

# AGING

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# MAGAZINE

The in-house magazine for the IAS Private Members Club



## BREAKTHROUGHS

### In this issue:

#### 4MU and prostate cancer

An article by Jonathan Wright, M.D.

#### The healthy gas

The benefits of nitric oxide

#### Wash your mouth out!

How peptides improve dental health

#### Viagra® for the brain

Dr. Ward Dean details modafinil

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# WELCOME

Occasionally, a true breakthrough comes to the fore. We have listed a few of them in this issue.

First and foremost, our lead article is written by the highly respected Jonathan Wright, M.D. Dr. Wright describes a dietary supplement called 4MU and its major impact on prostate cancer, at least for animals.

But what does this mean for humans? Dr. Wright explores the possibilities and as his own patients are undergoing treatment in his Washington clinic with 4MU, we will be intrigued to report on those outcomes when they become available.

Meanwhile, the role of the gas nitric-oxide (NO) has been known for a while, at least since the Nobel Prize for its

discovery in 1998 was announced. Our article looks at how NO improves cardiovascular health and erectile dysfunction and how it encourages stem cell release from bone marrow.

Other topics herein include the role of peptides in mouth health and Dr. Ward Dean reminds us that modafinil is still number one when it comes to its attention/ stimulatory effects.

All are breakthroughs in their own right.

**Phil Micans, MS, PharmB**  
Editor, Aging Matters™ Magazine

**Ward Dean, M.D.**  
Medical Director



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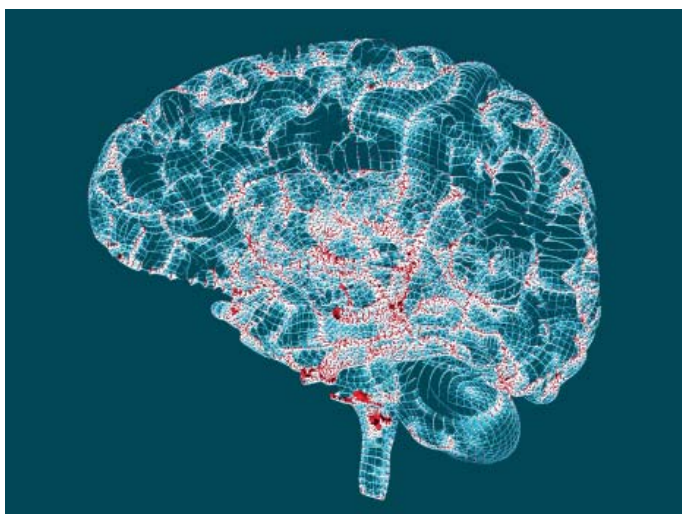
# RAPAMYCIN INHIBITS THE EFFECTS OF SENESCENT CELLS

Rapamycin is one of the most well-known longevity drugs under study. It was initially discovered as an antifungal metabolite produced by *Streptomyces hygroscopicus* from a soil sample of Easter Island<sup>(1)</sup>.

Prior research has revealed it could impact on something called the senescence – associated secretory phenotype or SASP. The increase in cellular senescence associated with aging, and the inflammation also associated, can help set the stage for a variety of degenerative diseases, such as dementia and Alzheimer's. In laboratory animals, once senescent cells are cleared out, they are known to live longer and contract fewer diseases. Rapamycin can have similar effects.

New research has shown that Rapamycin acts through an additional mechanism and is able to directly act on the SASP itself through another pathway. This reveals that Rapamycin works via a two-pronged approach and effectively inhibiting the SASP produced by the senescent cells.

Other studies have shown that astrocyte cells that aid to protect neuron function and health can be damaged by SASP. This may be one of the causes of neurologic diseases, including Alzheimer's.



## Further Reading

1. Jing Li, Sang Gyun Kim, and John Blenis Rapamycin: one drug, many effects *Cell Metab.* 2014 Mar 4; 19(3): 373–379. Published online 2014 Feb 6. doi: 10.1016/j.cmet.2014.01.001
2. Rong Wang, Zhen Yu, Bharath Sunchu, James Shoaf, Ivana Dang, Stephanie Zhao, Kelsey Caples, Lynda Bradley, Laura M. Beaver, Emily Ho, Christiane V. Löhr, Viviana I. Perez. **Rapamycin inhibits the secretory phenotype of senescent cells by a Nrf2-independent mechanism.** *Ageing Cell*, 2017; DOI: 10.1111/acel.12587

# WITHOUT A CURE ON THE HORIZON, ARE HERPES SUFFERERS MISSING OUT ON BHT (BUTYLATED HYDROXYTOLUENE)?

According to the World Health Organisation (Jan 2017); an estimated 3.7 billion people under the age of 50 (60%) worldwide have the HSV-1 infection (Herpes Simplex Virus type 1). HSV-1 is mainly transmitted through oral-to-oral contact resulting in oral herpes, which includes symptoms more commonly known as 'cold sores,' but is also known to cause genital herpes. The HSV-2 (Herpes Simplex Virus type-2) is a sexually transmitted infection that causes genital herpes, which estimates that 417 million people aged 15-49 (11%) are infected with HSV-2.

HSV-1 (oral herpes) and HSV-2 infections are highly contagious and generally asymptomatic, with many sufferers unaware they have been infected with the virus. When symptoms are present they include painful blisters or ulcers/sores around the mouth commonly referred to as 'cold sores.'

With no known cure, and a substantial amount of treatments to suppress and mask outbreaks rather than eradicate, much to the frustration of sufferers. A natural supplement called BHT (butylated hydroxytoluene) has been known in the industry for years but doesn't get the recognition or attention that maybe it deserves.

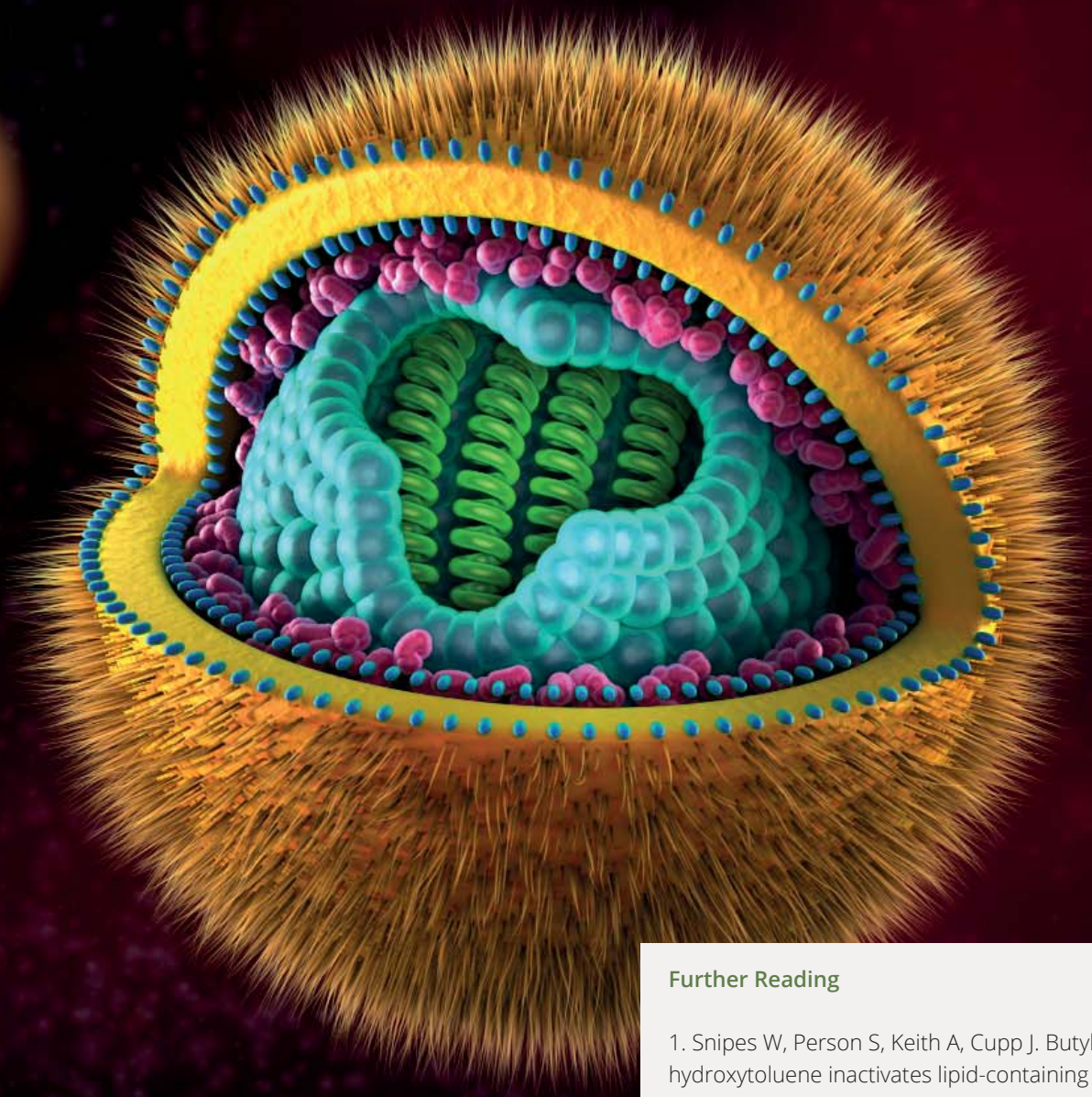
BHT (butylated hydroxytoluene) is a common, inexpensive compound that is approved by the FDA as a food additive, yet although doctors have the authority to prescribe BHT, it is possible they may face disputes from peers and malpractice insurance issues for prescribing an unapproved treatment for herpes. The large pharmaceutical companies don't appear to be interested in investing money into researching and certifying its value as a herpes medicine, which could possibly be due to BHT (butylated hydroxytoluene) being a natural supplement – therefore un-patentable – and inexpensive.

A paper published in the journal of science over 25 years ago, presents research that BHT (butylated hydroxytoluene) could inactivate herpes simplex (HSV-1 and HSV-2) and other lipid coated viruses in lab dishes<sup>(1)</sup>. Herpes has a lipid envelope, meaning the virus has a nuclear acid core and is coated with a fatty membrane. A virus of this type needs an intact lipid membrane in order to pierce through cell walls and infect other living cells.

BHT (butylated hydroxytoluene) works against the virus by disrupting the lipid membranes, in turn making them vulnerable to the immune system and damaging their ability to penetrate human cells. BHT (butylated hydroxytoluene) also eliminates the binding proteins that the virus uses to pierce through cell membranes. Acting as an antioxidant, BHT (butylated hydroxytoluene) neutralizes free radicals that damage cell membranes and cause inflammation.

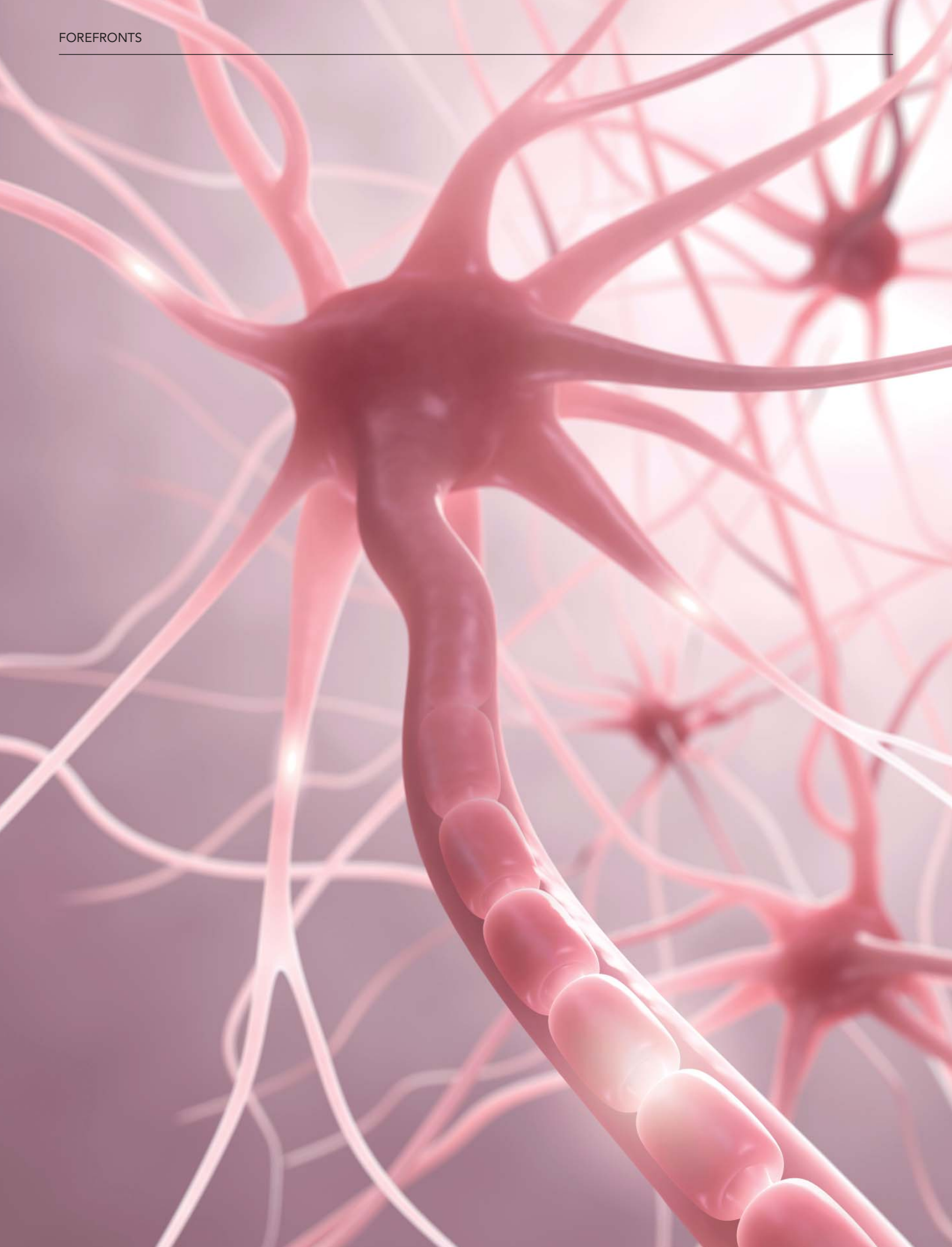
Due to these early scientific findings, some individuals suffering with the herpes virus began an experimental trial taking BHT (butylated hydroxytoluene). Dosage was between 250mg to 3000mg per day with the results presenting a reduction in herpes outbreaks. Some participants virus outbursts remained suppressed for as long as they sustained the daily dose, whilst a number of participants were able to ultimately cease the dosage without a single recurrence.

There is no way of knowing the exact number of patients who have treated their herpes using BHT (butylated hydroxytoluene), the estimates range it is just a fraction of the number of sufferers, ranging from only tens of thousands to hundreds of thousands, meaning there are potentially hundreds of millions of sufferers missing out on this affordable and potentially highly effective treatment.



#### Further Reading

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2. Fowkes, SW 'The BHT book, a practical guide to resolving viral disease' 2008
3. Mann JA, Fowkes SW. *Wipe Out Herpes with BHT*. Manhattan Beach, Calif: MegaHealth Society; 1983.





# ARE PIG'S BRAIN CELLS THE ANSWER TO THOSE WITH PARKINSON'S?

Living Cell Technologies, based in Auckland New Zealand have been developing a procedure that uses cells from the choroid plexus in pigs. The construction of this brain combines growth factors and signalling molecules known to help keep nerve cells healthy.

Patients suffering with Parkinson's disease have had pigs brain cells implanted in their brains, in hope that it will stop the disease progressing.

This method is still in the primary stages of tests and trails. Although, initial results from four patients is looking encouraging, with all showcasing improvements 18 months after the surgery.

Last month, 18 patients completed the operation in a placebo-controlled trail, using the choroid plexus cell implants. The goal is that compounds created by these cells will nourish the remaining dopamine-producing cells in the participant's brains, hopefully slowing further loss.

Ken Taylor of Living Cell Technologies stated "It's putting in a little neurochemical factory to promote new nerve cell growth and repair," as this method has been seen to be successful in the rat version of Parkinson's disease.

