



Brain Care II Fact Sheet

Since the Millennium-TBI Centers inception in 2004, we have been providing assessment and treatment for all forms of head trauma associated with the development of post-concussion syndrome, CTE, mild TBI, symptomatic TBI, and PTSD. Our patient population consists of civilians, professional athletes, Veterans, active military, law enforcement and fire department individuals. Each has a different and unique story, but all suffer with the same or similar complaints.

In 2009, we entered the world of Translational Medicine taking incredible research from the bench to clinical application and monitored the results. Those results have been incorporated into the development of Brain Care II which is now available to consumers.

The Science behind Brain Care II

DHA – One of the major building blocks of the brain, the omega-3 fatty acid **docosahexaenoic acid (DHA)** is critical for optimal brain health and function at all ages of life. Researchers are now finding that DHA provides brain-boosting benefits in infants and aging adults. A key mechanism of DHA is the protection of neural tissue by the production of Resolvin and Protectin D1.

Tocopherol – Also known as Vitamin E (alpha, delta, and gamma) which has been found to reduce the production of inflammation by downregulating the production of the transcriptional factor NFkB responsible for signaling DNA to manufacture the inflammatory chemicals.

Ascorbic Palmitate – Unique to the different formulations of Vitamin C is this fat-soluble form which can easily enter into the blood supply feeding the brain. Once in the brain, Vitamin C is a major anti-inflammatory and free radical scavenger reducing inflammation.

Quercetin – This is a natural polyphenolic, flavonoid antioxidant and has a number of important effects on the metabolism of the brain and reduction of inflammation. First, Quercetin can increase the production of mitochondria starting within 7 days yielding a higher production of energy as ATP (adenosine triphosphate). This ATP is used to run cellular functions which can be perceived as clearing thoughts, more energy and loss of fogginess. Second, Quercetin downregulates the production of the transcriptional trigger for inflammation, the notorious NFkB.

N-Acetyl-Cysteine – This is the two amino acid precursor of Glutathione that functions as the front-line defense against oxidative stress in the brain. After trauma, the levels of Glutathione are reduced, through consumption and damage to the enzyme system that regenerate it, and this allows for the accumulation of free radicles. This increased Oxidative Stress, which damages neurons and alters the molecular chemistry in the brain, is the focus of this and the entire Brain Care II product.

EGCG - Epigallocatechin gallate is the active agent in Green Tea. Studies on post-stroke patients and those with dementia and Alzheimer's disease all benefited with an improvement in cognitive functioning when placed on EGCG.



How to take Brain Care II

A. Standard Protocol

Initial 2-Weeks: One teaspoon upon arising. Place in mouth and swish around for 30 seconds before swallowing. Repeat prior to dinner using one teaspoon, swish for 30 seconds and then swallow.

Subsequently: One teaspoon upon arising. Place in mouth and swish around for 30 seconds before swallowing.

B. CME Protocol w/Brain Care II

Combination: Same as the Standard Protocol except you add Clear Mind & Energy to the morning serving of Brain Care II. This can be separated by minutes making sure you swish each around the mouth for 30seconds.

