that it shows the activity by acting on COX-2 enzyme [3]. In-vivo rat foot pad edema studies have also shown promising results. phycocyanin also exerted anti-inflammatory and anti-arthritic effects in zymosan-induced arthritis in mice.[4]

It was found that Pc (50-200 mg/kg p.o) inhibited in a dose-dependent manner edema as well as PGE2 and LTB4 levels in the mouse ear treated with arachidonic acid most probably by selectively reducing COX-2 activity.

It is well known that enhanced platelet activation induced by various inducers such as platelet activating factor (1-O-alkyl-2-acetyl-sn-glycero-3-phosphocholine) plays an important role in the initiation and development of atherothrombosis and CVD. Studies by various groups have also shown that phycocyanin inhibits platelet aggregation. Phycocyanin also attenuated PGH2-induced TXB2 formation and platelet aggregation, implying that phycocyanin may also be a thromboxane synthase inhibitor.[5]

Role of Phycocyanin in Immune System

Phycocyanin has shown potential therapeutic benefits for improvement of weakened immune functions caused by use of toxic drugs. Phycocyanin has shown enhancement of proliferation and differentiation of bone marrow hematopoietic cells thereby increasing the levels of various cytokines like IL-1ß, IFN-γ, GMCSF and IL-3. [7]

Expression of Essential Enzymes and Detoxification

Phycocyanin has been shown to increase the expression of essential enzymes and biochemicals related to the balanced function of liver and kidney. This further leads to the detoxification. [8, 9]

Cytochrome P-450 (CYP)

The cytochrome P450 super family (officially abbreviated as CYP) is a large and diverse group of enzymes. The function of most CYP enzymes is to catalyze the oxidation of organic substances. The substrates of CYP enzymes include metabolic intermediates such as lipids and steroidal hormones, as well as xenobiotic substances such as drugs and other toxic chemicals. CYPs are the major enzymes involved in drug metabolism and bioactivation, accounting for ~75% of the total metabolism.

Super Oxide Dismutase (SOD)

Superoxide dismutases are a class of enzymes that catalyze the dismutation of superoxide into oxygen and hydrogen peroxide. As such, they are an important antioxidant defense in nearly all cells exposed to oxygen. Simply stated, SOD outcompetes damaging reactions of superoxide, thus protecting the cell from superoxide toxicity.

Catalase

Catalase is a common enzyme found in nearly all living organisms that are exposed to oxygen, where it functions to catalyze the decomposition of hydrogen peroxide to water and oxygen. Catalase has one of the highest turnover numbers of all enzymes; one molecule of catalase can convert 40 million molecules of hydrogen peroxide to water and oxygen each second. Hydrogen peroxide is a harmful by-product of many normal metabolic processes: to prevent damage, it must be quickly converted into other, less dangerous substances. To this end, catalase is frequently used by cells to rapidly catalyze the decomposition of hydrogen peroxide into less reactive gaseous oxygen and water molecules.

Alanine transaminase ALT/SGPT

Alanine transaminase (ALT), also called Serum Glutamic Pyruvate Transaminase (SGPT) or Alanine aminotransferase (ALAT) is an enzyme present in hepatocytes (liver cells). When a cell is damaged, it leaks this enzyme into the blood, where it is measured. ALT rises dramatically in acute liver damage, such as viral hepatitis or paracetamol (acetaminophen) overdose. Elevations are often measured in multiples of the upper limit of normal (ULN).

Aspartate transaminase AST/SGOT

Aspartate transaminase (AST) also called Serum Glutamic Oxaloacetic Transaminase (SGOT) or aspartate aminotransferase (ASAT) is similar to ALT in that it is another enzyme associated with liver parenchymal cells. It is raised in acute liver damage, but is also present in red blood cells and cardiac and skeletal muscle and is therefore not specific to the liver. The ratio of AST to ALT is sometimes useful in differentiating between causes of liver damage. Elevated AST levels are not specific for liver damage, and AST has also been used as a cardiac marker.

Phycocyanin Toxicity

Although the effective dosage range of Phycocyanin in various animal models of inflammation was from 25 to 300 mg/kg p.o, the safety of the phycobiliprotein is good. The measured LD50 values were estimated to be greater than 3 g/kg for rats and mice. No mortality was induced even at the highest dose of Pc tested (3 g/kg p.o). However, further preclinical pharmacological and toxicological studies are required to determine the safety of Pc as potential drug. Also pharmacokinetic studies and of metabolism must be performed to the phycobiliprotein as previous stages to clinical trials.[6]

Summary

Consumption of phycocyanin in the form of spirulina or supplement leads to optimal health. In the current situation where the environment is full of toxins from pollution from oil, gas, heavy metals and nuclear isotopes, consumption of spirulina/phycocyanin is more than required.

References

1. **Ch. Romay,1, R. González1, N. Ledón1, D. Remirez1 and V. Rimbau2**
   Phycocyanin: A Biliprotein with Antioxidant, Anti-Inflammatory and Neuroprotective Effects
   Current Protein and Peptide Science, 2003, 4, 207-216

2. **Bhat, V.B. and Madyastha, K.M. (2000)**
   C-phycocyanin: a potent peroxyl radical scavenger in vivo and in vitro.
   Biochem. Biophys.Res. Commun., 275, 20-25.

3. **Madhava C. Reddy, J. Subhashini, S.V.K. Mahipal, Vadiraja B. Bhat, P. Srinivas Reddy, G. Kiranmai, K.M. Madyastha, and P. Reddanna**
   C-Phycocyanin, a selective cyclooxygenase-2 inhibitor, induces apoptosis in lipopolysaccharide-stimulated RAW 264.7macrophages
   Biochemical and Biophysical Research Communications 304 (2003) 385–392

4. **Diadelis RemirezCA, Ricardo Gonzalez, Nelson Merino, Sandra Rodriguez and Odelsa Ancheta**
   Inhibitory effects of Spirulina in zymosan-induced arthritis in mice
   Mediators of Inflammation, 11, 75–79 (2002)

5. **Hui-Fen Chiu1, Shih-Ping Yang2, Yu-Ling Kuo3, Yuan-Shu Lai4 and Tz-Chong Chou**
   Mechanisms involved in the antiplatelet effect of C-phycocyanin
   British Journal of Nutrition (2006), 95, 435–440

6. **C. Romay, N. Ledón and R. González V**
   Further studies on anti-inflammatory activity of phycocyanin in some animal models of inflammation
   Volume 47, Number 8, 334-338, Inflammation Research

7. **Osamu Hayashi1,*, Shoji Ono, Kyoko Ishii, YanHai Shi, Tomohiro Hirahashi & Toshimitsu Katoh**
   Enhancement of proliferation and differentiation in bone marrow hematopoietic cells by Spirulina (Arthrospira) platensis in mice
   Journal of Applied Phycology (2006) 18: 47–56

8. **Ou Y, Zheng S, Lin L, Jiang Q, Yang X**
   Protective effect of C-phycocyanin against carbon tetrachloride-induced hepatocyte damage in vitro and in-vivo. Chem Biol Interact. 2010 Apr 29;185(2):94-100. Epub 2010 Mar 12

9. **Roy KR, Nishanth RP, Sreekanth D, Reddy GV, Reddanna P. Hepatol**
   C-Phycocyanin ameliorates 2-acetylaminofluorene induced oxidative stress and MDR1 expression in the liver of albino mice.
   Res. 2008 May;38(5):511-20. Epub 2007 Nov 21.