The research team documented the average improvement among candidates, this was then measured on a 199-point scale of symptom severity, which gages how well participants can cut up their food and are able to walk. Steven Gill at the University of Bristol stated, that participants improved immediately after their surgery, this could be due to the placebo effect as "nerve cells do not regrow that fast".

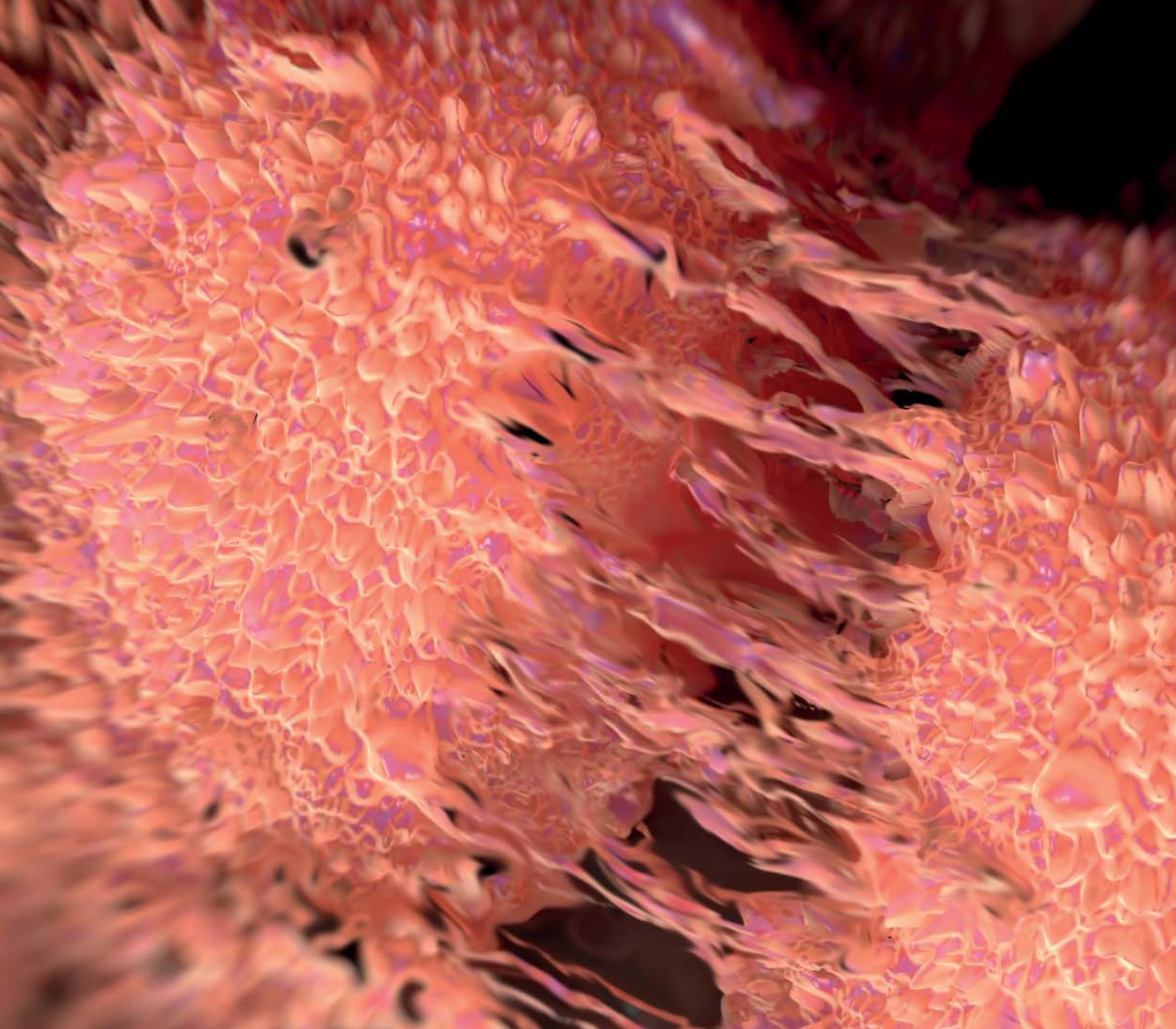
This is an ongoing research trial; participants have had up to 120 capsules put in both sides of their brains. Roger Barker from the University of Cambridge states, "The strategy is a good idea, the question is how competitive that will be compared with other cell therapies."

Additionally, pig's brain cells are being examined as treatments for other disorders caused by the nerve cells dying, in conditions such as Alzheimer's and Huntingdon's, where both diseases cause cognitive and mobility problems. The choroid plexus cells may prove to be helpful in treating other disorders where nerve cell damage has taken place.

## Further Reading

1. Cell therapy for neurodegenerative diseases: <http://www.lctglobal.com/>





# 4MU AND PROSTATE CANCER

# THE DIETARY SUPPLEMENT 4MU (4-METHYLUMBELLIFERONE) IS AN EFFECTIVE CHEMOPREVENTIVE AND THERAPEUTIC AGENT FOR PROSTATE CANCER

*By Jonathan V. Wright, M.D.*

Just in case any of us think the title of this can't be so, it must be nonsense—a dietary supplement that effectively prevents and treats prostate cancer—this was and is the title of an article published in the Journal of the National Cancer Institute (“JNCI”) in 2015. Yes, that’s the Journal of the National Cancer Institute of these United States, supported by taxes paid by you and me, and of course the printing presses (electronic and otherwise) at the Federal Reserve Bank.

So that was 2015....why haven't we seen this dietary supplement for sale in our health food stores, compounding pharmacies, on-line, or at the Tahoma Clinic Dispensary? Why—in 2017—would any of us be forced to go overseas for to buy a safe, natural product which the Journal of the National Cancer Institute told us in 2015 is “an effective chemopreventive and therapeutic agent for prostate cancer”, especially when the same JNCI article tells us that “4-MU is....non-toxic”?

It's likely you already know the answer to that.... so let's review the findings reported in this and other research publications concerning 4-MU (the short name for 4-methylumbelliferone). The researchers worked with mice deliberately bred to develop prostate cancer and prostate cancer

metastases at mouse puberty, which is (for these mice) twenty-eight weeks of age. Technically, these mice are termed “TRAMP” mice and no kidding, the prostate cancers they develop are considered to “closely mirror the pathogenesis of human prostate cancer”.

As expected, these mice all developed prostate cancer and metastases of prostate cancer at twenty-eight weeks. One group received a placebo; the other group were given 4-MU, 450 milligrams per kilogram per day. The researchers reported that both the original prostate cancers and metastases were “abrogated” (research-ese for eliminated) in the 4-MU treated group. The abstract of their publication concluded: “4-MU is an effective, non-toxic, oral chemopreventive and therapeutic agent that targets prostate cancer development, growth and metastasis....”

The opening sentence to the full article said: “Effective control of localized prostate cancer and of its metastatic spread by consumption of a non-toxic dietary supplement can potentially delay/avoid treatment of low-risk localized prostate cancer and halt progression in patients with advanced disease. 4-MU is a dietary supplement consumed in Europe and Asia for improving liver health.”





# 4MU AND PROSTATE CANCER

Prostate cancer isn't the only cancer against which 4-MU has been reported effective. Ovarian cancer appears to be another possibility, as reported by Japanese researchers. Rats were "inoculated" with human ovarian cancer cells injected into their abdominal cavities. One group was then given a "carrier base" only, and the other group got 4-MU with the "carrier base". All of the rats in the carrier base only group died in thirteen days. The rats in the 4-MU group were given this treatment for only fourteen days; then treatment was stopped; the researchers reported that survival time was significantly prolonged ( $p < 0.05$  for the statistically inclined) in the 4-MU group even though 4-MU treatment had been stopped at fourteen days.

Despite discontinuance, 4-MU also was reported to reduce dissemination of ovarian tumors throughout the rats' abdomens, as well as reducing ascites (scientese for edema fluid in the abdomen). The researchers concluded: "...this is the first study to report an inhibitory effect of 4-MU on ovarian cancer."

Breast cancer is affected by 4-MU. Using human breast cancer cells (MDA-MB-231 for the technically inclined) grown

in culture plates, researchers demonstrated that 4-MU "significantly inhibited cell growth and induced apoptosis (cell death)....4-MU treatment also inhibited cell motility as well as cell invasiveness..." The human cancer cells were then injected into the bones of mice. In the group of mice treated with 4-MU, the invasion of the human cancer cells into the bones was significantly inhibited.

4-MU has also been reported to inhibit breast cancer cells in dogs . In the article abstract, the researchers wrote: "We examined the antitumor effect of 4-MU on CF41 mesenchymal-like canine mammary tumor cells....since 4-MU exhibits anti-tumor activity in mesenchymal-like cells, it may be a useful inhibitor of canine mammary tumor invasion and metastasis."

Osteosarcoma is a bone cancer which occurs most frequently in adolescents and young adults. Not infrequently, it metastasizes (often to the lungs) "colonizing" other areas away from its original location. Investigating osteosarcoma in mice, the researchers reported: "4-Methylumbelliferone is a promising therapeutic agent targeting both primary tumors and distant metastasis of osteosarcoma..."

Melanoma (a skin cancer) frequently metastasizes from the skin to elsewhere in the body. Once again working with mice (doing such research in humans isn't ethical) researchers reported : "...4-methylumbelliferone has an inhibitory effect on the liver metastasis of....melanoma cells and therefore shows promise as an anti-metastatic agent."

Another research group wrote about squamous cell cancer of the esophagus, starting their report by writing: "Oesophageal cancer is a highly aggressive tumor entity with at present poor prognosis....the median survival time [after diagnosis] is less than one year." Once again, the "research subjects" were mice, about which the researchers wrote: "Treatment with 4-MU not only was associated with decreased tumor size, but also caused remarkable alterations in tumor morphology" (in English, the tumors in the 4-MU treated mice looked very different than tumors in mice not treated with 4-MU).

Steve Jobs, founder of Apple Computers, and famous Hollywood actor Patrick Swayze died relatively rapidly from pancreatic cancer. "Conventional" treatment rarely cures pancreatic cancer, at best adding one or more months to

a sufferer's lifetime. (More than a century ago, Dr. Joseph Beard of the UK discovered the reason for this, but that's a subject for another time.)

In February 2017, another group of researchers reported about what happened to human pancreatic cancer cells ("MIA PaCa-2" cells for the technically inclined) and the tumors they formed in mice. The researchers reported : "A suspension of tumor cells was injected into the abdomens of mice. Tumor-bearing mice were randomly divided into two groups that were treated with or without 4-MU.....After 72 hours of treatment, 4-MU inhibited cell proliferation... 4-MU also suppressed the amount of [cancer] cell migration and invasion.....the percentage of apoptotic [self-destructed] cancer cells was significantly increased in cells treated with 4-MU....in conclusion, our findings show that 4-MU had anti-cancer properties in a [human] pancreatic cancer cell line and improved survival times in mice with pancreatic tumors. The results of our study suggested that 4-MU may have effectiveness as a novel anticancer agent for the treatment of pancreatic cancer."

## 4-METHYLBELLIFERONE (4-MU) SAFETY

Maybe it's not safe? In addition to the statement in the JNCI article that 4-MU is effective and non-toxic, in 2015 another article was published concerning the safety of this dietary supplement , which is available over-the-counter in some (but not all) European countries where it goes by the names "hymecromone" and "cantabaline". Here are excerpts concerning safety of 4-methylumbelliferone ("4-MU") from this second publication:

"Several clinical trials in humans, including randomized placebo-controlled, have been published on hymecromone and all demonstrated

excellent safety during short-term administration of approved doses.... Taken together, at least 182 patients have been exposed in clinical trials and no serious adverse events from hymecromone were reported. The longest reported duration of administration of hymecromone was a multiple-dose study of oral administration of hymecromone (4-MU) at 1200 milligrams per day (400 mg three times/day) for three months in 20 participants with biliary dyskinesia..."

"The overall safety of hymecromone is further supported by animal data noted in the Italian Medicines Agency "package insert" which notes "acute toxicity has proved to be very low: the LD50 [the amount of a toxic agent sufficient to kill

50 percent of a population of animals] for oral administration is 7593 milligrams per kilogram [2.2 pounds] in mice and 6220 milligrams/kilogram in rats. Protracted oral administration in the range of 800–2400 milligrams/kilogram/day for three months, and in the rat 400–1000 milligrams/kilogram/day for four months has shown excellent tolerability..."

"Taken together, the clinical experience to date suggests hymecromone is a safe and well-tolerated oral medication. The safety of oral hymecromone doses as high as 2400 mg/day and treatment durations as long as 3 months have been demonstrated in humans and can serve as a benchmark for early stage clinical trials exploring new indications."

## AVAILABILITY AND USE OF 4-METHYLU BELLIFERONE

As the last part of this article is being written on the 4th of July 2017, where we are all encouraged to celebrate “freedom”, it’s sad to report that 4-methylumbelliferone, reported by researchers in the Journal of the National Cancer Institute to be “an effective, non-toxic oral chemopreventive and therapeutic agent” against prostate cancer is not freely available here in these United States. (George Washington, Thomas Jefferson, James Madison and all the other signers of the Declaration of Independence would be both sad and aghast!)

However, 4-MU (labelled with a myriad of trade-names) can be purchased over-the-counter in Italy, Turkey, Greece, Germany, the United Kingdom and Russia. In Austria and Czechoslovakia, a prescription is required. It can also be purchased on-line as “4-MU-Pro™” at [www.antiaging-systems.com](http://www.antiaging-systems.com)

Unfortunately, there are as yet no double-blind, placebo controlled clinical trials in humans using 4-MU against prostate cancer. We can’t be sure there ever will be; it’s doubtful that any man diagnosed with prostate cancer would volunteer to be in the placebo group! So what do you do if you’re a man with prostate cancer? Of course, discuss this with a physician skilled and knowledgeable in natural medicine.

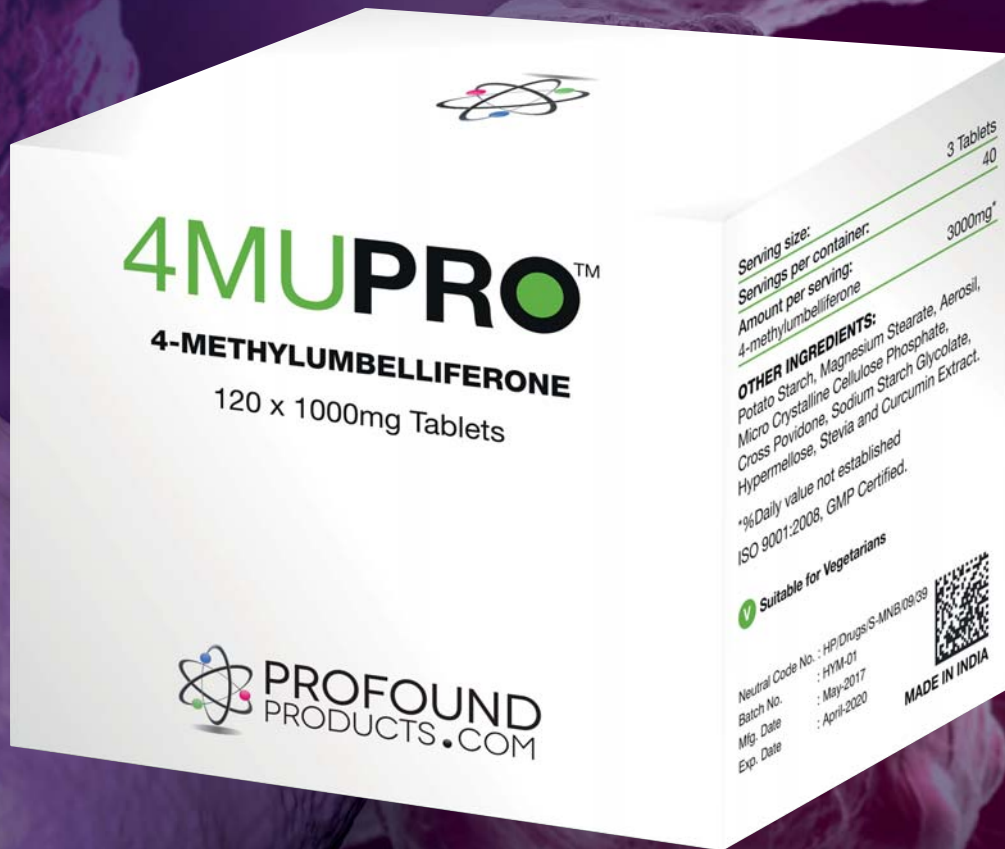
What about dosages and for how long? Again, discuss with a physician, but given the safety and duration-of-treatment reports noted above in animals (“7593 milligrams per kilogram in mice and 6220 milligrams per kilogram in rats”<sup>9</sup>, but “only” 450 milligrams per kilogram per day given for 28 weeks in the successful JNCI prostate cancer study<sup>1</sup>) and humans (“the safety of oral hymecromone [4-MU] doses as high as 2400 milligrams per day and treatment durations as long as 3 months have been demonstrated in humans”<sup>9</sup>).

