

The Science Behind Daytime Restore

By Dr. Nicholas Larkins

Introduction

Our bodies are made up of around 70 trillion (ie: 7 followed by 13 zeros !!!!) cells. When one multiplies that by the number of chemical reactions going on in a cell at any one time - 20,000 - one ends up with an unbelievably immense amount of chemical reactions each and every millisecond going on within us.

Bear in mind that we have yet to consider our 100 trillion resident communities of intestinal microbiota and their chemical reactions that helps provide the fuels that enables these reactions in the first instance.

Little wonder that when we are subjected to the daily never ending stressors that this wonderful machine can go a bit awry.

The even greater wonder is that it so rarely goes wrong.

Our bodies are subject to a myriad of daily life stressors, such as noise, decreased and/or poor quality oxygen supply (airplane/shopping malls, clubs, a/c, etc.), pain, malnutrition - lacking conditionally essential ingredients in the diet (eg: a McDonalds' diet), heat, cold, trauma, old age, drugs - including medically prescribed drugs, obesity (metabolic syndrome), disease, surgical interventions and responses to life events. These stressors deplete the body's energy level. Many so-called "energy" products address this energy depletion by providing large doses of caffeine, which is fine for a short-term response, but destructive and debilitating over time.

Daytime Restore has been formulated with ingredients that act together synergistically with to address these daily life stressors. They achieve this by assisting the body return to its healthy state of well-being: homeostasis. To do this, Daytime Restore addresses the body and its many trillions of cells as whole community rather than just focusing on one particular community area such as the heart.

In doing so, those high energy levels we once took for granted can again become a reality. This is real energy not short term artificially induced energy.

To again achieve this youthful energy state it must be appreciated that Daytime Restore does not function like a drug. The results are not instantaneous.

These conditionally essential nutrients provided by Daytime Restore are cumulative helping the human bipedal mammal returns to its healthy state of well-being. Once there Daytime Restore keeps it there.

Green Tea - *Camellia sinensis*

In Asia, green tea is a widely-consumed beverage and, for centuries, has been regarded to possess significant health-promoting effects. (Balentine DA et al. Crit Rev Food Sci Nutr 37 :693 -704,1997)

In recent years, scientists throughout the world have investigated the potential benefits of green tea. (Wolfram S, J Am Coll Nutr. 2007 Aug;26 84):373s-388s)

Green Tea is the unprocessed, dried, young leaves of *Camellia sinensis*. Green Tea is particularly rich in catechins, of which epigallocatechin gallate (EGCG) is the most abundant.(Graham HN. Prev Med 1992; 21: 334)

The green tea polyphenols have demonstrated potent antioxidant activity in vitro and in vivo and in volunteers. (Bushman JL. Nutr Cancer 1998; 31: 151) The polyphenols are absorbed rapidly after ingestion of Green Tea and cause an increase in plasma antioxidant status. (Benzie IF et al. Nutr Cancer 1999; 34: 83) Green Tea has demonstrated anticarcinogenic activity in experimental models, epidemiological studies and in patients. (Nakachi K et al. Jpn J Cancer Res 1998; 89: 254)

In a study examining the relationship between tea consumption and cognitive function in 716 adults green tea consumption were associated with better cognitive performance. However and interestingly in this study *there was no positive association between coffee consumption and cognitive function*. (Feng L et al., J Nutr Health Aging. 2010;14(6):433-8)

The results of an epidemiological study conducted among Japanese people found that a higher consumption of green tea is associated with a lower prevalence of cognitive impairment.

Cognitive function was assessed by using the Mini-Mental State Examination (MMSE). The results were significantly positive for green tea. (Kuriyama S, Hozawa A, Ohmori K et al. Am J Clin Nutr 2006; 83(2): 355-361)

In a study by L C Yang and co-workers it was observed that daily consumption of green tea per day for at least one year reduced the risk of developing hypertension. These results provide one possible explanation for the reduced cardiovascular mortality associated with habitual green tea consumption.(Yang YC et al. Arch Intern Med 164 :1534 -1540,2004)

A small population study undertaken in Japan between 1999 and 2001 found positive associations between healthy heart function and drinking green tea. It has been speculated by researchers that green tea flavonoids modify signalling between cells which is vital to cellular function so as to ensure healthy cells and tissues. (Borelli F et al. *Aliment Pharmacol Ther* 2004; 19(5):497-510, Williams RJ et al. *Free Radic Biol Med* 2004; 36 (7):838-849)