1. References - DHA

1. Yehuda S, Rabinovitz S, Carasso RL, Mostofsky DI. Essential fatty acids preparation (SR-3) improves Alzheimer's patient's quality of life. *Int J Neurosci*. 1996 Nov;87(3-4):141-9.
2. Soderberg M, Edlund C, Kristensson K, Dallner G. Fatty acid composition of brain phospholipids in aging and in Alzheimer's disease. *Lipids*. 1991 Jun;26(6):421-5.
3. Prasad MR, Lovell MA, Yatin M, Dhillon H, Markesbery WR. Regional membrane phospholipid alterations in Alzheimer's disease. *Neurochem Res*. 1998 Jan;23(1):81-8.
4. Hashimoto M, Hossain S, Shimada T, et al. Docosahexaenoic acid (DHA) provides protection from impairment of learning ability in Alzheimer's disease model rats. *J Neurochem*. 2002 Jun;81(5):1084-91.
5. Neuringer M, Connor WE. omega-3 fatty acids in the brain and retina: evidence for their essentiality. *Nutr Rev*. 1986 Sep;44(9):285-94.
6. Gamoh S, Hashimoto M, et al. Chronic administration of docosahexaenoic acid (DHA) improves reference memory-related learning ability in young rats. *Neuroscience*. 1999;93(1):237-41.
7. Enslen M, Milon H, Malnoe A. Effect of low intake of omega-3 fatty acids during development on brain phospholipid fatty acid composition and exploratory behavior in rats. *Lipids*. 1991 Mar;26(3):203-8.
8. Ozias MK, Carlson SE, Levant B. Maternal parity and diet (omega-3) polyunsaturated fatty acid concentration influence accretion of brain phospholipid docosahexaenoic acid (DHA) in developing rats. *J Nutr*. 2007 Jan;137(1):125-9.
9. McCann JC. Is docosahexaenoic acid (DHA), an omega-3 long-chain polyunsaturated fatty acid, required for development of normal brain function? An overview of evidence from cognitive and behavioral tests in humans and animals. *Am J Clin Nutr*. 2005 Aug;82(2):281-95.
10. Colombo J, Kannas KN, Shaddy DJ, et al. Maternal DHA and the development of attention in infancy and toddlerhood. *Child Dev*. 2004 Jul;75(4):1254-67.
11. Youyou A, Durand G, Pascal G, et al. Recovery of altered fatty acid composition induced by a diet devoid of omega-3 fatty acids in myelin, synaptosomes, mitochondria, and microsomes of developing rat brain. *J Neurochem*. 1986 Jan;46(1):224-8.
12. Connor WE, Neuringer M, Lin DS. Dietary effects on brain fatty acid composition: the reversibility of omega-3 fatty acid deficiency and turnover of docosahexaenoic acid in the brain, erythrocytes, and plasma of rhesus monkeys. *J Lipid Res*. 1990 Feb;31(2):237-47.
13. Moriguchi T, Loewke J, Garrison M, Catalan JN, Salem N, Jr. Reversal of docosahexaenoic acid deficiency in the rat brain, retina, liver, and serum. *J Lipid Res*. 2001 Mar;42(3):419-27.
14. Anderson GJ. Developmental sensitivity of the brain to dietary omega-3 fatty acids. *J Lipid Res*. 1994 Jan;35(1):105-11.
15. Stillwell W, Shaikh SR, Zerouga M, Siddiqui R, Wassall SR. Docosahexaenoic acid (DHA) affects cell signaling by altering lipid rafts. *Reprod Nutr Dev*. 2005 Sep;45(5):559-79.
16. Stillwell W, Wassall SR. Docosahexaenoic acid: membrane properties of a unique fatty acid. *Chem Phys Lipids*. 2003 Nov;126(1):1-27.
17. Horrobin DF. Interactions between lipid metabolism and schizophrenia: the biochemical changes which may have made us human. *Lipids*. 1999;34 SupplS255.
18. Litman BJ, Niu SL, Polozova A, Mitchell DC. The role of docosahexaenoic acid containing phospholipids in modulating G protein-coupled signaling pathways: visual transduction. *J Mol Neurosci*. 2001 Apr;16(2-3):237-42.
19. Turner N, Else PL, Hulbert AJ. Docosahexaenoic acid (DHA) content of membranes determines molecular activity of the sodium pump: implications for disease states and metabolism. *Naturwissenschaften*. 2003 Nov;90(11):521-3.
20. Salem N, Jr., Litman B, Kim HY, Gawrisch K. Mechanisms of action of docosahexaenoic acid (DHA) in the nervous system. *Lipids*. 2001 Sep;36(9):945-59.
21. Sergeeva M, Strokin M, Reiser G. Regulation of intracellular calcium levels by polyunsaturated fatty acids, arachidonic acid and docosahexaenoic acid, in astrocytes: possible involvement of phospholipase A2. *Reprod Nutr Dev*. 2005 Sep;45(5):633-46.