If we use the JNCI “mouse dosages” of 450 milligrams per kilogram (2.2 pounds) for a 175 pound (79.5 kilogram) man, that’s almost 36 grams of 4-MU per day (likely split into three or four daily dosages) taken for 28 weeks, roughly four months. Once again, that’s a “heck of a lot” of 4-MU for quite a while. Discuss that with your physician skilled and knowledgeable in natural medicine, too!

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10. <https://biomonde.org/contact/contacts.htm>

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# THE BENEFITS OF NITRIC OXIDE



# SUPPORT YOUR HEART, SEX LIFE AND OVERALL HEALTH WITH NITRIC-PRO™

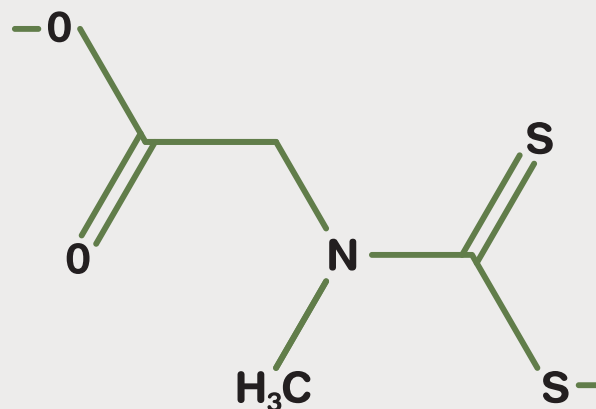
Protecting against cardiovascular disease and enhancing one's sex life are two health-related goals high on almost everyone's list. An overall strategy to reaching these goals, while supporting health in general, includes promoting optimal levels of an endogenously produced molecule crucial to our physiology; deficiencies have been linked to high blood pressure, angina, heart attack, erectile dysfunction (ED), diabetes, even aging.

This structurally simple, though multifaceted molecule, is nitric oxide, a potent vasodilator that plays a range of key roles in the body, including regulating blood flow and blood pressure, reducing cardiovascular risk factors, mediating immune defense and stem cell release, enhancing sexual function, and even reducing waist size. Fortunately, research shows that it's possible to boost circulating

levels of this essential substance by supplementing with an amino acid precursor, the major ingredient of a cutting-edge dietary supplement called Nitric-Pro.

## NITRIC OXIDE IS A POTENT VASODILATOR CRUCIAL TO VASCULAR FUNCTION

Nitric oxide is, by chemical definition, a free radical that exerts multiple physiological effects for seconds before undergoing degradation in the bloodstream. It functions as a cellular signaling molecule; i.e., it transmits information between cells to elicit a physiologic response, and it's one of the few gaseous signaling molecules known. Because of its biological significance, nitric oxide has been extensively studied, yielding over 100,000 scientific papers in the fields of chemistry, molecular biology, gene therapy, and physiology.



**Figure 1:**

The chemical molecule of Nitric-Oxide.

# THE BENEFITS OF NITRIC OXIDE

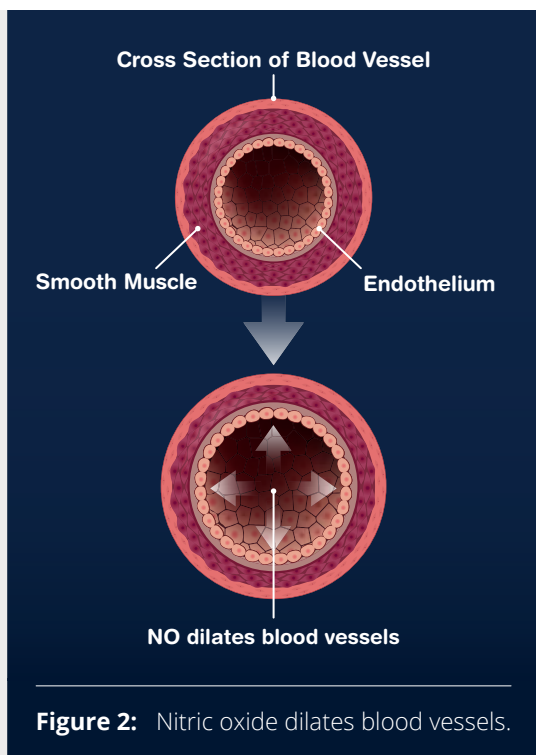
Nitric oxide plays a major role as the body's most powerful vasodilator, signaling blood vessels to relax and expand when necessary to facilitate blood flow and maintain normal blood pressure. More than just tubes transporting blood, arteries are active, dynamic muscular structures that must expand and contract to support the body's changing needs. For example, arteries that supply the heart can enlarge in diameter up to 50 percent during exercise in the presence of an adequate nitric oxide supply. The manufacturing site of nitric oxide is the endothelium, a thin layer of cells that line the interior of blood vessels.

Before its chemical structure was identified, the substance we now know as nitric oxide was originally named "endothelium-derived relaxing factor," denoting its role in regulating blood vessel elasticity.

Since Nitric oxide has a transient half-life, a continual supply is required; any disruption or impairment in the manufacture of nitric oxide can lead to endothelial dysfunction, the inability of arteries and blood vessels to dilate in response to the body's need for increased blood flow. This can precipitate a cascade of events including inflammation, clotting, plaque formation, constricted blood

vessels, and the development of diseases such as cardiovascular disease (including angina, heart attack, atherosclerosis and stroke), diabetes, and ED. In fact, endothelial dysfunction is the common mechanism that leads to both ED and heart disease; men with one condition will often exhibit the other, and both are due to impairment in nitric oxide production that lowers the capacity to dilate arteries and ensure blood flow to vital parts of the body. A major reason for this impairment is a deficit of a precursor for nitric oxide synthesis, as we'll see next.

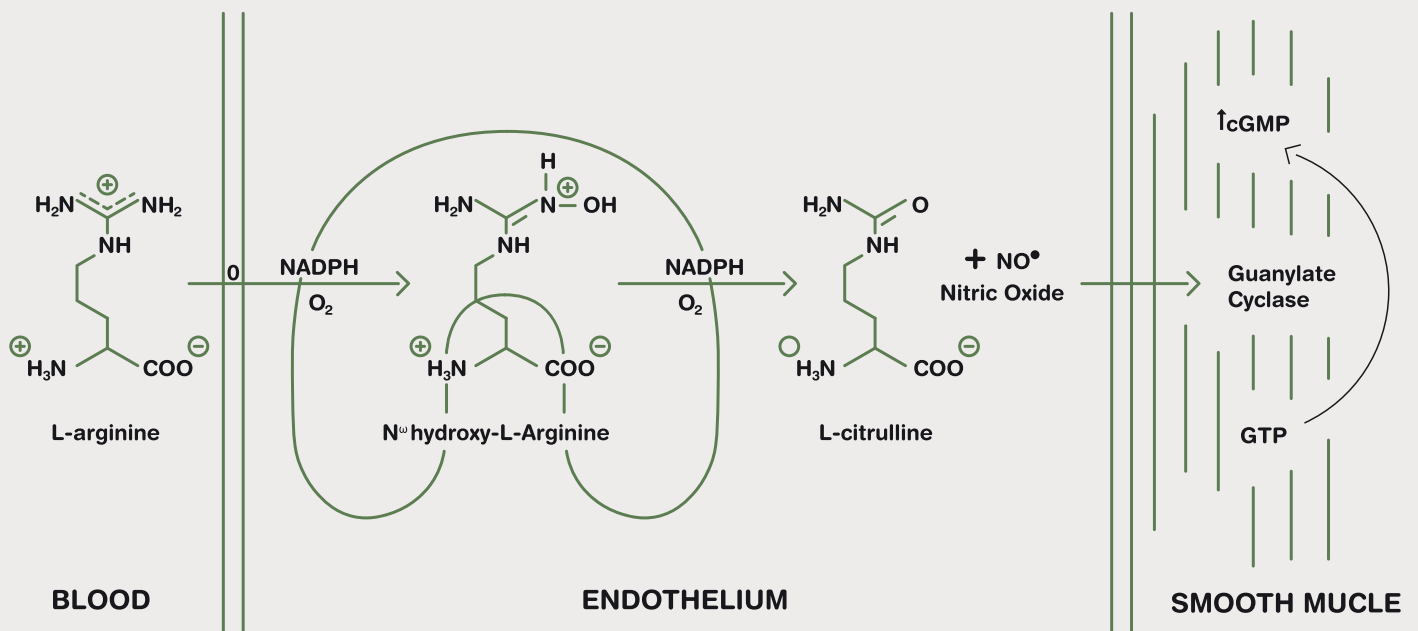
*[Note: in this discussion, "ED" is used as the abbreviation for erectile dysfunction, not to be confused with endothelial dysfunction.]*



**Figure 2:** Nitric oxide dilates blood vessels.

## AMINO ACID L-ARGININE, A CRUCIAL PRECURSOR FOR NITRIC OXIDE SYNTHESIS

Drugs such as nitroglycerine, used to treat angina and Viagra®, prescribed for ED, act on the nitric oxide pathway, but they do not actually undo the underlying snag in the metabolic pathway that manufactures nitric oxide. An alternate approach that corrects the root problem in endothelial dysfunction and resulting ED, heart disease and other disorders, is to restore nitric oxide bioavailability by supplementation with the amino acid L-arginine, the primary ingredient in Nitric-Pro, and the physiological starting material for nitric oxide synthesis. In the body, endothelial cells release enzymes that catalyze the manufacture of nitric oxide from L-arginine and oxygen. As mentioned, this metabolic pathway relies on adequate stores of L-arginine; deficiencies set the stage for alterations in blood vessels and resulting disorders. L-arginine has been found to be a safe and effective first-line therapy for many health conditions, particularly vascular diseases, as shown in several clinical studies which we'll now examine.



**Figure 3:** Nitric oxide synthesis.

## CLINICAL STUDIES ON L-ARGININE: TREATING ED AND IMPROVING CARDIOVASCULAR RISK FACTORS

A 2017 study proved that men with arteriogenic ED (ED resulting from the inability of arteries and blood vessels to dilate) had significantly lower levels of serum L-arginine and L-citrulline, (an amino acid also contained in Nitric-Pro) than controls or patients whose ED resulted from another cause. The authors concluded that low serum levels of these amino acids reduced circulating concentrations of nitric oxide and increased ED risk. <sup>(1)</sup> An earlier double-blind placebo-controlled study evaluated the effect of “high-dose” L-arginine supplementation (5 g/day – the approximate L-arginine dose in Nitric-Pro) for 6 weeks in 50 men with ED. After 6 weeks, one third of the men in the treatment group reported significant improvements in their sexual function which corresponded to a doubling of levels of urinary nitric oxide metabolites, (resulting from increased nitric oxide production). These results indicate that L-arginine is effective in certain cases of ED, namely those that result from decreased nitric oxide synthesis (i.e., arteriogenic ED). <sup>(2)</sup> (ED can stem from a variety of causes besides vascular problems,

which is why more men in this study did not experience an improvement in symptoms, even though L-arginine supplementation likely enhanced their overall health.) In addition to alleviating symptoms of ED in men, raising nitric oxide levels may enhance sexual function in women too, as shown in a study in which 108 women, aged 22-73, who reported a lack of sexual interest, received a supplement containing L-arginine and other ingredients, or placebo. After 4 weeks, women receiving the supplement reported improvements in different aspects of sexual health. <sup>(3)</sup>

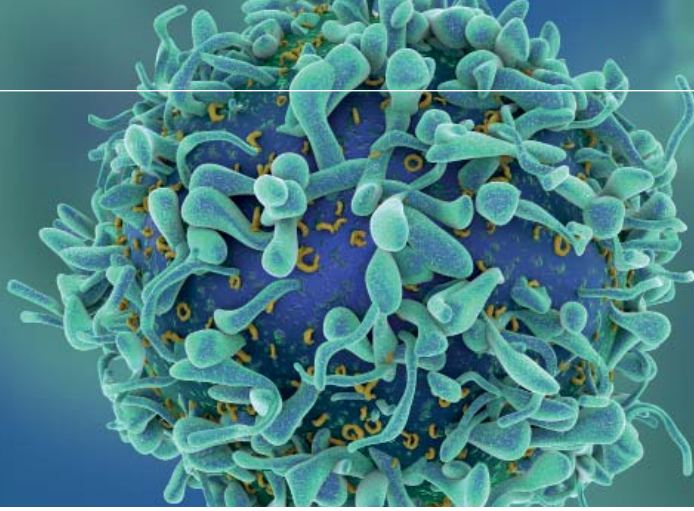
Positive outcomes in patients with multiple cardiovascular risk factors have also been obtained using L-arginine as primary therapy. In one trial, 6 months of L-arginine treatment led to improvements in arterial flexibility (as measured by a test known as the “large artery elasticity index”) and a reduction in systolic blood pressure, leading researchers to conclude that “long-term L-arginine supplementation has beneficial vascular effects in pathologic disease states associated with endothelial dysfunction.” <sup>(4)</sup> A couple of studies looked at L-arginine and its effect on cardiovascular risk factors in obese patients. (Obesity is a risk factor for fatal heart attacks and heart disease, as well as other conditions such as diabetes.)



In one trial, 90 obese patients received either L-arginine (3 or 6 g, 3 times daily) or placebo for 8 weeks. After 8 weeks, the treatment group showed significant decreases in not just blood pressure, but also fasting blood sugar, glycated hemoglobin (HbA1c), LDL cholesterol, triglycerides and total cholesterol, with a significant increase in HDL (“good”) cholesterol. And, as if these results weren’t impressive enough, the patients also lost weight and inches, as evidenced by decreases in body mass index and waist circumference – a remarkable outcome! <sup>(5)</sup> This weight-reducing potential of L-arginine was confirmed in another trial on women with central (abdominal) obesity administered L-arginine at 5 g/day, combined with selenium and a low calorie diet <sup>(6)</sup>. These studies establish L-arginine as a novel and effective treatment for weight loss and lowering cardiovascular risk factors (blood pressure, blood sugar, HbA1c, and cholesterol) in obese patients, and potentially in diabetics and patients with metabolic syndrome. (Metabolic syndrome is characterized by a group of risk factors including high blood pressure, high blood sugar, unhealthy levels, and abdominal fat. The syndrome is increasingly common and raises the risk of heart disease and diabetes.)

Amazingly, L-arginine supplementation can reduce certain cardiovascular risk factors even in young healthy adults. In a double-blind placebo controlled trial, 52 men, aged 21 (on average), received either L-arginine (2 g daily) or placebo for 45 days. At the end of the study, those in the treatment group showed significant reductions in fasting blood sugar, triglycerides, and cholesterol, though systolic and diastolic blood pressure remained unchanged, <sup>(7)</sup> probably because these numbers were already in the optimal range in these young, healthy subjects; as we saw earlier, L-arginine lowers blood pressure when it is elevated, in cases of obesity and hypertension.

So, to recap what we’ve covered so far: boosting nitric oxide production by supplementing with precursor L-arginine has the capacity to normalize blood flow and blood vessel elasticity, lower cardiovascular risk factors, shave inches and promote weight loss, and enhance sexual function in both men and women. But keep in mind – it’s not just those with obesity, diabetes, heart disease or ED who suffer the effects of a dwindling nitric oxide supply; the aging process itself is associated with altered endothelial function and impaired nitric oxide synthesis, resulting in continual stiffening and blockage of arteries, a leading health risk in the West.