Green tea consumption has been shown to increase antioxidant capacity in lymphocytes. (Erba D et al. *J Nutr Biochem* 16 :144 -149,2005). A different concept was used in the study by Nagao et al. Who demonstrated that after a 12-week supplementation with green tea catechin-enriched oolong tea in 35 overweight, but otherwise healthy subjects, the reduction in body weight and body fat was significant compared to the control group. (Nagao T et al. *Am J Clin Nutr* 81 :122 -129,2005)

In a paper published by the International Journal of Vitamin Research discussing the health potential for green tea it stated that many 'functional foods' and ingredients are advocated for their effects on body composition but few have consistent scientific support for their efficacy. However, an increasing amount of mechanistic and clinical evidence is building for green tea. Green tea has been suggested to have a number of potential health benefits in areas such as cardiovascular disease, cancer prevention, glucose homeostasis and dental health. Small cumulative effects on energy metabolism could also be responsible for the longer-term effects of green tea on body composition. (Boon N. *Int J Vitam Nutr Res.* 2008 Dec;78(6):275-81.)

An intriguing heading in the Journal of Preventative Medicine 'Can green tea do that? A literature review of the clinical evidence' by Clement and co-workers who evaluate studies that show that habitual green tea consumption is associated with health benefits including chemoprevention and cardiovascular protection. This non-systematic literature review presents positive clinical evidence in support of green tea consumption. (Clement Y. *Prev Med.* 2009 Aug-Sep;49(2-3):83-7)

Findings in relation to regular green tea consumption were published in late 2006 in the prestigious Journal of the American Medical Association (JAMA). (Kuriyama S, Shimazu T, Ohmori K et al. *JAMA* 2006; 296(10): 1255-1265). It was found that regular Green Tea Consumption lowers cardiovascular mortality. The massive study undertaken over 11 years was population-based and which involved 40,350 Japanese adults .

Siberian Ginseng - *Eleutherococcus senticosus*

The root of *Eleutherococcus senticosus* was introduced into traditional practice in the Soviet Union in the mid-1950s.(Baranov AI. J Ethnopharmacol 1982; 6: 339) Soviet researchers were the first to establish that certain plants had the ability to support the body's normal adaptive responses. They called these herbs adaptogens.

Adaptogens are defined as having (Davydov M, Krikorian AD. J Ethnopharmacol 2000; 72: 345)

- broad therapeutic activity increasing attention and endurance in fatigue,
- nonspecific action - providing resistance to the action of a wide variety of harmful factors (stressors)
- a stabilising action - return to homeostasis(the body's complex dynamic state of equilibrium) - independent of the direction of the previous changes.

Adaptogens increase the body's ability to adapt to changing environmental factors (stressors) and to provide non-specific resistance to these factors.(Panossian A, Wagner H. Phytother Res 2005; 19: 819, Lazarev NV. 1958.. Farmacol.Toxicol, 21(3): 81-86)

Adaptogens were shown to work (Davydov M, Krikorian AD. J Ethnopharmacol 2000; 72: 345)

- in healthy individuals and those experiencing stress,
- for those who were not well, for example, those requiring an increase in immunity after surgery, or to facilitate convalescence after a serious disease.

As an adaptogen and tonic Siberian Ginseng is used for temporary fatigue and general debility.(British Herbal Medicine Association. British Herbal Compendium. BHMA, Bournemouth, 1992)

Siberian Ginseng was included as a tonic for cosmonauts in the Soviet space program in 1977. (Halstead BW, Hood LL. Oriental Healing Arts Institute, Long Beach, 1984)

Indications supported by clinical trials have shown *Eleutherococcus senticosus* to improve physical performance, minimize the effects of stress in athletes, enhancement of immune function (NK-cells, T-helper cells) and reduce convalescence after antibiotic therapy. (Zykov M.P. Vladivostok; Far East Sci

Center Symposium. 164-169 1984. Wagner H. Advances in Chinese Medicinal Materials. Chang HM et al, editor. Singapore: World Scientific Publishing;1985. p.159-70)