23. Kim HY, et al. Inhibition of neuronal apoptosis by docosahexaenoic acid (DHA). Role of phosphatidylserine in antiapoptotic effect. *J Biol Chem.* 2000 Nov 10;275(45):35215-23.
24. Zhao G, Etherton TD, Martin KR et al. Anti-inflammatory effects of polyunsaturated fatty acids in THP-1 cells. *Biochem Biophys Res Commun.* 2005 Oct 28;336(3):909-17.
25. McGahon BM, Martin DS, Horrobin DF, Lynch MA. Age-related changes in synaptic function: analysis of the effect of dietary supplementation with omega-3 fatty acids. *Neuroscience.* 1999;94(1):305-14.
26. *Fujita S, Ikegaya Y, Nishikawa M, Nishiyama N, Matsuki N. Docosahexaenoic acid (DHA) improves long-term potentiation attenuated by phospholipase A(2) inhibitor in rat hippocampal slices. *Br J Pharmacol.* 2001 Apr;132(7):1417-22.
27. *Cao D, Xue R, Xu J, Liu Z. Effects of docosahexaenoic acid on the survival and neurite outgrowth of rat cortical neurons in primary cultures. *J Nutr Biochem.* 2005 Sep;16(9):538-.
28. de la Presa OS, Innis SM. Docosahexaenoic and arachidonic acid prevent a decrease in dopaminergic and serotonergic neurotransmitters in frontal cortex caused by a linoleic and alpha-linolenic acid deficient diet in formula-fed piglets. *J Nutr.* 1999. Nov;129(11):2088-93.
29. *Delion S, Chalon S, Guilloteau D, Besnard JC, Durand G. alpha-Linolenic acid dietary deficiency alters age-related changes of dopaminergic and serotonergic neurotransmission in the rat frontal cortex. *J Neurochem.* 1996 Apr;66(4):1582-91.
30. *Zimmer L, et al. The dopamine mesocorticolimbic pathway is affected by deficiency in omega-3 polyunsaturated fatty acids. *Am J Clin Nutr.* 2002 Apr;75(4):662-7.
31. *Mitchell DC, Niu SL, Litman BJ. Enhancement of G protein-coupled signaling by DHA phospholipids. *Lipids.* 2003 Apr;38(4):437-43.
32. Blaylock RL. Chronic microglial activation and excitotoxicity secondary to excessive immune stimulation: possible factors in gulf war syndrome and autism. *J Amer Phys Surg.* 2004 Summer;9(2):46-51.
33. *Yang K, et al. Levels of serum interleukin (IL)-6, IL-1beta, tumour necrosis factor-alpha and leptin and their correlation in depression. *Aust NZJ Psychiatry.* 2007 Mar;41(3):266-73.
34. Kim YK, et al. Cytokine imbalance in the pathophysiology of major depressive disorder. *Prog Neuropsychopharmacol Biol Psychiatry.* 2007 Jun 30;31(5):1044-53.
35. *Kiecolt-Glaser JK, Belury MA, Porter K, et al. Depressive symptoms, omega-6: omega-3 fatty acids, and inflammation in older adults. *Psychosom Med.* 2007 Apr;69(3):217-24.
36. Craddock D, Thomas A. Cytokines and late-life depression. *Essent Psychopharmacol.* 2006;7(1):42-52.
37. Spalletta G, Bossu P, Ciarabella A, et al. The etiology of post-stroke depression: a review of the literature and a new hypothesis involving inflammatory cytokines. *Mol Psychiatry.* 2006 Nov;11(11):984-91.
38. Beilin B, Greenfeld K, Abiri N, et al. Anesthesiologists at work: an increase in pro-inflammatory and Th2 cytokine production, and alterations in proliferative immune responses. *Acta Anaesthesiol Scand.* 2006 Nov;50(10):1223-8.
39. O'Brien SM, Scully P, Fitzgerald P, Scott LV, Dinan TG. Plasma cytokine profiles in depressed patients who fail to respond to selective serotonin reuptake inhibitor therapy. *J Psychiatr Res.* 2007 Apr;41(3-4):326-31.
40. Basterzi AD, Aydemir C, Kisa C, et al. IL-6 levels decrease with SSRI treatment in patients with major depression. *Hum Psychopharmacol.* 2005 Oct;20(7):473-6.
41. O'Brien SM, Scott LV, Dinan TG. Antidepressant therapy and C-reactive protein levels. *Br J Psychiatry.* 2006 May; 188:449-52.
42. von KR, Hepp U, Kraemer B, et al. Evidence for low-grade systemic proinflammatory activity in patients with posttraumatic stress disorder. *J Psychiatr Res.* 2007 Nov;41(9):744-52.
43. Kodas E, Galineau L, Bodard S, et al. Serotonergic neurotransmission is affected by omega-3 polyunsaturated fatty acids in the rat. *J Neurochem.* 2004 May;89(3):695-702.
44. Kodas E, Vancassel S, Lejeune B, Guilloteau D, Chalon S. Reversibility of omega-3 fatty acid deficiency-induced changes in dopaminergic neurotransmission in rats: critical role of developmental stage. *J Lipid Res.* 2002 Aug;43(8):1209-19.
45. Sontrop J, Campbell MK. Omega-3 polyunsaturated fatty acids and depression: a review of the evidence and a methodological critique. *Prev Med.* 2006 Jan;42(1):4-13.
46. De Vriese SR, Christophe AB, Maes M. Lowered serum omega-3 polyunsaturated fatty acid (PUFA) levels predict the occurrence of postpartum depression: further evidence that lowered n-PUFAs are related to major depression. *Life Sci.* 2003 Nov 7;73(25):3181-7.
47. Terao T, Soya A. Cholesterol, essential fatty acids, and suicide. *Pharmacopsychiatry.* 2003 Mar;36(2):86-7.
48. *Sublette ME, et al. Omega-3 polyunsaturated essential fatty acid status as a predictor of future suicide risk. *Am J Psychiatry.* 2006 Jun;163(6):1100-2.
49. McCullumsmith RE, Meador-Woodruff JH. Striatal excitatory amino acid transporter transcript expression in schizophrenia, bipolar disorder, and major depressive disorder. *Neuropsychopharmacology.* 2002 Mar;26(3):368-75.
50. Mathew SJ, Keegan K, Smith L. Glutamate modulators as novel interventions for mood disorders. *Rev Bras Psiquiatr.* 2005 Sep;27(3):243-8.
51. *Relton JK, Strijbos PJ, Cooper AL, Rothwell NJ. Dietary N-3 fatty acids inhibit ischemic and excitotoxic brain damage in the rat. *Brain Res Bull.* 1993;32(3):223-6.
52. *Hogyes E, et al. Neuroprotective effect of developmental docosahexaenoic acid supplement against excitotoxic brain damage in infant rats. *Neuroscience.* 2003;119(4):999-1012.
53. Hamazaki T, et al. Administration of docosahexaenoic acid influences behavior and plasma catecholamine levels at times of psychological stress. *Lipids.* 1999;34 SupplS33-7.
54. Hamazaki T, Sawazaki S, Itomura M, et al. Effect of docosahexaenoic acid on hostility. *World Rev Nutr Diet.* 2001; 88:47-52.
55. Itomura M, et al. The effect of fish oil on physical aggression in schoolchildren—a randomized, double-blind, placebo-controlled trial. *J Nutr Biochem.* 2005 Mar;16(3):163-71.
56. Sawazaki S, et al. The effect of docosahexaenoic acid on plasma catecholamine concentrations and glucose tolerance during long-lasting psychological stress: a double-blind placebo-controlled study. *J Nutr Sci Vitaminol. (Tokyo).* 1999 Oct;45(5):655-65.