## NITRIC OXIDE ENHANCES IMMUNE RESPONSE AND STIMULATES STEM CELL RELEASE

Besides its dramatic effect in promoting vascular health and normalizing metabolic parameters, nitric oxide also mediates immune response and stem cell release.

A noteworthy meta-analysis evaluating 321 patients enrolled in 11 trials found that those supplemented with L-arginine showed significantly greater CD4+ T-cell proliferation and lower rates of infection than controls. <sup>(8)</sup> (CD4+T cells are a type of white blood cell crucial to achieving a regulated and effective immune response to pathogens.) And a fascinating study in the journal *Cell* showed that cellular concentrations of L-arginine directly impact the integrity and survival capacity of T cells that are crucial for anti-tumor activity, <sup>(9)</sup> which means increased protection from cancer. The positive effects obtained in both studies, at least in part, may have resulted from enhanced cell signaling capacity in response to L-arginine-induced increases in nitric oxide production.

In a ground-breaking study at the University of Pennsylvania, researchers using a technique called hyperbaric oxygen therapy (HBOT), discovered that nitric oxide stimulates the release of stem cells from bone marrow. Stem cells are undifferentiated “primary” cells from which all other cell types in the body descend. These undeveloped cells have the ability, when needed, to proliferate and generate a variety of specialized cell types, such as muscle, blood, or nerve cells, with the overall function of continuously maintaining, repairing, and regenerating the body’s tissues and organs. Ongoing tissue and organ repair is a critical function and relies on effective activation, differentiation, and mobilization of stem cells, particularly in bone marrow. Hyperbaric oxygen therapy (HBOT) involves exposing the body to 100

percent oxygen at a level higher than atmospheric pressure, either in a specialized chamber or through use of a gas mask, for the purpose of promoting the healing of wounds, injuries, infections and burns, as well as other medical applications.

It appears that the increased healing capacity resulting from this technique is not due to enhanced oxygenation of tissues, as once thought, but rather to a boost in nitric oxide bioavailability which stimulates the release of stem cells from bone marrow, as determined by the University of Pennsylvania study.

In the study, subjects undergoing HBOT exhibited a doubling of CD34+ cells in the bloodstream after only one treatment, and a dramatic eight-fold increase after 20 treatments. (Bone marrow CD34+ cells contain stem and progenitor cells and can differentiate into all the various blood cell types.) In mice, HBOT also increased circulating stem cells, as expected, but in addition, researchers made a fascinating discovery: HBOT raised bone marrow nitric oxide concentration. In mice lacking genes for endothelial nitric oxide synthase (an enzyme crucial to the production of nitric oxide), stem cell release from bone marrow was hindered, which was also the case in mice pre-treated with a nitric oxide synthase inhibitor. These last findings indicate that nitric oxide was the factor responsible for the mobilization of stem cells from bone marrow during exposure to hyperbaric oxygen. <sup>(10)</sup>

These results have huge implications in the field of regenerative medicine, using HBOT as a means to increase circulating stem cells for the purpose of repairing and regenerating damaged tissues and organs. Although no studies to date have been published on the direct effect of L-arginine supplementation on stem cell release, the likelihood is that the amino acid, through its stimulation of the nitric oxide pathway, also has the capacity to induce stem cell proliferation.

## NITRIC-PRO – A TARGETED AND COMPREHENSIVE NITRIC OXIDE ENHANCER

If you're excited about reaping all of the impressive health benefits of increased levels of nitric oxide circulating in your bloodstream, an ideal product to include in your regimen is Nitric-Pro, which contains a sizable 4.75 g L-arginine per sachet, in the range of doses used in the clinical studies (i.e., approximately 2 to 6 g). Nitric-Pro is formulated as a convenient powder, pre-measured in individual sachets for precise dosing, which can be mixed with fruit juice or water. This comprehensive formula also contains a combination of other proven ingredients to further support vascular and overall health including:

- **L-citrulline:** an amino acid converted to L-arginine in the body.
- **B-complex vitamins:** necessary to the pathways involved in energy production and cell metabolism; in particular, Vitamins B12, B6, and folate maintain healthy homocysteine levels which promote cardiovascular health.
- **Vitamin D:** a fat-soluble prohormone crucial to overall health, including immune function, reduction of inflammation, bone health, modulation of cell growth, and cardiovascular protection.
- **Vitamin C:** a potent antioxidant which has been shown to protect against many aspects of cardiovascular disease, including endothelial dysfunction, altered lipid profiles, and plaque build-up. Vitamin C also stimulates the production of collagen, a major connective tissue protein that imparts blood vessels with strength and flexibility. Vitamin C regenerates other antioxidants in the body, including vitamin E, and also plays an important role in immune function.
- **Vitamin E:** another powerful antioxidant that may reduce risk factors for cardiovascular disease. Vitamin E is also involved in immune function, cell signaling, regulation of gene expression, and other metabolic processes.
- **Magnesium:** a cofactor in more than 300 enzyme systems that regulate diverse processes, including protein synthesis, muscle and nerve function, blood glucose control, and blood pressure regulation. Magnesium helps relax the smooth muscle layer of the endothelium and promotes normal heart

rhythm and blood pressure. Magnesium is also a co-factor in the synthesis of nitric oxide.

- **Chromium:** an essential trace element that enhances the action of insulin and improves blood sugar control in prediabetes and diabetes.
- **Selenium:** another essential trace element and a constituent of compounds known as selenoproteins that support thyroid hormone metabolism, DNA synthesis, heart and brain health, and protect against oxidative damage and infection.
- **CoQ10:** coenzyme Q10 is a well-known supplement that supports cardiovascular health and has a significant role in the energy production of the mitochondria.

## SUMMING UP

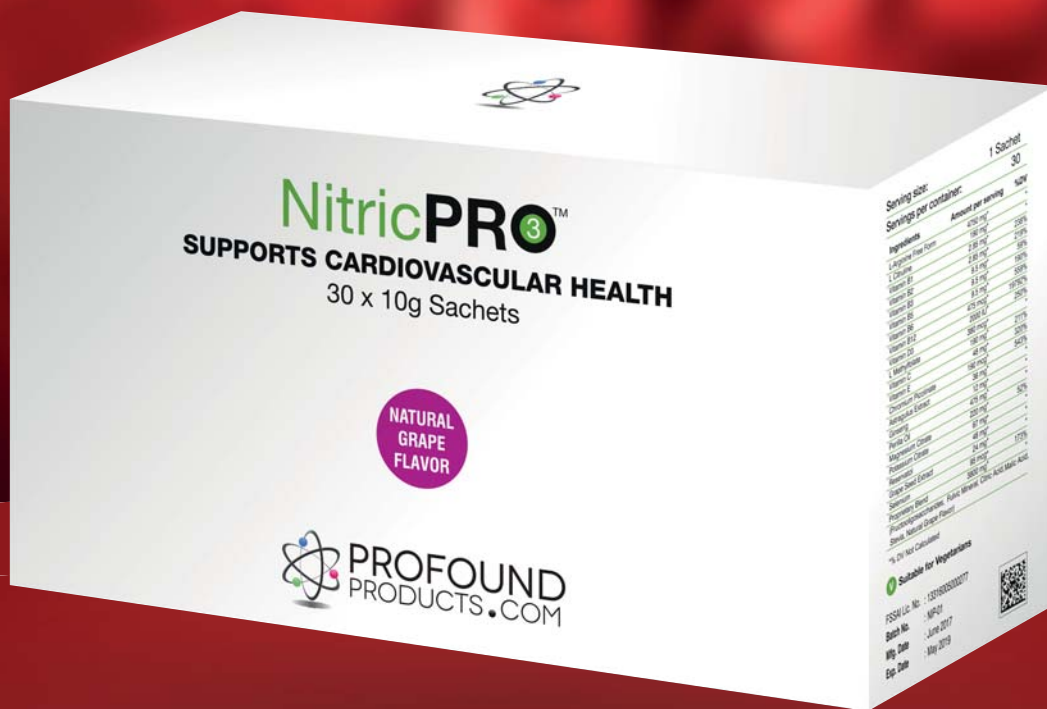
We've just examined the many roles that nitric oxide plays in the body, from vasodilator promoting arterial health and blood flow to stimulator of stem cell release. It's amazing that such a simple molecule, a free radical produced as a gas, modulates such a diverse array of physiological functions. Also amazing is the fact that its precursor, an amino acid commercially available as a dietary supplement, can be used as a first-line therapy to dramatically improve cardiovascular risk factors, alleviate symptoms of ED, induce weight loss, and boost immune function, as shown in clinical studies.

Supplementing with Nitric-Pro is an ideal and convenient way to ensure that you produce and maintain optimal nitric oxide levels; your heart, and the rest of your body, will thank you.

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# WASH YOUR MOUTH OUT!



# 8 THINGS THAT YOU SHOULD KNOW ABOUT YOUR MOUTH

## 1. BACTERIA GROWTH

A once and for all cure to get rid of bad bacteria doesn't exist, they will always be present and your priority should be to protect your mouth from invasion!

The bacteria streptococci and staphylococci are commonly known and present in most serious diseases and conditions. Just because you don't see the bacteria, doesn't mean to say you don't have them. Having bacteria in your mouth is normal but do not ignore their existence. The consequences could be devastating. Managing the bacteria community in your mouth can be done by daily brushing, flossing your teeth and using a mouth wash. Sometimes even this is not enough, so regular visits to the dentist is very important.

It isn't just your teeth and gums that you should be concerned about when it comes to bacteria. Complications from bacteria in your mouth could be connected to life threatening diseases. Always seek advice if you have concerns. It's not just brushing your teeth and using a mouth wash that is important, it's what you put in your mouth too. Bad management of oral bacteria can lead to oral infections and viruses. The Dental Clinics of North America produced a very insightful article about oral viral infections caused by bacteria. It details the commonly seen viral infections in the oral cavity with associated systemic manifestations. It encompasses viral infections discussing clinical features, histopathology, diagnosis, treatment and prevention.<sup>(1)</sup>

# WASH YOUR MOUTH OUT!

## 2. ORAL INFECTIONS

There are many types of bacteria related oral infections:

- **Dental caries** or **cavities** caused by a build-up of bacteria are the leading cause of tooth loss
- **Gingivitis** is when bacteria settle in the gum's crevices and the bacteria turn into toxins. The gums react by becoming inflamed and swollen
- **Gingivitis** that spreads below the gum line and effects the bones and tissues can result in periodontal disease. The teeth can loosen and is another common cause of tooth loss in adults
- **Hand, Foot and Mouth Disease** is most likely to develop in children and the virus Coxsackie A16 is usually responsible. Symptoms start with a fever, slightly painful blisters can appear inside the cheeks and the tongue
- **Herpangina** is related to hand, foot and mouth disease. Most frequently infects children aged 3-10. Symptoms start with a sore throat and difficulty swallowing. Tiny blisters develop at the back of the mouth which form large ulcers and eventually they rupture
- **Thrush** is an overgrowth of the naturally occurring bacteria 'Candida albicans'. It requires medical treatments such as antibiotics. Symptoms are a white curd-like plaque which can appear on the tongue, inner cheeks, palate and back of the mouth
- **Canker sores** are lesions that start on the gums and other mouth tissues. Medically known as aphthous ulcers
- **Oral Herpes** is caused by the herpes simplex virus. Symptoms can be much like flu, blisters and ulcers may be present on the tongue



The American Society of Clinical Oncology (ASCO) produced one of the first large studies to explore the possible impact of HPV vaccination on oral HPV infections; researchers found it may confer a high degree of protection. The study of young adults in the United States showed that the prevalence of high-risk HPV infection was 88% lower among those who reported getting at least one vaccine dose than among those who were not vaccinated. <sup>(2)</sup>



### 3. GUM DISEASE

Gum disease is otherwise known as Gingivitis or Periodontal disease and it is a common dental problem. Nearly 3 out of 4 people over the age of 35 have it to some degree. It is the common reason for tooth loss in adults. It can be identified by swelling, inflammation or infection of the gums and other tissue that holds your teeth in place.

Gingivitis is inflamed gum tissue around the teeth, caused by dental plaque which is responsible for cavities. Healthy gums are generally coral-pink in color and firmly attached to the teeth. The first sign of gingivitis is bleeding gums during brushing and the gums may be tender to touch. This is a reversible condition that can be improved by good dental hygiene. Periodontal disease is a more severe form of the condition. This is where the bone and other foundations that hold the teeth in place are stripping away.

The University of Louisville School of Dentistry researchers have found a

bacterial species responsible for gum disease, *Porphyromonas gingivalis*, is present in 61 percent of patients with esophageal squamous cell carcinoma (ESCC). The findings, published recently in *Infectious Agents and Cancer*, only detected *P. gingivalis* in 12 percent of tissues adjacent to the cancerous cells, while this organism was undetected in normal esophageal tissue.

“These findings provide the first direct evidence that *P. gingivalis* infection could be a novel risk factor for ESCC, and may also serve as a prognostic biomarker for this type of cancer,” said Huizhi Wang, M.D., Ph.D., assistant professor of oral immunology and infectious diseases at the UofL School of Dentistry. “These data, if confirmed, indicate that eradication of a common oral pathogen may contribute to a reduction in the significant number of people suffering with ESCC.”

This is the first study to evaluate the association of bFGF and TGF- $\beta$  on human periodontal ligament cells. Based on previous reports, two concentrations of these growth factors were used

in order to assess a possible dose-response effect. A dose-dependent effect on cell proliferation was expected for bFGF, whereas a time-dependent effect was anticipated for TGF- $\beta$  stimulation. Surprisingly, neither of the concentrations of bFGF stimulated cell proliferation. Since bFGF had other biological effects on these cells we assume the hPDL fibroblasts express the adequate receptors.

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#### Things that will increase the risk of gum disease are:

- Smoking – this greatly increase the risk of developing problems and also increases the severity and rate of the tissue destruction
  - Poorly controlled diabetes
  - Pregnancy
  - Certain medications
  - Age – problems increase as you age
-

## 4. BAD BREATH

Halitosis is otherwise known as bad breath. It is when a bad odour comes from the mouth. There are a variety of causes, eating certain foods or bad dental hygiene. Halitosis is normally caused by bacteria. Bacteria builds up, forming plaque on the teeth, on the gums and also on the tongue. Bacteria grow well in a warm and wet oral environment, when levels are high, smelly odours are released. Our breath odour varies throughout the day, after drinks or food or morning breath.

### These are some of the factors that can cause bad breath:

- Bad oral hygiene
- Gaps between the teeth that fill up with plaque
- Gum disease
- Smoking
- Strong flavoured foods such as garlic or onions
- Coffee
- Alcohol
- Medications that cause dry mouth
- Infections in the respiratory tract such as infections in the lungs or throat
- Illnesses from other parts of the body, kidney failure, diabetes, liver disease or lung disease
- Eating disorders

A study was conducted by Francisco Wilker Mustafa Gomes Muniz, Stephanie Anagnostopoulos Friedrich, Carina Folgearini Silveira and Cassiano Kuchenbecker Rösing for the Journal of Breath Research. They aimed to analyze the impact of chewing gum on halitosis parameters. Three databases were searched with the following focused question: 'Can chewing gum additionally

reduce halitosis parameters, such as organoleptic scores and volatile sulfur compounds (VSC), when compared to a control treatment? Chewing gum containing sucrose was able to reduce the VSC levels, in comparison to xylitol and zinc citrate chewing gum, but only for 5 min. It was concluded that chewing gums containing probiotics Lactobacillus, zinc acetate and magnolia bark extract, eucalyptus-extract, and AITC with zinc lactate may be suitable for halitosis management. (4)

## 5. YOUR MOUTH AND TONGUE

Whatever mouth and tongue discomfort you experience whether it's from dental problems or mouth ulcers it is important that you deal with it straight away. A build-up of bacteria can cause abscesses or be an indication of something even more serious. One condition that is a cause for concern is burning mouth syndrome. The symptoms may last for months or years! Or in some cases symptoms may suddenly disappear on their own, or become less frequent. Some sensations can be alleviated during eating or drinking. The condition doesn't normally show physical changes to your tongue or mouth.