In a study involving 36 volunteers a placebo controlled study on the effect of an eleutherococcus extract on the immune system showed a highly significant increase in the absolute number of immunocompetent cells especially T lymphocytes ($p < 0.00001$), predominantly on the helper subtype but also on cytotoxic and natural killer (NK) cells. Pharmacokinetic studies indicate that eleutheroside B is enriched in the adrenal cortex. This suggested a complicated network involving effects on steroidogenesis which in turn causes interactions with the immune system leading to a conclusion that Eleutherococcus senticosus was capable of non-specific immunostimulation. (Bohn B. Nebe C T, Birr C. *Arzneim-Forsch/Drug Research*. 10:1193-1196 1987)

In controlled trials, Siberian Ginseng:

- reduced cardiovascular responses to stress in healthy young volunteers.(Facchinetti F et al. *Stress Health* 2002; 18:31)
- reduced absenteeism and general illness over a one year period in those working in a Siberian factory who were exposed to mean daily temperatures of -5°C (23°F), (Farnsworth NR et al. *Eleutherococcus senticosus: Current Status as an Adaptogen*. In: Farnsworth NR et al. (eds): *Economic and Medicinal Plant Research*, Volume 1. London:Academic Press, 1985)
- improved well being and selective memory in middle-aged volunteers. (Winther K et al. *J Neurol Sci* 1997; 150(Supp 1): S90)

In uncontrolled trials, Siberian Ginseng extract:

- improved the mental and physical performance and stamina of workers. (Fulder S. *New Scientist* 1980; 87: 576)
- caused faster activation in healthy participants exposed to heat stress. (Novozhilov GN, Silchenko KI. *Fiziol Chel* 1985; 11:303)
- improved light and colour perception in healthy volunteers. (Arushanian EB, Shikina IB. *Eksp Klin Farmakol* 2004; 67: 64)
- assisted resettled people to adapt to their new and harsh environment in the mountainous, desert area of Mongolia as measured by normalisation in the parameters measured, including work capacity.(Zhekalov AN. *Rastit Resur* 1995; 31:87)

Siberian Ginseng was used by Soviet athletes to prepare for the Olympic games in the late 1970s and early 1980s. (Fulder S. New Scientist 1980; 87: 576)

Trials in the Soviet Union had previously found it increased stamina and performance in athletes, as well as reflexes and concentration.(Fulder S. New Scientist 1980; 87: 576)

In other trials, Siberian Ginseng:

- increased concentration in track and field athletes, gymnasts and weight lifters (uncontrolled trial).(Fulder S. New Scientist 1980; 87: 576)

Administration of Siberian Ginseng was shown to increase the stress response in male endurance athletes, as evidenced by a significant increase in the serum testosterone to cortisol ratio. (Gaffney BT et al. Life Sci 2001; 70: 431)

In a randomised, double-blind trial, 20 patients received either Siberian Ginseng extract or placebo for 8 weeks. After 4 weeks of therapy patients receiving Siberian Ginseng achieved significantly higher scores for social functioning and mental health compared to placebo.(Cicero AF et al. Arch Gerontol Geriatr Suppl 2004; (9):69)

The beneficial effects of chronic (ongoing) administration of adaptogens are mainly associated with the hypothalamic-pituitary-adrenal axis and the subsequent regulation of the immune and neuroendocrine systems. This allows the body to better respond to repeated stress.(Panossian A, Wagner H. Phytother Res 2005; 19: 819)

In acute (single) doses the effects of adaptogens are associated with another part of the stress system: the sympatho-adrenal-system. This system provides a rapid response mainly to control the acute reaction to a stressor.(Panossian A, Wagner H. Phytother Res 2005; 19: 819)

Turmeric - Curcuma longa

Curcuma longa, a perennial herb, is a member of the Zingiberaceae (ginger) family. Turmeric has a long tradition of use in the Chinese and Ayurvedic systems of medicine, particularly as an anti-inflammatory agent. Current research focuses on turmeric's antioxidant, hepatoprotective, anti-inflammatory, anticarcinogenic, and antimicrobial properties. All these activities are in addition to its use in cardiovascular disease and gastrointestinal disorders. (Chainani-Wu N. J Altern Complement Med 2003; 9(1): 161-168)

Turmeric, derived from Curcuma longa, is a gold-coloured spice commonly used in the Indian subcontinent, not only for health care but also for the preservation

of food and as a yellow dye for textiles. Curcumin, which gives the yellow colour to turmeric, was first isolated almost two centuries ago. Its structure as diferuloylmethane was determined in 1910. Since the time of Ayurveda (circa 1900 BC) numerous therapeutic activities have been assigned to turmeric for a wide variety of diseases and conditions, including those of the skin, pulmonary, and gastrointestinal systems, aches, pains, wounds, sprains, and liver disorders. (Aggarwal BB et al., *Adv Exp Med Biol.* 2007;595:1-759).