2. Reference - Tocopherols

1. Hoskins A, Roberts JL III, Milne G, Choi L, Dworski R. Natural-source d-alpha-tocopherol acetate inhibits oxidant stress and modulates atopic asthma in humans in vivo. *Allergy* 2012; 67:676-82.
2. Miller ER III, Pastor-Barriuso R, Dalal D, Riemersma RA, Appel LJ, Guallar E. Meta-analysis: high-dosage vitamin E supplementation may increase all-cause mortality. *Ann Intern Med* 2005; 142:37-46.
3. Jiang Q, Ames BN. Gamma-tocopherol, but not alpha-tocopherol, decreases proinflammatory eicosanoids and inflammation damage in rats. *FASEB J* 2003;17: 816-22.
4. Patel A, Liebner F, Netscher T, Mereiter K, Rosenau T. Vitamin E chemistry: nitration of non-alpha-tocopherols: products and mechanistic considerations. *J Org Chem* 2007; 72:6504-12.
5. Wisner J, Alexis NE, Jiang Q, Wu W, Robinette C, Roubey R, et al. In vivo gamma-tocopherol supplementation decreases systemic oxidative stress and cytokine responses of human monocytes in normal and asthmatic subjects. *Free Radic Biol Med* 2008; 45:40-9.
6. Berdnikovs S, Abdala-Valencia H, McCary C, Somand M, Cole R, Garcia A, et al. Isoforms of vitamin E have opposing immunoregulatory functions during inflammation by regulating leukocyte recruitment. *J Immunol* 2009; 182:4395-405.
7. Marchese ME, Kumar R, Colangelo LA, Avila PC, Jacobs DR Jr, Gross M, et al. The vitamin E isoforms alpha-tocopherol and gamma-tocopherol have opposite associations with spirometric parameters: the CARDIA study. *Respir Res* 2014; 15:31.
8. Wagner JG, Birmingham NP, Jackson-Humbles D, Jiang Q, Harkema JR, Peden DB. Supplementation with gamma-tocopherol attenuates endotoxin-induced airway neutrophil and mucous cell responses in rats. *Free Radic Biol Med* 2014; 68:101-9.
9. Hernandez ML, Wagner JG, Kala A, Mills K, Wells HB, Alexis NE, et al. Vitamin E, gamma-tocopherol, reduces airway neutrophil recruitment after inhaled endotoxin challenge in rats and in healthy volunteers. *Free Radic Biol Med* 2013;60: 56-62.

3. Reference - Ascorbyl Palmitate

1. Pryor WA, ed. *Free radicals in biology*. Vol 1-VI. New York: Academic Press, 1976-1984.
2. Halliwell B, Gutteridge JMC, eds. *Free radicals in biology and medicine*. 2nd ed. Oxford, UK: Clarendon Press, 1989.
3. Sies H, ed. *Oxidative stress*. London: Academic Press, 1985.
4. Tolbert BM. Metabolism and function of ascorbic acid and its metabolites. *IntJ Vitam Nuts Res* 1985;27:122-38.
5. Levine M. New concepts in the biology and biochemistry of ascorbic acid. *N Engl J Med* 1986;314:892-901.
6. Bendich A, Machim U, Scandurra O, Burton GW, Wayner DDM. The antioxidant role of vitamin C. *Adv Free Radic Biol Med* 1986;2: 419-44.
7. Burns JJ, Rivers JM, Machlin U, eds. *Third conference on vitamin C*. *Ann N Y Acad Sci* 1987;498:1-538.
8. Niki E. Vitamin C as an antioxidant. *World Rev Nutr Diet* 1990;64: 1-30.
9. Yamamoto Y, Niki E, Kamiya Y, Mild M, Tamai H, Mino M. Free radical chain oxidation and hemolysis of erythrocytes by molecular oxygen and their inhibition by vitamin E. *J Nutr Sci Vitaminol (Tokyo)* 1986;32:475-9.
10. Miki M, Tamai H, Mino M, Yamamoto Y, Niki E. Free-radical chain oxidation of rat red blood cells by molecular oxygen and its inhibition by a-tocopherol. *Arch Biochem Biophys* 1987;258:373- 80.