### Symptoms of burning mouth syndrome:

- A sensation of a dry mouth with increased thirst
- A burning or scalded sensation that has an effect the tongue the lips, gums, palate, throat or whole mouth. It depends on the severity
- Taste changes such as a metallic or bitter taste
- A loss of taste altogether

### Causes of burning mouth syndrome:

- When no clinical abnormalities are identified the condition is called idiopathic burning mouth syndrome. In this instance the condition could just be nerve related
- Sometimes the condition can develop from an underlying medical condition
- Various medications
- Fungal infection – oral thrush or lichen planus
- Nutritional deficiencies
- Dentures
- Allergies or reactions
- Reflux
- Oral bad habits
- Endocrine disorders
- Excessive tooth brushing or abrasive toothpastes
- Anxiety, depression or stress
- Abrasive toothpastes, overusing mouthwashes or having too many acidic drinks

The main symptom of burning mouth syndrome (BMS) is pain in the mouth that is burning, scalding, or tingling. Or, the pain may be a feeling of numbness. Other symptoms include dry mouth or altered taste in the mouth. BMS is a painful condition. Usually, the tongue is affected, but the pain may also be in the lips or roof of the mouth, or throughout the mouth. BMS pain can last for months or years. Some people feel constant pain every day. For others, pain increases throughout the day. For many people, the pain is reduced when eating or drinking. The National Institute of Dental and Craniofacial Research explain that the diagnosis of BMS is difficult to do. Multiple tests would have to be done – blood, oral swab, allergy and salivary flow tests. (5)

## 6. DAMAGED ENAMEL AND CAVITIES

Tooth decay is also known as dental caries or cavities. It is the destruction of teeth caused by plaque acids. There are three main causes of tooth decay, bad bacteria, food and drinks. Bacteria are found in dental plaque, plaque is the thin white film that is constantly forming on your teeth after you brush. The bacteria produces harmful acid which erodes the tooth, this can lead to cavities. Sugars and carbohydrates in food are the main dangers to the teeth, bacteria and plaque loves them! They feed on the sugars and carbohydrates and turn them into plaque acids. This attack can last for at least an hour until saliva helps to neutralize the acid. The frequency of taking on those types of foods and drinks is more harmful than the amount.

Typical foods and liquids would be: Candy, chocolate, fizzy drinks, juice, biscuits, ice cream, jam, jelly, fruits, potato chips, cereals, pretzels and yoghurts. There are a lot of hidden sugars in foods too.

Decay is a gradual process. Decay occurs in different areas of the tooth. Grooves, pits or fissures, the surface between teeth, near the gum line, around fillings, crowns, partial dentures and bridgework

Acid erodes the tooth enamel, a small white spot may be seen and at this point it is still possible to reverse the damage. But, if left untreated, the damage will continue through to the softer part of the tooth called dentine, this is when the cavity is formed. The decay will eventually reach the dental pulp where the nerves are and potentially a root canal or tooth extraction could be required.

### **Tooth decay symptoms:**

- Sensitivity to cold or hot food or drinks
- Toothache
- Bad breath
- Throbbing in the mouth
- Discomfort when eating

Tooth decay is a common disorder, second only to the common cold. It usually occurs in children and young adults, but it can affect anyone. (6)



## 7. ENAMEL REMINERALIZATION

Our saliva has healing properties. Naturally occurring proteins, enzymes and cellular compounds in saliva can fight some infections and slow down tissue loss as infection penetrate open or broken layers of skin. Those compounds help our teeth, they work to harden or ‘remineralize’ the enamel on the teeth.

Teeth are strong on the exterior because of tight mineral bonds of enamel. It’s one of the strongest substances in the human body. Saliva is watery but has properties strong enough to help keep the teeth strong. It keeps calcium and phosphates flowing around the mouth so teeth can remineralize. If it wasn’t for saliva and its healing properties, teeth would lose their hard-coated enamel covering; bad bacteria and acids would penetrate the enamel to the dentin. Teeth would become soft and chewing would be difficult. Soft teeth would be no match for food that needs to be broken down before getting digested in the stomach and the very nutrients needed to keep the body and the teeth healthy would be hard to absorb.

In a regular or normal mouth, teeth will stay tough and protected but sometimes bacteria and acids win the battle and overtake the saliva balance, leading to plaque, tooth decay and cavities. Poor hygiene, a high-sugar or acidic diet, and tooth damage increase demineralization, as can illness and medication, so knowing how remineralization works can help you keep your enamel and teeth strong.

A recent study from Scientific Reports - In vivo remineralization of dentin using an agarose hydrogel biomimetic mineralization system reported the use of an agarose hydrogel biomimetic mineralization system loaded with calcium and phosphate to induce dentin remineralization and formation of a oriented densely parallel packed HA layer on dentin surface in a rabbit model in vivo. The results indicated a potential clinical use for repairing dentin-related diseases, such as erosion, wear, and dentin hypersensitivity. (7)

## 8. SHRINKING GUMS

Shrinking gums or ‘receding gums’ refer to exposure of the roots of your teeth. Roots are normally coated in healthy tissue called gingiva. Shrinking gums are a common problem in adults who are over 40, although, in some cases it can start in teenage years. Symptoms develop over time, teeth appear longer, teeth and gums become sensitive and a bump or series of bumps can be felt along your gum line. If the gingival tissue appears swollen, it could result in bleeding gums or bad breath. The gaps between crowns or bridges may become wider too and the dark line of the crown will be revealed.

### The cause:

- Poor oral hygiene, smoking, medical conditions, trauma to the gums
- Over-aggressive brushing – this action can wear down enamel
- Crowding – this can lead to one or more teeth lying out of line of the arch
- Grinding – the action of grinding or clenching is another possible cause
- Anug – a nasty infection that is more common in younger people
- Periodontal disease - a progression from gingivitis
- Genetic predisposition – some people have thin or insufficient gingival tissue and some develop high frenum. These are little tags that connect your gums to the cheeks/lips
- Dental treatments – ill-fitting crowns or dentures

There are easy steps that you can take to reduce the risk of oral bacterial infections. Good oral hygiene, flossing, mouthwash, dental check-ups and dental scaling. Seek advice about correct brushing techniques and using an appropriate toothbrush that suits your mouth and gums. Ill-fitting dental work should be fixed and sensitive teeth should be dealt with. With more serious conditions there are further treatments that you can have:

- Saliva replacement products
- Specific oral rinses or lidocaine
- Capsaicin, a pain reliever that comes from chili peppers
- An anticonvulsant medication called clonazepam (Klonopin)
- Certain antidepressants
- Medications that block nerve pain
- Cognitive behavioural therapy

It is reported that one hundred and fourteen million Americans don't have insurance coverage for their teeth!

### The American debate on oral health

According to an article in the New York Times, Americans are debating medical coverage and the problem of their teeth has remained almost entirely unaddressed. About 114 million Americans don't have insurance coverage for their teeth. That is more than the number of people who didn't have health insurance before the Affordable Care Act.

“Oral health is a neglected issue nationally,” said Julia Paradise, an associate director of the program on Medicaid and the Uninsured at the Kaiser Family Foundation. “This is a big problem. The mouth and the head – mental health and dental health – somehow remain outside of what people think of as general health.” (8)

A healthy mouth is about good dental hygiene, regular dental check-ups and a healthy diet.

Wash your mouth out because prevention is better than cure! OralTide-Pro is a mouthwash containing DPR (Dental Bond Peptide) and AGDP (Anti-gingival Degenerate Peptide).

Dental Bond Peptide is refined and obtained from mass production of enriched fermented peptides using patented hydrolysis technology to yield a high concentration of precise DRP fragments and then purified via ultrafiltration membrane technology.

Anti-gingival peptide is refined and obtained from mass production of enriched fermented peptides using patented hydrolysis technology to yield high concentration of precise AGDP fragments and then purified via ultrafiltration membrane technology. AGDP can increase synthesis of type 1 collagen and extracellular matrix repairs the fracture and breakage of collagen organization. It promotes growth of shrinking gums, accelerates mouth tongue wound healing, and relieves symptoms of inflammation of the gums by activating gingival connective tissue and periodontal ligament fibroblasts.

### The 4 guarantees of OralTide-Pro:

- 1. No bactericide and no alcohol.**  
Bactericide may be carcinogenic (a substance that promotes formation of cancer) and excessive alcohol can thin the oral mucosa which may lead to being carcinogenic.
- 2. No fluoride.**  
Excessive fluoride may cause fluorosis on the teeth (a mottled effect), nerve injury of the brain, spinal cord or sciatic nerve.
- 3. No potassium nitrate.**  
Potassium nitrate has a narcotic effect which will reduce the sensitivity of the tooth nerve potentially leaving tooth decay unnoticed.
- 4. Qualified by SGS.**

### Q&As

#### What are AGDP/DRP sources?

Edible AGDP/DRP are refined and obtained from mass production of enriched fermented peptides using patented hydrolysis technology to yield a high concentration of precise peptide, and then purified via ultrafiltration membrane technology.

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#### Have AGDP/DRP got any side effects?

Peptides in the body within 4-8 hours will be metabolized into amino acids and it does not build up in your organs. Compared with other drugs, peptides are less likely to cause side effects. What is the role of peptides in dental care therapy? A peptide is a protein fragment consisting of two or more amino acids. Specific sequence AGDP/DRP can act directly on the affected area and have high efficacy and specificity in the mouth.

#### What is the role of peptides in the enamel?

DRP can transport and deposit calcium ion into the damaged enamel microstructure to remineralize, fill the slot, reduces bacterial growth and prevents etching.

#### What is the role of peptides in the gum?

Promoting collagen and extracellular matrix (ECM) synthesis, activating growth factors to accelerate mouth healing such as tongue wounds. Healing, promoting growth of shrinking gums and relieving symptoms of inflammation of the gums.

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Anti-sensitive teeth: 1 week of continued use. Wound healing/ anti-inflammation: 6 times of continual use. Growth of shrinking gums: 2 months of continual use.

### HOW TO USE ORALTIDE-PRO:

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- It is reported that one hundred and fourteen million Americans don't have insurance coverage for their teeth! Sam Hodgson for The New York Times. Our teeth are making us sick. May 23rd 2017. Zoe Greenberg. [https://kristof.blogs.nytimes.com/2017/05/23/our-teeth-are-making-us-sick/?\\_r=0](https://kristof.blogs.nytimes.com/2017/05/23/our-teeth-are-making-us-sick/?_r=0)



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# EUGORICS, VIAGRA FOR THE BRAIN?

# EUGEROICS - VIAGRA® FOR THE BRAIN?

*By Ward Dean, M.D.*

Adrafinil (Olmifon®/ Adra-Pro™), modafinil (Provigil®/ Moda-Pro™), and armodafinil (Nuvigil®) are three members of a class of drugs known as eugeroic's ("eugregorique" means "good arousal" in French).<sup>1</sup> The term was proposed in 1987 by Jouvett, to characterize the arousal, vigilance-enhancing, anti-depressant effects of adrafinil, the first drug in this class. Adrafinil was developed in France in the late 1970s by Louis Lafon Laboratories. One of the most striking behavioral responses first noted with adrafinil was increased activity in mice,<sup>2</sup> monkeys<sup>3</sup> and rats.<sup>4</sup> Human studies followed, indicating that adrafinil had clinical efficacy as a vigilance-promoting, mood-enhancing agent in the elderly. But since most of the studies were published in French, where it was indicated for increasing alertness/vigilance-enhancement (similar-to, but without the excessive stimulating effects or abuse potential of amphetamines), adrafinil was largely unknown outside of France. Nevertheless, adrafinil soon gained a popular off-label reputation as a cognitive enhancing, nootropic agent.

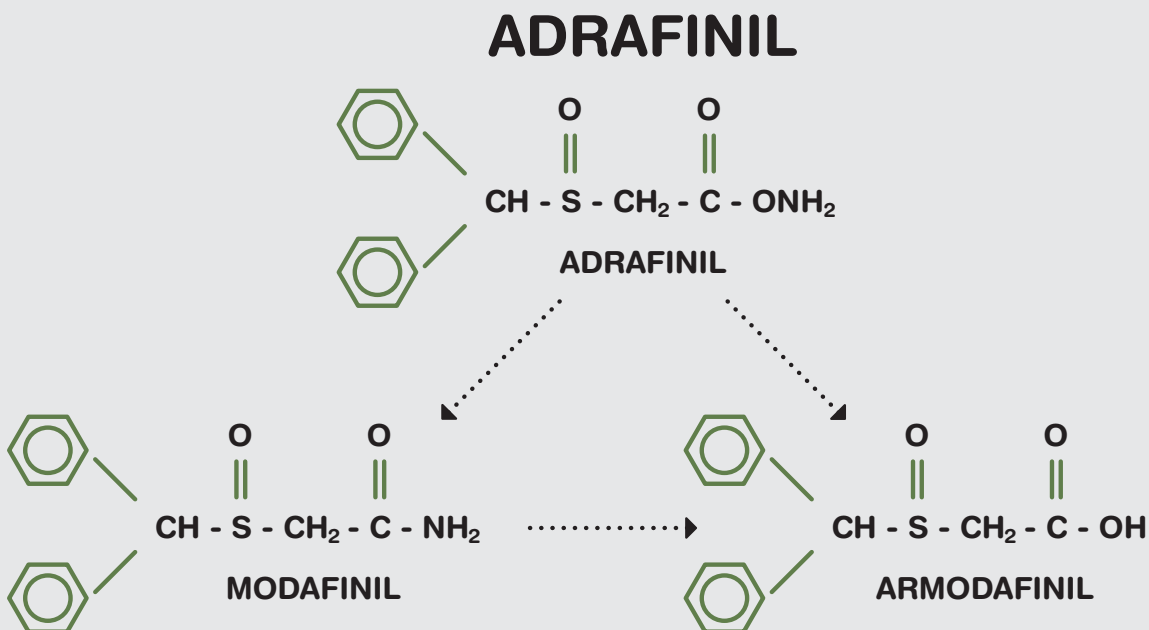
In the late 1980s, modafinil --the primary metabolite of adrafinil-- was developed (and was marketed in France in the early 1990s), was finally approved by the FDA in 1998 for the treatment of narcolepsy, shift work sleep disorder (excessive daytime sleepiness due to changes in working hours or job requirements) and obstructive sleep apnea. In 2007, armodafinil -the third eugeroic --was approved by the FDA for the same indications.

Because these drugs are so structurally similar (Fig. 1), and because the wakefulness-producing effects of adrafinil were later attributed to its metabolite, modafinil, the rest of this article will focus on modafinil. The main differences with the three drugs are their relative strengths, pharmacokinetics and availability.



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# EUGORICS, VIAGRA® FOR THE BRAIN?