The active constituents of *Curcuma longa* include yellow pigments (3–5%) known as curcuminoids and which consist of curcumin and curcumins. (Bisset NG (ed). *Herbal Drugs and Phytopharmaceuticals: A Handbook for Practice on a Scientific Basis.* Medpharm Scientific Publishers, Stuttgart, 1994. 90)

Curcumin has a surprisingly wide range of beneficial properties, including anti-inflammatory, antioxidant, chemopreventive and chemotherapeutic activity. The pleiotropic activities of curcumin derive from its complex chemistry as well as its ability to influence multiple signalling pathways within cells. Curcumin is a free radical scavenger and hydrogen donor, and exhibits both pro- and antioxidant activity. It also binds metals, particularly iron and copper, and can function as an iron chelator. Curcumin is remarkably non-toxic. (Hatcher H et al., *Cell Mol Life Sci.* 2008 Jun;65(11):1631-52).

A study investigating the pharmacological actions of curcumin in liver diseases found that this bioactive compound obtained from this plant, has shown anti-inflammatory, anti-oxidant, antifungal, antibacterial and anticancer activities. (Rivera-Espinoza Y, Muriel P. *Liver Int.* 2009 Nov;29(10):1457-66).

Most of the medicinal effects of turmeric have been attributed to curcumin, the principal curcumanoid found in turmeric. Recent evidence that curcumin exhibits strong anti-inflammatory and antioxidant activities and modulates the expression of transcription factors, cell cycle proteins, and signal transducing kinases has prompted the mechanism-based studies on the potential of curcumin to primarily prevent and treat cancer and inflammatory diseases. Little work however has been done to study the effect of curcumin on the development of immune responses. This review discusses current knowledge on the immunomodulatory effects of curcumin on various facets of the immune response, including its effect on lymphoid cell populations, antigen presentation, humoral and cell-mediated immunity, and cytokine production. (Gautam SC et al., *Adv Exp Med Biol.* 2007;595:321-41).

Professor Aggarwal and co-workers from The University of Texas in a paper entitled "Curcumin: the Indian solid gold" in which they acknowledged that targeting multiple cellular pathways to provide a greater therapeutic benefits is better than mono-targeted therapy. In undertaking such a therapeutic approach

they concluded that curcumin can be considered the ideal "Spice for Life" (Aggarwal BB et al. *Adv Exp Med Biol.* 2007;595:1-75)

The combination of turmeric and green tea has been found to be more effective than using the individual components. This study provided scientific evidence of synergetic activity when both were used collectively. (Schwarz K et al. *Unters Forsch* 1992; 195: 104)

A review paper investigated the anti-inflammatory properties of curcumin, one of the major constituents of *Curcuma longa*. From an anti-inflammatory perspective curcumin's effect on cancer was also discussed. It was concluded that research has shown curcumin to be a highly pleiotropic molecule capable of interacting with numerous molecular targets involved in inflammation. (Jurenka JS, *Altern Med Rev.* 2009 Jun;14(2):141-53.)

Scientific evidence suggests that curcumin has neuroprotective efficacy, including anti-inflammatory, antioxidant, and antiprotein-aggregate activities. In this review new evidence for the potential role of curcumin providing neuroprotective activity was presented. (Li Y, Wang P. *Zhongguo Zhong Yao Za Zhi.* 2009 Dec;34(24):3173-5).