4. Reference – Quercetin

1. Aggarwal, B. B. 2000. Tumour necrosis factor receptor associated signaling molecules and their role in activation of apoptosis. JNK and NF-kappa B. *Ann. Rheum. Dis.* 59:6–16.
2. Aggarwal, B. B., A. Samanta, and M. Feldmann. 2001. TNF- α , p. 413. In J. J. Oppenheim, M. Feldman, S. K. Durum, T. Hirano, J. Vilcek, and N. A. Nicola (ed.), *Cytokine reference*, vol. I. Academic Press, San Diego, Calif.
3. Bremner, P., and M. Heinrich. 2002. Natural products as targeted modulators of the nuclear factor-kappaB pathway. *J. Pharm. Pharmacol.* 54:453– 472.
4. Busse, W. W., D. E. Kopp, and E. Middleton, Jr. 1984. Flavonoid modulation of human neutrophil function. *J. Allergy Clin. Immunol.* 73:801–809.
5. Calamia, K. T. 2003. Current and future use of anti-TNF agents in the treatment of autoimmune, inflammatory disorders. *Adv. Exp. Med. Biol.* 528:545–549
6. Camuesco, D., M. Comalada, M. E. Rodriguez-Cabeza, A. Nieto, M. D. Lorente, A. Concha, A. Zarzuelo, and J. Galvez. 2004. The intestinal anti-inflammatory effect of quercitrin is associated with an inhibition in iNOS expression. *Br. J. Pharmacol.* 143:908–918.
7. Celec, P. 2004. Nuclear factor kappa B—molecular biomedicine: the next generation. *Biomed. Pharmacother.* 58:365–371.
8. Cho, S. Y., S. J. Park, M. J. Kwon, T. S. Jeong, S. H. Bok, W. Y. Choi, W. I. Jeong, S. Y. Ryu, S. H. Do, C. S. Lee, J. C. Song, and K. S. Jeong. 2003. Quercetin suppresses proinflammatory cytokines production through MAP kinases and NF-kappaB pathway in lipopolysaccharide-stimulated macrophage. *Mol. Cell. Biochem.* 243:153–160.
9. Chomczynski, P., and N. Saachi. 1987. Single step method of RNA isolation by acid guanidinium thiocyanate-phenol-chloroform extraction. *Anal. Biochem.* 162:156–159.
10. Coligan, J. E., A. M. Kruisbeek, D. H. Margulies, E. M. Shevach, and W. Strober (ed.). 1991. *Current protocols in immunology*, p. 145–186. Wiley, New York, N.Y.