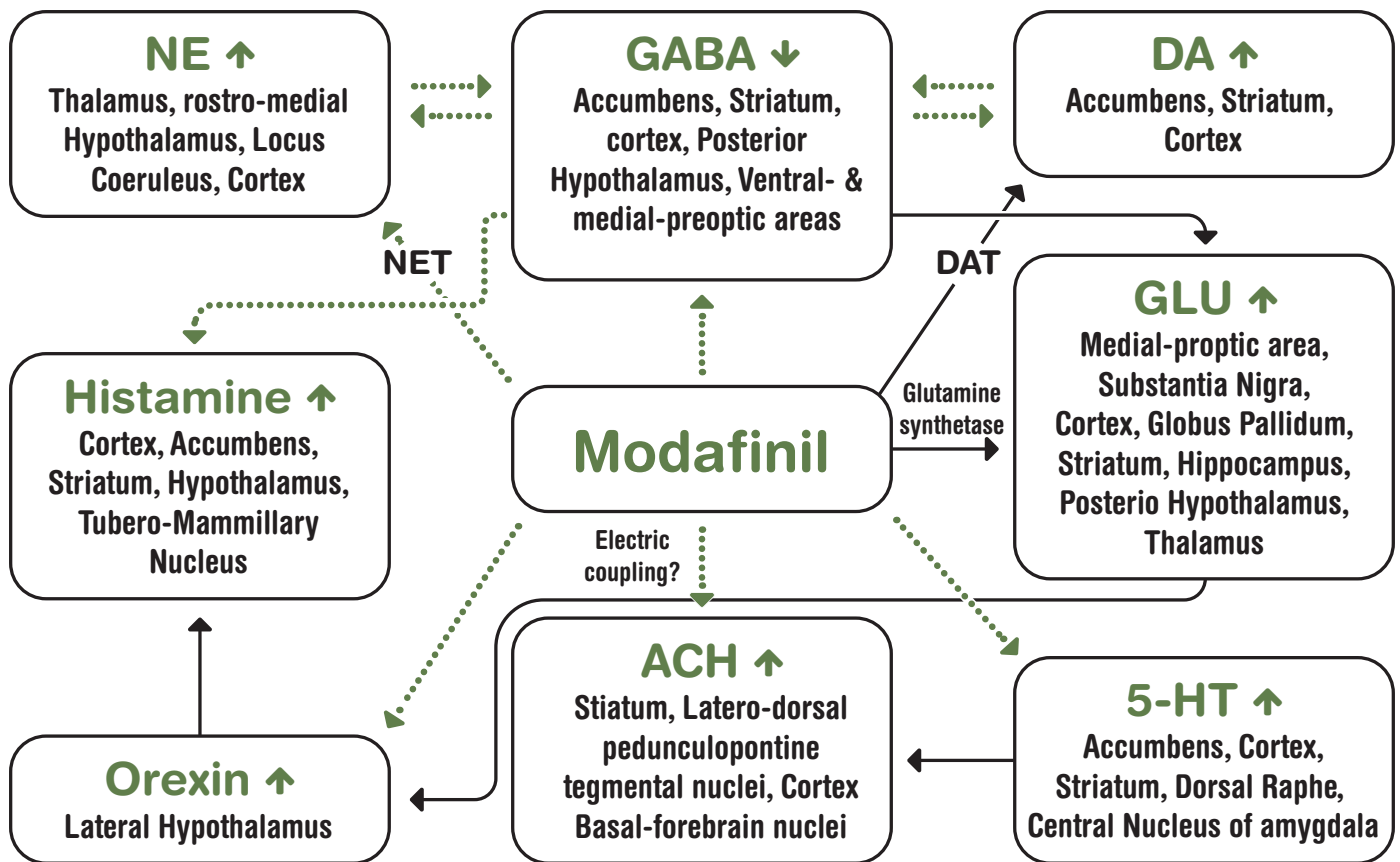
## STRUCTURE OF ADRAFINIL, MODAFINIL AND ARMODAFINIL

**Figure 1:** After oral ingestion, adrafinil is metabolized into modafinil, and its longer-acting R-enantiomer (mirror-image analog) armodafinil. Although this sequence was known as early as 1986,<sup>5</sup> it took another 10-20 years for the clinical efficacy of each of the two metabolites to be appreciated.

## MECHANISMS OF ACTION

The exact mechanism(s) that explain modafinil's wake-promoting, cognitive-enhancing properties have not been definitively identified. Modafinil increases histamine (HA), norepinephrine (NA), serotonin (5-HT) dopamine (DA) and orexin systems, and inhibits GABA and glutamate systems in

the brain.<sup>6</sup> Scientists from the National Institutes of Health (NIH) determined that modafinil's varied effects on different conditions were due to multiple effects on different brain areas and neurotransmitter systems (see Fig. 2).<sup>7</sup>



**Figure 2:** Targets of MOD's actions as a cognitive enhancer. Brain areas and related neurotransmitter systems that are potentially involved in the therapeutic actions of MOD as a cognitive enhancer. NE= norepinephrine; DA= Dopamine; GABA= gamma-amino-butyric-acid; GLU= glutamate; NET= norepinephrine transporter; DAT= dopamine transporter, 5-HT=serotonin; Ach= Acetylcholine. Solid lines indicate direct interactions, while dashed lines indicate observed effects that appear to be via indirect interactions or for which a mechanism has not yet been elucidated.

## APPROVED INDICATIONS

So far, the only approved indications for modafinil and armodafinil in the US are for sleep-related disorders such as narcolepsy, obstructive sleep apnea and shift work sleep disorder, although it is often used for a growing number of off-label uses.<sup>8</sup>

## UNAPPROVED/OFF-LABEL USES

Among the off-label uses for which modafinil and the other eugeroics have been tested are fatigue, cocaine addiction, depression, seasonal affective disorder, bipolar disorder, multiple sclerosis, and schizophrenia. In fact, the range of off-label uses for modafinil was reported by several researchers to be outpacing the growth of the empirical literature.<sup>9</sup>

## ADHD

To date, the strongest evidence for off-label use for modafinil is for attention deficit/hyperactivity disorder (ADHD) in children and adults.<sup>10</sup> The first study to evaluate modafinil for ADHD in the U.S. revealed that for 22 adults, twice-daily 200 mg of modafinil was equivalent to 20 mg twice-daily of dextroamphetamine. The authors concluded that modafinil may be a viable alternative to conventional stimulants for adults with ADHD.

In 2003, physicians at the Children's Specialized Hospital, Toms River, NJ conducted a double-blind study of modafinil versus placebo on 22 children with ADHD. Ten of 11 treatment patients were "significantly improved," whereas 8 of 11 control subjects manifested "no" or "slight" improvement.<sup>11</sup> The following year, in the UK, scientists at the University of Cambridge School of Medicine, conducted a double-blind study of 20 patients with ADHD, treated with a single dose of modafinil 200 mg or placebo. Modafinil produced a pattern of cognitive enhancement similar to that observed in healthy adults, with improvements in tests of short-term memory, visual memory, spatial planning, and stop-signal motor inhibition.<sup>12</sup>

In 2005, at the University of California, Irvine, 246 children and adolescents 6-17 years old with ADHD were treated with modafinil (n=164) or placebo (n=82) for 9 weeks. A unique aspect of this study was the use of an 85 mg modafinil tablet, and the dosage was individually titrated. The minimum and maximum dosages used in the study were 170-425 mg, respectively. Modafinil once daily improved the full spectrum of symptoms of ADHD, including inattention, impulsivity and hyperactivity and were evident both at school and at home. Improvement occurred by the first week of the study, and continued throughout the 9-week study.<sup>13</sup>



## COGNITIVE ENHANCEMENT IN NORMAL INDIVIDUALS

This is the subject of greatest interest to the majority of healthy off-label modafinil users/potential users—will it improve my mental performance? The answer from most of the studies appears to be “yes.”

In 2003, scientists from Cambridge University School of Medicine, who—as described above demonstrated modafinil's benefit in ADHD—were interested in assessing whether modafinil might act as a cognition-enhancer in normal subjects, without the side effects experienced by those who used amphetamines for alerting purposes. Sixty healthy young adult male volunteers received either a single oral dose of placebo, or 100 or 200 mg modafinil prior to performing a comprehensive battery of neuropsychological tests of memory and attention. Modafinil significantly enhanced performance on the majority of the tests and the subjects reported feeling more alert, attentive and energetic on the drug, compared to those on placebo, indicating that modafinil selectively improves neuropsychological task performance.<sup>14</sup>

A meta-analysis of studies of modafinil for neuroenhancement in healthy individuals by scientists in Germany revealed **that modafinil's use as a cognitive enhancer for “non-medical uses” was widespread.** Although they admitted that modafinil improved attention for well-rested individuals and maintained wakefulness, memory and executive functions to a significantly higher degree in sleep-deprived individuals, they cautioned that expectations by many users exceeded the drug's actual effects.<sup>15</sup>

The Cambridge doctors relentlessly performed another double-blind placebo controlled study of sixty-four healthy male (n=31) and female (n=33) volunteers, age range 19-36 years. Modafinil 200 mg or placebo was given to the participants. Two-hours post-drug administration, the subjects completed a battery of computerized neuropsychological tasks, which evaluated executive function, working memory, objective creativity and motivation to complete the tasks. Although modafinil demonstrated improvements in certain tests of “cold cognition,” the most striking improvements were noted for the most difficult of these computerized tasks. Another important finding was a striking increase in task motivation. Participants on modafinil felt considerably more pleasurable after

performing individual tasks. The main finding of the study in healthy volunteers is a clear performance improvement in the most difficult stages of computerized tests of working memory, visual memory and problem solving.<sup>16</sup>

A team from the University of Oxford recently performed a meta-analysis of studies conducted between January 1990 through December 2014 that evaluated the cognitive-enhancing effects of modafinil in healthy adults. They found that modafinil intake clearly enhances executive function and that when the most complex assessments are used, modafinil consistently enhances attention, and improves executive functions and learning.<sup>17</sup>

## MILITARY USES OF MODAFINIL

Perhaps even more significant than evaluations of modafinil's effects on healthy unstressed normal subjects, would be tests of modafinil's effects on above-average healthy normals, subject to sleep-deprivation and required to perform complex, stressful maneuvers. Those in the military, (especially pilots) are routinely required to perform under such conditions. Consequently, military services around the world were quick to appreciate the potential benefit of a wakefulness-promoting drug like modafinil.

A year after modafinil was approved in France, but 7 years prior to its approval in the U.S., the U.S. Air Force was keenly interested in its vigilance-improving effects, especially in sleep-deprived aviators, with its minimal peripheral side effect profile, low to absent abuse potential and lack of interference with normal sleep.<sup>18</sup>

In 2000, researchers at the U.S. Army Aeromedical Laboratory at Fort Rucker, Alabama, exposed six pilots to two 40-hour periods of continuous wakefulness during which they were required to complete several simulator flights. In one period, they were administered three 200 mg doses of modafinil and in the other, matching placebo. Modafinil attenuated sleep deprivation effects on four of six flight maneuvers, reduced slow-wave EEG activity and lessened self-reported problems with mood and alertness- in comparison to placebo. The most noticeable benefits occurred between 0330 and 1130 hours, when the combined impact of sleep loss and the circadian trough was most severe. The authors concluded that; “modafinil is a promising countermeasure for sleep loss in normals.”<sup>19</sup>



In Canada, scientists at the Defense Research and Development Center in Toronto, conducted a double-blind placebo controlled study of modafinil 300 mg or placebo, in a group of 18 healthy, non-sleep-deprived adults. The scientists wanted to evaluate the effectiveness of modafinil for use during sustained military operations to ameliorate the effects of fatigue due to sleep loss. Three 50-minute computerized cognitive assessment test batteries were given, (before drug ingestion and at 90 and 180 min after drug ingestion). Relative to placebo, modafinil improved fatigue levels, motivation, reaction time and vigilance.<sup>20</sup>

Two years later, a review of the performance- and alertness-sustaining/restoring effects of modafinil during sleep deprivation in normal, healthy adults was conducted at the Walter Reed Army Institute of Research. Researchers concluded that modafinil is efficacious for sustaining/restoring objective

performance and alertness during sleep deprivation with few adverse effects, and that modafinil restores performance and alertness to non-sleep-deprived levels.<sup>21</sup>

Two back-to-back studies were published an issue apart in the journal, *Aviat Space Environ Med*, from researchers at the U.S. Army Aeromedical Research Laboratory. The first study involved 18 helicopter pilots, with two 40-hour periods of sustained wakefulness, during which time each pilot completed 18 helicopter flights and other evaluations. During each 40-hour iteration, the pilots ingested 3 doses at 4-hour intervals of modafinil (100 mg), dextroamphetamine (5 mg) or placebo. Modafinil and dextroamphetamine maintained alertness, feelings of well-being, cognitive function, judgement, risk perception, and situational awareness of sleep-deprived aviators consistently better than placebo.<sup>22</sup> The other study was a meta-analysis of studies of modafinil which met inclusion criteria relevant to military

research, to summarize the current state of knowledge of potential cognitive-enhancing drugs, with the conclusion that the results supported the efficacy of modafinil.<sup>23</sup>

In a review of the appropriateness of modafinil for military use, a scientist at the Korean Air Force Academy summarized modafinil's effects. He stated that modafinil not only has waking, mood-brightening and memory-enhancing effects, but also has been used for disease-related fatigue, attention-deficit-disorder, Alzheimer's disease, age-related memory decline, depression, idiopathic hypersomnia, cognitive impairment in schizophrenia, myotonic dystrophy, post-anesthesia grogginess, everyday cat-napping, and jet lag treatments. He summed up by stating that; "modafinil can be used by anyone who wishes to work late, stay awake, enhance their cognitive reactions, or brighten their moods."<sup>24</sup>



## SAFETY

These drugs are generally considered very safe, with minimal abuse potential. As one indication of the safety of modafinil, Bastuji and Jouvet described a subject who unsuccessfully attempted to commit suicide by taking forty-five 200 mg modafinil tablets (a dosage 15 times that of a very high dose).<sup>25</sup> Allergic reactions are rare, but can be severe. If one develops a rash with any of these medications, further use should be immediately discontinued, and medical care sought. If renal or hepatic impairment is present, the dosage should be reduced.

## DOSAGE AND PHARMACOKINETICS

Plasma levels of adrafinil peak about one hour after consumption, and peak EEG and behavioral effects appear about an hour later.<sup>26</sup> Modafinil and armodafinil reach peak plasma levels 2 hours after consumption when taken on an empty stomach, and may take up to 4 hours when taken with a meal.<sup>27, 28</sup>

Recommended bio-equivalent dosages of adrafinil are 300-600 mg in the morning, and possibly another 300 mg at noon; modafinil is 100-200 mg in the morning (max dose 400 mg/day); and armodafinil 150-250 mg in the morning.

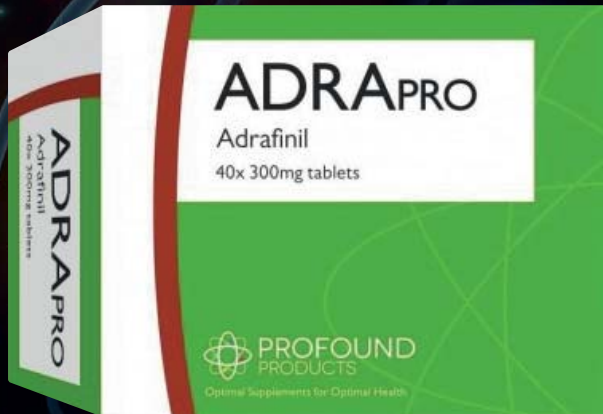
## AVAILABILITY

Modafinil and armodafinil are now generic and a prescription is required when obtaining them from a pharmacy in the U.S. Adrafinil, having never been approved in the U.S., (and not being a scheduled drug in France), may be freely imported into the U.S. using the FDA's personal-use drug import policy. Adrafinil has the additional advantage of being less expensive than the other two, newer eugorics.

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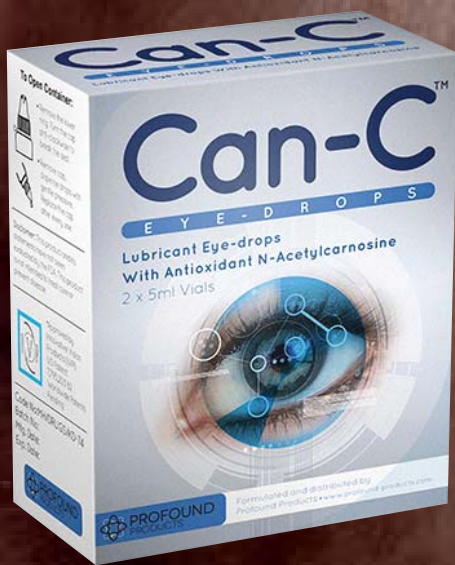
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In this complete new textbook "Reversing Physical Aging", discover how to reset or reduce all aspects of physical aging of the head – hair, face – and the 5 senses – vision, hearing, smell, taste and touch. This practical guide is full of ready-to-use information for medical therapies that reverse each physical aging signs and assesses the efficiency of each treatment. "Reversing physical aging" is the best way to make your patients healthier.

« A practical and complete textbook on the aging of the head and the senses that every physician needs. »



Dr HERTOGHE MEDICAL SCHOOL



# Can-C™

## 2x5ml Eye drop bottles

**\$39.99**

Buy 3 Save 10%

Buy 6 Save 20%



Can-C™ Plus is the perfect accompaniment to Can-C™ Eye Drops.