The potential of curcumin has been examined on a pharmacological basis for its potential alleviating anti-inflammatory role. This study investigated the crucial role of inflammation in most chronic states. The pharmacodynamics and pharmacokinetics of curcumin were examined and it concluded its findings with a discussion on the various anti-inflammatory pharmacological dynamics of curcumin. (Aggarwal BB et al., *Trends Pharmacol Sci.* 2009 Feb;30(2):85-94)

A wealth of research in curcumin has attributed its cardio-protective benefits to its anti-inflammatory and antioxidative properties. This paper concluded and confirmed that these activities can lead to preservation of myocardial function following ischemic or biochemical insult to the heart. (Srivastava G, Mehta JL. *J Cardiovasc Pharmacol Ther.* 2009 Mar;14(1):22-7)

Studies in India have explored its anti-inflammatory and anti-oxidant potentials with the recent investigations focusing on its preventive effect on pre/carcinogenic, anti-inflammatory and anti- atherosclerotic effects in biological systems both under in vitro and in vivo conditions in animals and humans. Both turmeric and curcumin have been found to increase detoxifying enzymes, prevent DNA damage, improve DNA repair, decrease mutations and tumour formation and exhibit antioxidative potential. (Krishnaswamy K. *Asia Pac J Clin Nutr.* 2008;17 Suppl 1:265-8)

Maidenhair tree - Ginkgo biloba

Ginkgo biloba is a dioecious (possessing male and female flowers on separate trees) fossil tree: indigenous to China and possibly Japan. Ginkgo biloba has survived unchanged from the Triassic period (some 150 million years ago). The trees are long lived: up to 1000 years. Ginkgo trees are grown in large scale plantations in China, France and in South Carolina (USA).

The medicinal use of the leaves was recorded by the Chinese in 'Chen Houng Pen T'sao' published in 2800 BC and a monograph exists in the modern Chinese pharmacopoeia. Leaves and the seeds from the fruit are mentioned in ancient Chinese pharmacopoeias.

In the 1960s German researchers found an extract of Ginkgo biloba leaves to be particularly beneficial for conditions characterised by disturbed blood flow. This led to the development of a special extract (EGb 761) standardised to contain 24% flavonoid glycosides (ginkgo flavone glycosides) and eventually 6% terpenoids (ginkgolides and bilobalide). (DeFeudis FV. Ginkgo biloba Extract (EGb 761): Pharmacological Activities and Clinical Applications. Elsevier, Amsterdam, 1991)

Since that time a large number of Ginkgo products have become available. Not all of them, however, reflect the phytochemical profile of this clinically-trialled extract.

A 2005 meta-analysis, conducted by the Cochrane Collaboration, assessed controlled trials for the effect on neurological deficit. Other measures of disability (such as the activities of daily living) and quality of life were not evaluated. Analysis of the results of 10 trials indicated that Ginkgo was associated with a significant increase in the number of improved patients. No major side effects were reported in any of these trials. (Zeng X et al. Cochrane Database Syst Rev 2005; (4): CD003691)

A placebo-controlled trial using standardised Ginkgo extract produced a modest, but not statistically significant, increase in maximal walking time. (Gardner CD et al. J Cardiopulm Rehabil Prev 2008; 28: 258)

A positive review published in 2009 examined the cognition-enhancing effects of standardised Ginkgo extract. Included in the analysis were 29 randomised, double-blind, placebo-controlled studies of chronic (greater than 4 weeks) administration providing data on function-specific cognitive tests in healthy and cognitively impaired volunteers of any age. Objective psychometric test results were examined for 4 cognitive domains (memory, attention, executive functions, intelligence) comprising 14 sub-functions (e.g. for the domain of memory: the

subfunctions were short- and long-term, visual and verbal memory).(Kaschel R. Hum Psychopharmacol 2009; 24: 345)

There is consistent evidence from studies investigating mild cognitive impairment, depression, multiple sclerosis in both healthy young and elderly volunteers. Ginkgo improves selective attention, some executive processes (working memory, cognitive flexibility), long-term memory for verbal and non-verbal (visual) material. The results of a trial with rigorous patient selection, indicated that standardised Ginkgo extract was shown to be beneficial to those patients showing apathy, depression and agitation/aggression. Up to 80% of patients with dementia, irrespective of cause, exhibit such symptoms. (Napryeyenko O et al. *Arzneim Forsch* 2007; 57:49)

In late 2008, the German Institute for Quality and Efficiency in Health Care (IQWiG) which assessed Ginkgo biloba trials for meta-analysis noted that there is consistent evidence showing positive benefits from standardised Ginkgo extracts when taken over extended periods (for at least 16 weeks) particularly with respect the goal of coping with daily activities. (IQWiG Reports - Commission No. A05-19B, Executive Summary, Version 1.0, September 2008)