11. Comalada, M., D. Camuesco, S. Sierra, I. Ballester, J. Xaus, et al. 2005. In vivo quercitrin anti-inflammatory effect involves release of quercetin, which inhibits inflammation through down-regulation of the NF-kappaB pathway. *Eur. J. Immunol.* 35:584–592.
12. Dempsey, P. W., S. E. Doyle, J. Q. He, and G. Cheng. 2003. The signaling adaptors and pathways activated by TNF superfamily. *Cytokine Growth Factor Rev.* 14:193–209.
13. Duh, E. J., W. J. Maury, T. M. Folks, A. S. Fauci, and A. B. Rabson. 1989. Tumor necrosis factor alpha activates human immunodeficiency virus type 1 through induction of nuclear factor binding to the NF-kB sites in the long terminal repeat. *Proc. Natl. Acad. Sci. USA* 86:5974–5978.
14. Hsu, H., J. Xiong, and D. V. Goeddel. 1995. The TNF receptor 1-associated protein TRADD signals cell death and NF-kB activation. *Cell* 81:495–504.
15. Hubbard, G. P., S. Wolffram, J. A. Lovegrove, and J. M. Gibbins. 2004. Ingestion of quercetin inhibits platelet aggregation and essential components of the collagen-stimulated platelet activation pathway in humans. *J. Thromb. Haemost.* 2:2138–2145.
16. Kandaswami, C., and E. Middleton, Jr. 1994. Free radical scavenging and antioxidant activity of plant flavonoids. *Adv. Exp. Med. Biol.* 366:351–376.
17. Kawada, N., S. Seki, M. Inoue, and T. Kuroki. 1998. Effect of antioxidants, resveratrol, quercetin, and N-acetylcysteine, on the functions of cultured rat hepatic stellate cells and Kupffer cells. *Hepatology* 27:1265–1274.
18. Kim, H. P., K. H. Son, H. W. Chang, and S. S. Kang. 2004. Anti-inflammatory plant flavonoids and cellular action mechanisms. *J. Pharmacol. Sci.* 96:229–245.
19. Korkina, L. G., and I. B. Afanas'ev. 1997. Antioxidant and chelating properties of flavonoids. *Adv. Pharmacol.* 38:151–163.
20. Krakauer, T. 2004. Molecular therapeutic targets in inflammation: cyclooxygenase and NF-kappaB. *Curr. Drug Targets Inflamm. Allergy* 3:317–324.
21. Li, B. Q., T. Fu, Y. Dongyan, J. A. Mikovits, F. W. Ruscetti, and J. M. Wang. 2000. Flavonoid baicalin inhibits HIV-1 infection at the level of viral entry. *Biochem. Biophys. Res. Commun.* 276:534–538.
22. Mahajan, S. D., S. A. Schwartz, and M. P. Nair. 2003. Immunological assays for chemokine detection in in-vitro culture of CNS cells. *Biol. Proced. Online* 5:90–102.
23. Mamani-Matsuda, M., J. Rambert, D. Malvy, H. Lejoly-Boisseau, S. Daulouede, D. Thiolat, S. Coves, P. Courtois, P. Vincendeau, and M. D. Mossalayi. 2004. Quercetin induces apoptosis of *Trypanosoma brucei* gam-biense and decreases the proinflammatory response of human macrophages. *Antimicrob. Agents Chemother.* 48:924–929.
24. Manjeet, K. R., and B. Ghosh. 1999. Quercetin inhibits nitric oxide and tumor necrosis factor-alpha production in murine macrophages. *Int. J. Immunopharmacol.* 21:435–443.
25. Middleton, E., Jr. 1998. Effect of plant flavonoids on immune and inflammatory cell function. *Adv. Exp. Med. Biol.* 439:175–182.
26. Middleton, E., Jr., C. Kandaswami, and T. C. Theoharides. 2000. The effects of plant flavonoids on mammalian cells: implications for inflammation, heart disease, and cancer. *Pharmacol. Rev.* 52:673–751.
27. Nair, H. K., K. V. Rao, R. Aalinkel, S. Mahajan, R. Chawda, and S. A. Schwartz. 2004. Inhibition of prostate cancer cell colony formation by the flavonoid quercetin correlates with modulation of specific regulatory genes. *Clin. Diagn. Lab. Immunol.* 11:63–69.

5. Reference – NAC

1. Hoffer ME, Balaban C, Slade MD, Tsao JW, Hoffer BJ (2013) Amelioration of acute sequelae of blast induced mild traumatic brain injury by N-Acetyl Cysteine: A double-blind, placebo controlled study. *PLoS One* 8(1):e54163. doi: 10.1371/journal.pone.0054163.
2. Faul M, Xu L, Wald MM, Coronado VG (2010) Traumatic Brain Injury in the United States: Emergency Department Visits, Hospitalizations and Deaths 2002–2006. Atlanta (GA): Centers for Disease Control and Prevention, National Center for Injury Prevention and Control.
3. Comper P, Bisschop SM, Carmide N, Tricco A (2005) A systematic review of treatments for mild traumatic brain injury. *Brain Inj* 19(11):863–80.
4. Rutland-Brown W, Langlois JA, Thomas KE, Xi YL (2003) Incidence of traumatic brain injury in the United States. *J Head Trauma Rehabil* 2006 Nov– Dec;21(6):544–8.
5. Yi JH, Hazell AS (2006) Excitotoxic mechanisms and the role of astrocytic glutamate transporters in traumatic brain injury. *Neurochem Int* Apr;48(5):394–403.
6. Morganti-Kossmann MC, Rancan M, Stahel PF, Kossmann T (2002) Inflammatory response in acute traumatic brain injury: a double-edged sword. *Curr Opin Crit Care* Apr;8(2):101–5.
7. Farkas O, Povlishock JT (2007) Cellular and subcellular change evoked by diffuse traumatic brain injury: a complex web of change extending far beyond focal damage. *Prog Brain Res* 161:43–59.
8. Lenzlinger PM, Morganti-Kossmann MC, Laurer HL, McIntosh TK (2001) The duality of the inflammatory response to traumatic brain injury. *Mol Neurobiol* 24(1–3):169–81.
9. Chen G, Shi J, Hu Z, Hang C (2008) Inhibitory effect on cerebral inflammatory response following traumatic brain injury in rats: a potential neuroprotective mechanism of N-acetylcysteine. *Mediators Inflamm* Article ID 716458, 8 pages.
10. Ellis EF, Dodson LY, Police RJ (1991) Restoration of cerebrovascular responsiveness to hyperventilation by the oxygen radical scavenger n-acetylcysteine. *J Neurosurg* Nov;75(5):774–779.
11. Hicdonmez T, Kanter M, Tiryaki M, Parsak T, Cobanoglu S (2006) Neuroprotective effects of N-acetylcysteine on experimental closed head trauma in rats. *Neurochemistry Research* 31:473–481.
12. Bergold P, Haber M, Dash P, Grill R, Grin'kina N, et al. (2012) Minocycline and N-Acetylcysteine modulates neuroinflammation and produces remyelination following controlled cortical impact. *J Neurotrauma* 29:A109–A110.
13. Dixon CE, Lyeth BG, Povlishock JT, Findling RL, Hamm RJ, et al. (1987) A fluid percussion model of experimental brain injury in the rat. *J Neurosurg* 67(1):110–9.