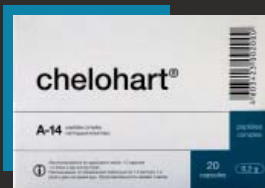
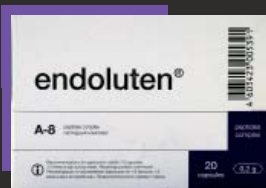
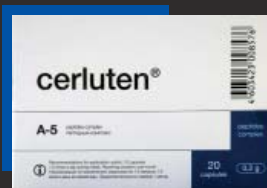
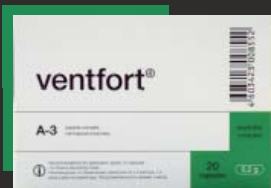
Maximise the benefit from day one of the Can-C eye-drops. Those who have very dense cataract and severely diminished vision to start with should combine the tablets with the eye-drops from day one.

*All side effects and contraindications are available on the IAS website.*

Restrictions may apply, please see IAS terms and conditions for full details. Offer valid until 1<sup>st</sup> March 2018



# PEPTIDE BIOREGULATORS



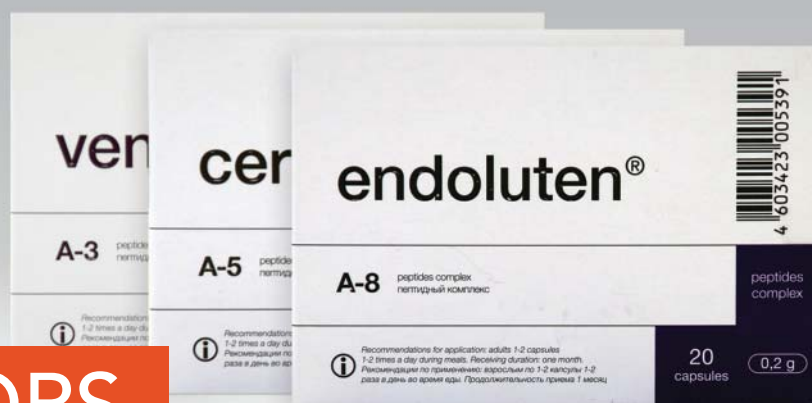
**20 x 200mg capsules**  
**Buy 3+ and save \$9.99 per pack**

Peptide Bioregulators, gene switches  
that could replace stem cells!

Restrictions may apply, please see IAS terms and conditions for full details. Offer valid until 1<sup>st</sup> March 2018

*All side effects and contraindications are available on the IAS website.*

# PEPTIDE BIOREGULATORS



## THE DISCOVERY OF GENE SWITCHES IN FOOD

Today Professor Vladimir Khavinson is the president of the European Academy of Gerontology and Geriatrics, but in the 1980's he was a Colonel in Soviet Union military medical corps. At the time, he and his team were approached by Kremlin officials, they wanted them to find a way to protect their troops from a myriad of problems; issues such as radiation for submariners in nuclear submarines to troops that may be blinded from known ( but thankfully unused) new weapons such as battlefield lasers

### A former Soviet military secret!

What their research uncovered- that was for two decades on many thousands of men and women-was a remarkable link between short chain peptides and DNA. This former military secret is now available to the public as peptide bioregulators. Their published research has identified that each organ/gland/ tissues use a highly specific short chain peptide, obtained from food, to act as a 'short-cut' to initiate protein synthesis. These peptides, unlike proteins, can enter the blood through the stomach.

Though a comprehensive list of patents and even copyrighted PowerPoint slides, the Russian research group have shown that each of the concentrated peptide bioregulators so far examined, interact with particular strands of DNA-effectively and very specifically activating repair and regenerative processes. This is a remarkable story since what we are describing here are peptides that act as individualised gene switches. To date, they have been tested for many years on thousands of individuals, without report of any serious side effects or contradictions. We believe that they could be set to 'out do' stem cells.

Why? Because this peptide therapy is relatively cheap, highly specific, can be taken orally and doesn't require any suppression of the immune system to operate fully ( as stem cells do).

### Oral material from the trails

The peptide bioregulators available via IAS are the bovine originals; sourced from carefully chosen Danish calves and processed through pharmaceutical processes and filters. They are not the synthetic versions which have not been studied/proven. Peptide bioregulators act as they sound-to regulate; for example, Thyreogen® the thyroid

peptide would increase thyroid activity if it were too low, but decrease it if it were too high.

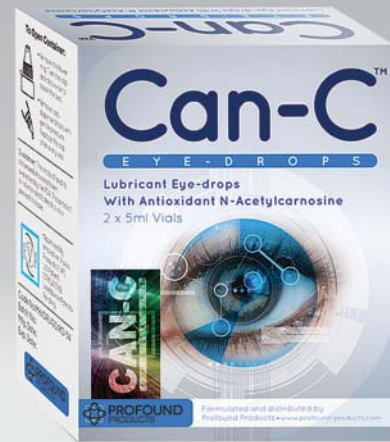
### Dosing

Doses are very dependent upon the need and unlike hormones these peptides do not have to be taken every day, hence making them a cost effective regime. A typical/ average use could be considered as follows:

- Start with an intensive course: 2 capsules once a day for 30 days
- Thereafter use 2 capsules once a day for 10-days, repeat every 2,3,4 or even as little as 6 months

The story of peptide bioregulators is a remarkable one and we recommend that you read the articles, interviews and see the video on the IAS website.

# CAN-C



## A BREAKTHROUGH FOR CATARACTS

Can-C™ eye-drops are the original™ brand-developed by Innovative Vision Products (IVP). This group were the first to research, publish and prove how eye drops can reduce and even eradicate cataracts. Accordingly there are active US and EU patents (and others pending) on this unique and special product.

### Unique Formula:

Can-C™ eye-drops are the formula from the original published human trials. They contain a purified and racemized form of n-acetylcarnosine (made in Japan); this natural di-peptide has potent anti-glycating and anti-oxidant properties that prevents lipid peroxidation. Note that the formula is important-it's not all about the n-acetylcarnosine; the specific carrier agents and their purity are also important. If you look at the Can-C™ formula you will see the differences to the copycats, (remember it is only Can-C™ that is patented in recognition of the original work). If you want the best possible results in the fastest possible time, then choose Can-C™ to deliver them according to the clinical trials.

### Clinical Trail:

Patients placed two-drops of Can-C™ into their eyes twice a day for a 6 month period, the outcome was:

- 90% saw an improvement in their visual acuity
- 88.9% of patients showed improvement in the clarity of their lens.

There have always been numerous reports on cataract shrinkage and even disappearance with documented evidence that Can-C™ eye-drops remain effective (and safe) more than 24-months later. The most commonly expressed initial reports are that glare is significantly improved, (for example night driving is much safer) and colour perception is enhanced.

### Improving Eye-Sight:

More evidence is mounting that Can-C™ is efficacious for many conditions including:

- Cataracts (particularly in senile vision)
- Glaucoma
- Presbyopia
- Corneal Disorders
- Eye Strain
- Ocular Inflammation
- Blurred Vision
- Vitreous opacities and lesions
- Diabetes mellitus complications
- Contact lens users
- Dry eye syndrome

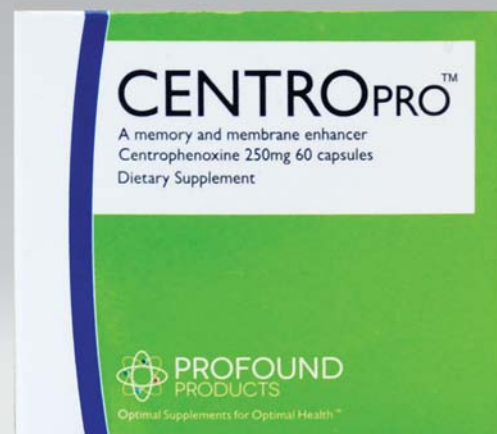
Of special interest may be to persons who wear contact lenses. This is because Can-C™ inhibits the accumulation of lactic acid and therefore contacts can be worn for longer periods without pain. We have also received reports that Can-C™ not only aids dry-eye syndrome with its lubricants, but that Can-C™ helps to unclog proteins from the lacrimal ducts, thus releasing more natural tears onto the eye. In a similar way it is also believed that the unclogging of proteins in the eye's drain, (the Schlemm valve), helps to reduce intraocular pressure and this aids glaucoma.

### Can-C™ Plus Capsules

In addition to the eye-drops, Can-C™ Plus capsules are also available. They are strongly recommended to be used in combination with the eye-drops- if you have ripe (long existing) cataracts.



# CENTROPHENOXINE



## CENTROPHENOXINE, (PRONOUNCED, CENT, ROW-FEN, OX-IN) IS A CLASSIC 'SMART DRUG'

The term 'smart drugs' has become synonymous with substances that aid memory and cognition although the correct medical terminology is 'nootropics' (which when translated from Greek is - 'towards the mind'). Centrophenoquine is an ester of PCPA (a plant compound) and DMA which is a natural choline-based substance found in the diet.

### About Centrophenoquine

Centrophenoquine has been studied over decades. Principally in Europe and one of its leading experts is Professor Imr Zs-Nagy. He said, "Centrophenoquine has shown many facets to improve conditions related to my membrane hypothesis of aging. For example, its ability to improve brain performance, survival time in animal experiment and to remove the cell-aging pigment called lipofuscin. It has been my anti-aging supplement for more than 30 years."

Centrophenoquine improves acetylcholine levels in the brain. It is this neurotransmitter that declines in Alzheimer's disease. The target is at the early stage of dementia or even before then at the anti-aging stage, wherein smart drugs like centrophenoquine improve/enhance and protect the performance of an aging but otherwise recognised as a healthy individual.

Lipofuscin is a waste material that accumulates in aging cells especially those in the brain, heart, lungs and skin. In skin cells, Lipofuscin can form part of the pigmented spots that are often referred to as 'age or liver spots'. Lipofuscin accumulation can be very troublesome for the cell because it inhibits proper functioning taking place, reducing the transference of chemicals through cell walls thus damaging both messaging and detoxification abilities. When there are significant amounts of Lipofuscin present in the brain they are then referred to as 'plagues' and then become a recognised trait of Alzheimer's.

Centrophenoquine's primary mode of action is to help remove lipofuscin deposits. Patients that take Centrophenoquine possibly over a couple of weeks can see aging spots fade or disappear. Whilst knowing, at the same time, Lipofuscin is reducing in their heart, lungs and brain.

### General cognitive benefits

further evaluation. Which of the following is your issue?

Short term memory

Medium term memory

Long term memory

Do you get bored easily?

Do you lack focus/attention?

Does your mind quickly become tired?

Is the problem remembering new experiences?

Does it take you too long to recall memories?

Centrophenoquine is best suited to the last one. It can help people especially those over 40 to hasten their recall speed, bringing clarity and order to both speech and thought. A typical dose for the average person is 250mg once or twice daily.

# DEPRENYL



## DEPRENYL FOR FOCUS AND CONCENTRATION

Deprenyl is also known as selegiline, it was created in the 1960s by Professor Joseph Knoll, principally as an aid to Parkinson's patients - because deprenyl has a significant benefit to improve dopamine levels in the brain.

### Significant longevity studies

Professor Knoll's experiments on rats produced incredible longevity benefits. When fed deprenyl in their food, they lived longer than those that were not. After the last non-treated rat died, the first of the deprenyl treated rats hadn't! These results were in another study conducted from research by Dean, Fowkes and Morgenthaler - published in the book, 'Smart Drugs and Nutrients'. It highlights that the loss of dopamine in humans with age, can be mapped against the development of Parkinson's and even death.

Deprenyl has been expressed as a MAO-b inhibitor. Preventing the enzyme monoamine-oxidase type-b from destroying dopamine, ergo leading to its greater availability in the brain.

The inhibition of the more common MAO-a can be problematic, leading to something called 'the cheese effect,' not a side effect of deprenyl, although it should be noted that dopamine can inhibit type-a, usually at very high doses of 20mg. Professor Knoll has noted that there is another significant action of deprenyl and this is the raising of PEA levels. PEA is a catecholamine activity enhancer that raises norepinephrine levels, it's a significant attention agent that is behind the primary mechanism of the famous Eugeroic drug- modafinil (Provigil). Read Professor Knoll's books - 'The brain and its self', or 'How selegiline/ deprenyl slows brain aging.'

### Typical patient responses

A patient who has mild cognitive impairment, or age related minor cognitive dysfunction, the most common report is a significant improvement in their focus and concentration. Persons with higher dopamine levels often appear more 'driven' and 'dedicated.'

Avoid overuse since it can lead to what may appear to be an oppressive behavior, as others around you are not so focused and 'on the ball' as you! We recommend breaks from deprenyl use.

Some advocate one week off in the month and others use it during the weekdays but not at the weekends.

Doses are based on need and age. Parkinson's patients will require large doses. A person wanting to improve their cognitive performance may want to consider 1mg to 3mg per day, with occasional breaks. These doses do not take into account synergy with other dopamine enhancing agents and persons using anti-depressants should consult with their physician. Deprenyl tablets are provided in 5mg form (Jumex), some like to take ½ to 1 of these tablets 3-times a week. The use of the deprenyl liquid (Dep-Pro) is particularly attractive for those using deprenyl to generally support, protect and improve neurological function, since 1 drop = 1mg, the liquid can be dosed very precisely by placing those drops into a cold drink. Avoid use in the late evening to prevent any sleep disruption.

# ESNATRI AND PROGESTERONE



## BIOIDENTICAL HORMONES - NATURAL ESTROGENS AND PROGESTERONE FOR WOMEN

In this featured section we are focusing on the use of natural estrogens and progesterone for women, normally utilised to aid the menopause. IAS carries a wide range of bioidentical hormones - a term that means 'natural to and in the body'.

When hormone replacement therapy (HRT) was developed in the 1920s, estrogens had to be derived from horse urine because a laboratory solution was too difficult or expensive to synthesize. Facts pointed out by Dr. Wright in his best-selling book 'Stay Young & Sexy'. Estrogens can be easily produced now. Some people believe that the known side-effects from 'traditional HRT' are due to the fact that the hormones given are not correct.

## Introducing Esnatri

Esnatri is our bioidentical triple estrogen cream. One of the best bioidentical estrogen creams available. It comes directly from the work of Dr. Wright who has shown that the majority of women produce estrogens in the ratios of 90% estriol, 7% estradiol and 3% estrone.

Most tri-estrogen preparations attempt to replicate the human hormones estriol, estradiol and estrone, apply them in the ratio of 80:10:10, while some even entirely over-look estriol, claiming it is a weak estrogen. But, women naturally produce high levels of estriol and it is considered to have anticarcinogenic effects.

The Esnatri cream can be applied by daily rotation to your neck, upper chest, breasts and behind the knees, or inner thighs. A typical starting dose is 2 mg. Start from day one (of what would have been the start of your menstrual cycle) and continue until day 25. You should stop for five days, before repeating the application at the start of the next menstrual cycle. During these last few days, the estrogen receptors are being allowed to 'rest' as they have been accustomed.

## Combing Estrogen with Progesterone

Progesterone is the counterbalance to estrogens. Women can significantly decline in estrogen levels during menopause - they rarely reach zero production levels, whereas progesterone can sometimes not be measured at all in elderly women. It is also the low progesterone that most significantly impacts bone strength, leading onto osteoporosis. There are numerous reasons to ensure that progesterone is also taken alongside an estrogen therapy. IAS provides a 5% strength natural progesterone cream. Typical doses are 25 mg to 30 mg of progesterone applied on day 10 and continuing to 25. The start date varies according to the usual timing of your ovulation. As with the Esnatri cream, stop for the last five days of your cycle so that the estrogen receptors have their accustomed 'rest' period. Remember, your hormone replacement therapy should be overseen by a physician and should not be undertaken if you have undergone cancer treatment.

# OXYTOCIN



## FOR PASSION AND SEX

Oxytocin is a hormone produced by the hypothalamus, excreted via the pituitary gland. Its orthodox medicine role is to help women give birth, since the large dose that's injected helps relaxes the uterus and alleviates the passage of the child. Dr. Thierry Hertoghe's book, 'Passion, sex and longevity, the oxytocin adventure' highlights that it has many other roles too.