A systematic review examining cognitive function in the healthy assessed randomised clinical trials in which Ginkgo was ingested as a single dose (7 trials) or over longer periods of time (8 trials, ranging from 2 days to 12 weeks). No effect was found on the lower level physiological function of the visual system, but significant improvement was found when assessing higher order neural changes. The higher order visual system relies on additional cognitive processing, and may include cognitive aspects such as attention, recognition and memory.(Page JW et al. *J Gerontol A Biol Sci Med Sci* 2005; 60: 1246)

An epidemiological study conducted in France assessed 3534 elderly people from 1988 to 2001. Participants aged 65 years or over and without dementia were included in the study. The findings concluded that those who took Ginkgo had a significantly lower risk of mortality in the long term, compared to non-consumers. (Dartigues JF et al. *J Am Geriatr Soc* 2007; 55: 395)

A prospective, cohort study conducted in Vienna from 2000 to 2002 examined 526 individuals without dementia aged around 75 years to investigate the influence of medication on plasma levels of amyloid beta protein 42 (A42). Increased plasma A42 may be a biological risk factor related to age. Plasma A42 levels are elevated in both late onset Alzheimer disease patients and their cognitively normal first-degree relatives. Users of Ginkgo biloba for at least 2 years had significantly decreased A42 plasma levels compared to non-users.(Blasko I et al. *Neurobiol Aging* 2005; 26: 1135)

Five randomised controlled trials were evaluated to determine the efficacy of standardised Ginkgo extract for the prevention of mountain sickness. Three of the trials demonstrated a beneficial effect.(Moraga FA et al. Wilderness Environ Med 2007;18 251). In a Chinese trial, Ginkgo leaf extract tablets improved lung ventilation and physical work capacity in young volunteers at high altitude.(Wang W et al. Chin J Clin Rehab 2005;9:36) In a randomised, double-blind, placebo-controlled, crossover study standardised Ginkgo extract demonstrated a protective effect when healthy volunteers were exposed to hypoxia induced as a result of reduced oxygen levels at high altitudes.(Schaffler K, Reeh PW. Arzneimittelforschung 1985; 35: 1283)

In other conditions standardised Ginkgo extract was shown to decrease anxiety in patients with defined anxiety disorders (Woelk H et al. J Psychiatr Res 2007; 41: 472), had a beneficial effect on sleep patterns in patients with depression. (Hemmeter U et al. Pharmacopsychiatry 2001; 34: 50), reduced the congestive symptoms of premenstrual syndrome, particularly breast symptoms (Tamborini A, Taurelle R. Rev Fr Gynecol Obstet 1993; 88: 447 73) and decreased capillary hyperpermeability in women with idiopathic oedema. (DeFeudis FV. Ginkgo biloba Extract (EGb 761): Pharmacological Activities and Clinical Applications. Elsevier, Amsterdam, 1991)

Standardised Ginkgo extract has been shown to improve word recognition and reading in children with dyslexia (Donfrancesco R, Ferrante L. Phytomedicine 2007; 14:367). In a two case study Ginkgo biloba extract improved cognitive function and social behaviour in children with Down syndrome (Donfrancesco R, Dell'umomo A. Phytomedicine 2004; 11:469). Standardised Ginkgo extract improved behaviour, hyperactivity, inattention and immaturity in young adults with attention deficit disorder (six cases) but not in autistic disorder (three cases). (Niederhofer H. Phytother Res 2009)

Administration of standardised Ginkgo extract significantly reduced plasma cortisol levels during 2-hour glucose-induced stress (oral glucose tolerance test) in healthy volunteers. In this double-blind, placebo-controlled, crossover trial participants received Ginkgo or placebo for 3-month periods. The author suggested that Ginkgo also may reduce blood cortisol levels in other types of stress.(Kudolo GB. Clin Chem 2007; 53(6, Suppl S): A186 81)

The main actions of standardised Ginkgo extract have been identified and examined in multiple experimental studies. (Ponto LL, Schultz SK. Ann Clin Psychiatry 2003; 15: 109: 94,95 and Smith JV, Luo Y. Appl Microbiol Biotechnol 2004; 64: 465) . Ginkgo biloba extracts: have strong antioxidant activity, increase blood flow/tissue perfusion enhancing, circulatory stimulant, are cognition enhancing, are neuroprotective, and life-span extending.