14. Prabhu A, Sujatha DI, Kanagarajan N, Vijayalakshmi MA, Ninan B (2009) Effect of N-acetylcysteine in attenuating ischemic reperfusion injury in patients undergoing coronary artery bypass grafting with cardiopulmonary bypass. *Ann Vasc Surg* 23(5):645–51.
15. West CA, Hart AM, Terenghi G, Wiberg M (2007) Analysis of the dose-response of N-acetylcysteine in the prevention of sensory neuronal loss after peripheral nerve injury. *Acta Neurochir Suppl* 100:29–31.
16. Morris RG, Garrud P, Rawlins JN, (1982) Place navigation impaired in rats with hippocampal lesions. *Nature* 297 (5868):681–683.
17. Milman A, Rosenberg A, Weizman R, Pick CG (2005) Mild traumatic brain injury induces persistent cognitive deficits and behavioral disturbances in mice. *J Neurotrauma* 22: 1003–1010.
18. Zohar O, Schreiber S, Getslev V, Schwartz JP, Mullins PG, et al. (2003) Closed-head minimal traumatic brain injury produces long-term cognitive deficits in mice. *Neuroscience* 118(4):949–955.
19. Tang Y, Mishkin M, Aigner TG (1997) Effects of muscarinic blockade in perirhinal cortex during visual recognition. *Proc Natl Acad Sci* 94:12667–12669.
20. Baratz R, Tweedie D, Rubovitch V, Luo WM, Yoon JS, et al. (2011) Tumor necrosis factor- α synthesis inhibitor, 3,69-dithiothalidomide, reverses behavioral impairments induced by minimal traumatic brain injury in mice. *J Neurochem* 118:1032–1042.
21. Dix SL, Aggleton J (1999) Extending the spontaneous preference test of recognition: Evidence of object-location and object-context recognition. *Behav Brain Res* 99:191–200.
22. Khan M, Sekhon B, Jatana M, Giri S, Gilg AG, et al. (2004) Administration of N-acetylcysteine after focal cerebral ischemia protects brain and reduces inflammation in a rat model of experimental stroke. *Journal of Neuroscience Research* 76:519–527.
23. Sekhon B, Sekhon C, Khan M, Patel SJ, Singh I, et al. (2003) N-Acetyl cysteine protects against injury in a rat model of focal cerebral ischemia. *Brain Research* 971:18.
24. Gilgun-Sherki Y, Rosenbaum Z, Melamed E, Offen D (2002) Antioxidant therapy in acute central nervous system injury: current state. *Pharmacological Reviews* 54:271–284.
25. Pahan K, Sheikh FG, Nambodiri AMS, Singh I (1998) N-acetyl cysteine inhibits induction of NO production by endotoxin or cytokine stimulated rat peritoneal macrophages, C6 glial cells and astrocytes. *Free Radical Biology & Medicine* 24:39–48.

6. Reference – EGCG

1. Butterfield D, Castegna A, Pocernich C, Drake J, Scapagnini G, Calabrese V: Nutritional approaches to combat oxidative stress in Alzheimer's disease. *J Nutr Biochem* 2002; 13: 444.
2. Wiseman SA, Balentine DA, Frei B: Antioxidants in tea. *Crit Rev Food Sci Nutr* 1997; 37: 705–718.
3. Higdon JV: Tea catechins and polyphenols: health effects, metabolism, and antioxidant functions. *Crit Rev Food Sci Nutr* 2003; 43: 89–143.
4. Jiang F, Dusting GJ: Natural phenolic compounds as cardiovascular therapeutics: Potential role of their anti-inflammatory effects. *Curr Vasc Pharmacol* 2003; 1: 135–156.
5. Hider RC, Liu ZD, Khodr HH: Metal chelation of polyphenols. *Methods Enzymol* 2001; 335: 190–203.
6. Guo Q, Zhao B, Li M, Shen S, Xin W: Studies on protective mechanisms of four components of green tea polyphenols against lipid peroxidation in synaptosomes. *Biochim Biophys Acta* 1996; 1304: 210–222.
7. Mandel S, Weinreb O, Amit T, Youdim MBH: Cell signaling pathways in the neuroprotective actions of the green tea polyphenol (–)-epigallocatechin-3-gallate: implications for neurodegenerative diseases. *J Neurochem* 2004; 88: 1555–1569.
8. Weinreb O, Mandel S, Amit T, Youdim MB: Neurological mechanisms of green tea polyphenols in Alzheimer's and Parkinson's diseases. *J Nutr Biochem* 2004; 15: 506–516.
9. Suganuma M, Okabe S, Oniyama M, Tada Y, Ito H, Fujiki H: Wide distribution of [3 H](–)-epigallocatechin gallate, a cancer preventive tea polyphenol, in mouse tissue. *Carcinogenesis* 1998; 19: 1771–1776.
10. Abd El Mohsen MM, Kuhnle G, Rechner AR, Schroeter H, Rose S, Jenner P, Rice-Evans CA: Uptake and metabolism of epicatechin and its access to the brain after oral ingestion. *Free Rad Biol Med* 2002; 33: 1693–1702.
11. Zecca L, Youdim MB, Riederer P, Connor JR, Crichton RR: Iron, brain ageing and neurodegenerative disorders. *Nat Rev Neurosci* 2004; 5: 863–873.
12. Blum D, Torch S, Lambeng N, Nissou M, Ben-abid AL, Sadoul R, Verna JM: Molecular pathways involved in the neurotoxicity of 6-OHDA, dopamine and MPTP: Contribution to the apoptotic theory in Parkinson's disease. *Prog Neurobiol* 2001; 65: 135–172.
13. Linazasoro G: Neuroprotection in Parkinson's disease: Love story or mission impossible? *Expert Rev Neurotherapeut* 2002; 2: 403–416.
14. McNaught KS, Belizaire R, Jenner P, Olanow CW, Isacson O: Selective loss of 20S proteasome alpha-subunits in the substantia nigra pars compacta in Parkinson's disease. *Neurosci Lett* 2002; 326: 155–158.
15. Lee JH, Song DK, Jung CH, Shin DH, Park J, Kwon TK, Jang BC, Mun KC, Kim SP, Suh SI, Bae JH: (–)-Epigallocatechin gallate attenuates glutamate-induced cytotoxicity via intracellular Ca modulation in PC12 cells. *Clin Exp Pharmacol Physiol* 2004; 31: 530–536
16. Lee S, Suh S, Kim S: Protective effects of the green tea polyphenol (–)-epigallocatechin gallate against hippocampal neuronal damage after transient global ischemia in gerbils. *Neurosci Lett* 2000; 287: 191–194.
17. Schroeter H, Spencer JP, Rice-Evans C, Williams RJ: Flavonoids protect neurons from oxidized low-density-lipoprotein-induced apoptosis involving c-Jun N-terminal kinase (JNK), c-Jun and caspase-3. *Biochem J* 2001; 358: 547–557.
18. Choi YT, Jung CH, Lee SR, Bae JH, Baek WK, Suh MH, Park J, Park CW, Suh SI: The green tea polyphenol (–)-epigallocatechin gallate attenuates beta-amyloid-induced neurotoxicity in cultured hippocampal neurons. *Life Sci* 2001; 70: 603–614.
19. Ishige K, Schubert D, Sagara Y: Flavonoids protect neuronal cells from oxidative stress by three distinct mechanisms. *Free Radic Biol Med* 2001; 30: 433–446.



Brain Care II*

Dietary Supplement

5.07 FL. OZ. (150mL)

Directions: Take 1 tsp (5 ml) 30 minutes before breakfast and 30 minutes before dinner. Shake before using. Refrigerate after opening. Use within 45 days of opening. For oral use only.

Warning: Do not use if you are pregnant, nursing, or under the age of 18. Consult a healthcare professional before using this, or any other dietary supplement, especially if you have a medical condition or if you are taking any medications. Immediately discontinue use and consult a healthcare professional if you experience any adverse reactions. **KEEP OUT OF REACH OF CHILDREN.** Do not use if safety seal is damaged or missing.

For more information:
www.dhpUSA.com

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

Supplement Facts
Serving Size: 1 tsp (5 ml)
Servings Per Bottle: 30

Amount Per Serving	%DV†
Vitamin C (as Vitamin C Palmitate)	50 mg 83%
Vitamin E (as D-Gamma-Tocopherol)	50 mg 167%
Proprietary Blend: 400 mg †	
DHA (from algae), N-Acetyl Cysteine, Quercetin, Green Tea Leaf Extract (45% EGCG)	

† Daily Value (DV) not established.

Other Ingredients: Purified water, phospholipids, glycerin, natural flavors, xanthan gum, acacia gum, stevia, potassium sorbate.

Manufactured for: Millennium Health Centers, Inc. Chatsworth, CA 91311

© 2018 Dynamic Health Products. All rights reserved.

Note: Sixty percent (60%) of the proceeds from the sale of this product goes to support our Veteran's Program. Present Supporters of this program: Access Medical Laboratories, Age Management Medicine Group, Warrior Angels Foundation, University Compounding Pharmacy, Empower Pharmacy of Houston, Millennium Health Centers, Inc., Pure Encapsulations, Enovex Pharmacy, Tailor Made Pharmacy, and ...