## The love hormone

Oxytocin has been dubbed 'the love hormone'. It can induce feelings of bonding and care. Its measurements have been taken between lovers, friends, relatives, parents and their children etc. It has been noted that oxytocin levels are higher when they are in their presence. Mothers naturally bond with their children, but even men, (especially those who experience the live birth), express their emotions as wanting to care and protect their off spring. These effects may be attributable to the release of oxytocin hence triggering the bond. However, psychopaths are notoriously low in their oxytocin levels, which may be a cause of their uncaring feelings towards other humans.

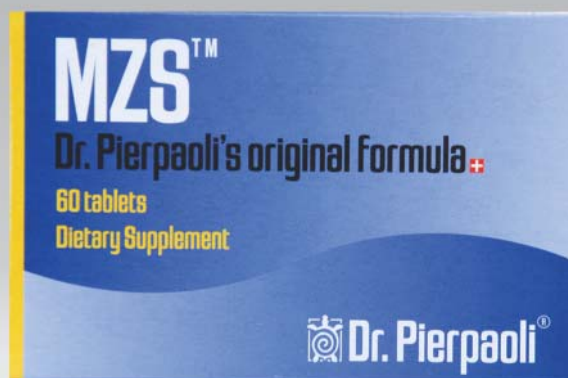
The pain and orgasm connection - Fibromyalgia can be a very debilitating disorder with a lot of pain, sometimes constant for those who suffer with it. In women, it was noted that when they were experiencing an orgasm they felt no pain at all. Women undergo a burst of oxytocin during orgasm. Trials were undertaken to see if oxytocin supplementation could alleviate the pain of fibromyalgia, there was some success, but the side-effect noted was that those women now enjoyed multiple orgasms!

## The effects of Oxytocin

Dr. Hertoghe explained that some will not feel the effects of Oxytocin. For two reasons, (if we consider that the dose is correct for that individual). Firstly, some people are 'low' in their own principal sex hormone, so if a man is low testosterone, or if a woman is low estrogen, it is possible that oxytocin will not elicit its full potential in those persons. The other issue could be low vasopressin, vasopressin is a counterpart to oxytocin, produced and released via the same glands. In cases of vasopressin deficiency, the patient may enhance the oxytocin experience by adding one or two sprays (10 IU each) of vasopressin via the Vaso-Pro nasal spray.

Doses are very dependent upon its use. For social or sexual enhancement, 5 IU to 10 IU is a 'typical' dose. Dr. Hertoghe reduced the doses that he recommends in his book, (transmitted via personal conversation to me). Currently, IAS is providing Oxy-Sub in 20 IU trouches (a soft sublingual tablet). These can be cut into half or quarter for a dose of 5 or 10 IU and should be placed under the tongue and allowed to melt. The other option is Oxy-Pro which is applied intranasally delivering 10 IU per spray.

# MZS



## BECAUSE NOT ALL MELATONINS ARE CREATED EQUAL

Melatonin is produced by the pineal gland at night to regulate our circadian rhythm, (sometimes called the sleep wake cycle). As we age the amount of melatonin we produce reduces, resulting in many older people sleeping less and having a lower quality of sleep. Our melatonin has been formulated by the world's foremost melatonin expert Dr. Walter Pierpaoli, his Melatonin Zn Se, or MZS, is totally unique since it is designed to mimic the natural night peak of melatonin to leave you feeling refreshed and alert the following day.

## What does Melatonin do?

Melatonin is vital to protect our hormonal system, regulate immunity and repair our body's cells. Commonly used by shift workers and to treat jet lag and age related sleep disorders. Melatonin is an extremely effective antioxidant, in fact on a molecule to molecule basis - melatonin has proved to be significantly more efficient in neutralizing toxic hydroxyl radicals than the two wellknown free radical scavengers, glutathione and mannitol. Its effect on longevity is well documented. Experts believe melatonin has a positive effect on aging.

Age related macular degeneration (ARMD) comes in two forms, wet and dry. It's a difficult disorder to treat and linked to blindness. A 24-month study, (published in NY Academy of Science, 2005, 1057:384-392) on 100 patients showed that after 3 months, the majority of patients taking 3 mg of Melatonin Zn Se nightly had halted the progression of their age related macular degeneration and at 6 months many showed reversal of their ARMD. True for both the wet and dry forms!

## Why is Dr. Pierpaoli's MZS more effective than other melatonin supplements?

Firstly, it is of pharmaceutical quality at a dose of 3 mg. Secondly, it contains the synergistic ingredients of selenium and zinc. Thirdly and most importantly- it is designed to release at a very specific time. Dr. Pierpaoli's research led him to perfect a formula that exactly mimics the pineal gland's release of melatonin. MZS is the only melatonin supplement to follow nature's own night peak. Take half to one 3 mg tablet at bedtime only; do not take more than two tablets. By taking MZS™ between 9pm and 11pm you will create a night peak between 1am and 3am, this is the most natural and normal time to have the highest melatonin levels.

MZS is much more than a sleep aid and melatonin has many published benefits. MZS comes with the endorsement of Dr. Pierpaoli. If you've tried other melatonin and didn't notice any significant effect, then we highly recommend you try Dr. Pierpaoli's MZS for a superior experience.

# STEM CELL WORX



## ENHANCING AND IMPROVING STEM-CELL ACTIVITY

Stem Cell Worx® is an intraoral spray that contains a very high-grade bovine colostrum, (with over 30% of the antibody IgG and over 54% protein) along with a 98% pure trans-resveratrol and 95% fucoidan ( a seaweed extract).

This natural health supplement is designed to activate the body's own adult stem-cells in order to provide a robust immunity. With 50 to 70 trillion cells in the body, cellular health is clearly crucial to overall well-being and good health. Hence, adult stem cells working at optimal levels provide the platform for many cumulative health benefits.

Unfortunately, as we age, our own adult stem cells decline rapidly, along with their release rates from the bone marrow, and our immune systems weakens. Whilst stem cell clinics are at the forefront of antiaging medicine today, the process of full adult stem cell therapy is very expensive and has many regulatory restrictions.

Adult stem cells are the master cells of the body that have the ability to maintain, self-renew and repair cells, tissue and muscle throughout an entire life-time. These cells are referred to as autologous, haematopoietic (blood), mesenchymal or stromal stem cells.

Adult stem cells should not be confused with embryonic stem cells that come from an embryo.

The Stem Cell Worx® supplement is designed specifically to enhance one's own adult stem cells naturally. Stem Cell Worx® is an intraoral spray providing an absorption rate of up to 95% of its nutrients. This is important because in order for adult stem cells to be stimulated, it is the blood that is the principal carrier of nutrients and oxygen to our cells. In order to enhance cell activation you need three key factors which are:

- Growth Factors
- Immune Factors
- Cytokines

Stem Cell Works® has all three of these factors in abundance and is scientifically proven they are most effective when administered by intraoral spray delivery.

Time takes its toll on adult stem cells. At 65 years of age, the release rate of adult stem cells entering the bloodstream has dropped by 80% compared to youth. It is important to keep them activated. The good news is it is now possible to reverse this statistic.

## Stem Cell Worx® Benefits

Stem Cell Worx® contains the greatest number of natural growth and immune

factors compared to any other health supplement currently on the market. This enables natural stem cells activation to be as much as 75% per 36mg of the formulation. This provides:

- Support to naturally increase adult stem cells, providing the platform for many cumulative health benefits including:

- Increased energy and endurance
- Boosting the immune system
- Improved alertness and mental clarity
- Faster recovery after your exercise regime and faster repair and recovery after surgery, injury or illness
- Helping to build muscle, burn fat and maintain natural weight loss in conjunction with a healthy diet and exercise regime

IAS chose Stem Cell Worx® over other purported stem-cell activators on the basis of evidence. Figure 2 demonstrates the benefits of supplementing daily with Stem Cell Worx.

## Dosing

Six sprays into the mouth provide 36mgs of formulation. This can be performed once or twice daily as required. Spray under the tongue, hold for 10 seconds, and then swallow the remainder. It's best taken on an empty stomach, at least 30 minutes before or after eating any food.

# THYROID SUPPORT



## FOR THE HYPOTHYROID EPIDEMIC

Dr. Broda Barnes in the 1970s estimated that 40% of the adult population was deficient in thyroid hormones. He published this statement in his excellent book - 'Hypothyroidism, the unsuspected epidemic.' Since then, pupils of Dr. Barnes, such as Dr. Richard Wilkinson, have suggested that this figure could be even greater now!

The thyroid gland is of pivotal importance to our overall health, as we age the production of thyroid hormones decline. This lack of thyroid function is the root cause of a variety of age related health disorders. Ergo, supplementation with a synthetic or a natural thyroid can have a significant positive effect on a wide range of age related problems.

## The importance of the thyroid gland

The hormones produced by the thyroid control the body's metabolism- the rate at which it burns calories for energy. It controls the body's utilization of fat, so a decline in the secretion of hormones from the thyroid gland, (known as hypothyroidism) can result in a range of symptoms such as poor concentration, confusion, memory problems, cold hands and feet and weight gain. Another serious condition which can be caused by and result from an underactive thyroid are painful musculoskeletal issues that affect tendons, muscles and ligaments. Your doctor can have your blood levels of thyroid checked. In addition to that, you can take your body temperature when you wake in the morning, it should be in the range of 97.8 to 98.2 degrees Fahrenheit. If it is regularly lower you could be hypothyroid and if higher then hyperthyroid.

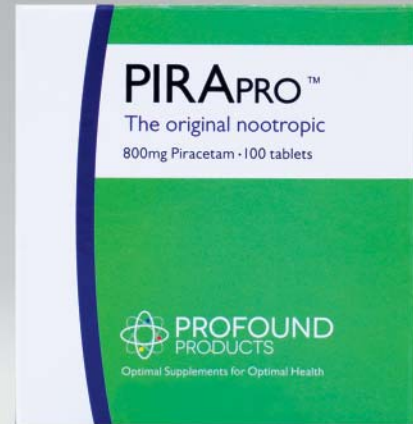
## Choosing between synthetic and natural thyroid supplements

IAS stocks a comprehensive range of both synthetic and natural thyroids, although we advocate the use of a natural supplement over a synthetic, this is because products such as Armour are of a porcine origin, so they naturally contain the full spectrum of T1, T2, T3 and T4 thyroid hormones, (note the bottles only list the amounts of T3 and T4 because very few physicians are familiar with T1 and T2).

Natural desiccated thyroids are measured in grains; with one grain being equivalent to approximately 60 mg. IAS carries doses from ¼ grain to 3 grains, with brands including Armour, ERFA and Nature. IAS also provides synthetic T3 in 20 mcg and T4 in 100 mcg tablets.

Thyroid supplements provide potent antiaging protection. Many aging individuals can benefit from taking a thyroid supplement because this remarkable hormone has such a profound affect across so many different conditions. Many antiaging physicians consider thyroid support an essential part of any serious attempt to improve a person's health-span and longevity.

# PIRACETAM



## PIRACETAM, THE ORIGINAL NOOTROPIC

Smart drugs and nutrients, or to give them their correct medical terminology, nootropics are agents that can improve conditions of senile dementias and have become popular for older individuals to improve their mental and cognitive processes. It was Ward Dean, M.D. who highlighted these facts through his very popular 'Smart Drug' series of books in the 1980s, since then the term 'smart drugs' has become mainstream.

## Piracetam, the original nootropic

This smart drug was first developed by Dr. Giurgea for UCB laboratories in Belgium in the 1960s. Originally it was designed to assist with travel and altitude sickness, but shortly afterwards individuals realised that piracetam had positive cognitive enhancement effects.

Piracetam is a cognition agent that has been used successfully to treat a wide range of conditions, for example, it has been shown to increase a person's attention levels and improve memory and intelligence. Piracetam can help to slow down 'senile involution', dementia and Alzheimer's disease. In tests and trials, piracetam induces significant improvement to memory consolidation and recall in those suffering from 'age-associated memory impairment'. It has also been used to improve patient's recovery from strokes, particularly improving post stroke speech impairment (aphasia). Another use has been in cases of acute and chronic cerebral ischaemia, (decreased blood flow to the brain). Using piracetam has restored speech and the use of limbs in these patients; it has also increased neuronal activity in the brain when measured with EEG.

For regular individuals, piracetam has been shown to enhance idea creation and the ability to 'see things through'. The level of clarity piracetam creates is often described, "the fog has lifted."

## How does piracetam work?

Piracetam's key and unique method of action is upon the Corpus Callosum, the region of the brain that links the two hemispheres. Most experts believe it is the key that gives piracetam users the ability to channel greater brain potential by connecting the logical side of the brain with the creative side more effectively.

What are the doses of piracetam? A common dose is 800mg tablets three times a day, then lowering to 800mg twice a day after the first month. The effects of piracetam can be enhanced if taken concurrently with centrophenoquine or Hydergine. Side effects are minimal and seldom experienced, but should you experience nausea or a headache then it is usually caused by an overdose. In which case reduce the dose and build up more slowly.



# YOUTH GEMS



## THE PEPTIDE BIROREGULATORS FOR SKIN

Four peptide bioregulators have now been combined into topical skin preparations so that their unique gene-switching performance can be brought to the field of aesthetic medicine.

### What does each peptide provide for?

The beauty product line Youth Gems contains the following four peptides and a ginseng extract called Neovitin. The latest developed program of complex skin care designed for the face, neck, hands and the body.

The line includes four unique active ingredients of short-chain peptides that have a directed tissue-specific action to improve all basic skin structures:

- **Thymus peptide:** Stimulates tissue regeneration and synthesis of tissue-specific proteins. Cells proliferative and metabolic activity is enhanced accelerating the renewal of cell tissues. Has an anti-inflammatory action, improving healing time of wounds, as well as antioxidant, immune stimulating and anti-stress actions.
- **Pineal peptide:** Regulates metabolic processes and increases protein synthesis in skin cells. It possesses potent antioxidant activity, normalizes the lipid peroxidation processes in skin

cells that promotes the elimination of negative influences on the skin from external factors.

- **Cartilaginous peptide:** Stimulates regeneration of fibroblasts and keratinocytes and interferes with the destructive changes in collagen skin structure. It strengthens collagen structure of elastic skin fibres and increases elasticity.
- **Blood vessel peptide:** Regulates metabolic processes in the vascular wall, normalizes vascular tone and restores disturbed skin microcirculation. It strengthens and regulates the permeability of the vascular walls of skin vessels and improves skin turgor.

Youth Gems contain beneficial natural agents. The range includes: Neovitin (a complex from ginseng), olive oil, raisin-seed oil, Argon oil, Soya oil, Jojoba oil, Bisabolol ( from chamomile), Peony extract, sodium hyaluronate (derivative of hyaluronic acid), green tea extract, cocoa oil, carrageenan (from seaweed), winter bloom, almond extract and vitamin E.

### What results have been seen?

Clinical trials and examinations have been conducted at the St. Petersburg Biogerontology Institute. They concluded that these short chain peptides have many beneficial activities.

Improved metabolism in vascular wall cells, growth of new skin cells, enhanced antioxidant activity, increased blood flow circulation and greater moisturization. The skin's appearance becomes smoother, fewer wrinkles and more elasticity, which helps to lift the face contours producing a more radiant, youthful appearance. These beneficial effects were noted in 100% of women who took part in the voluntary clinical trial.

### What's available?

**Body milk:** A very light cream that can be applied to most areas of the body.

**Day cream:** A core product designed to be applied to the face and hands.

**Serum:** To be used sparingly against the most noticeable skin aging effects on the face and neck.

**Tonic:** Used to help any area become more firm and taut and may be splashed on as required.

**Face pack:** An anti-aging facial mask with peptides and ginseng extract.

**Night cream:** This unique formula provides resilience against skin aging.

All of the Youth Gems products should be applied onto clean, dry skin - avoiding the eyes. Makeup can be applied after absorption - if required.

# TESTIMONIALS

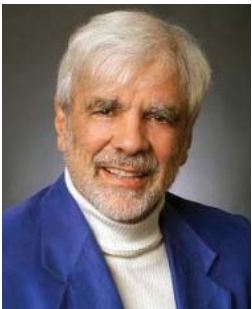


**DR. AUBREY DE GREY**

"IAS has shown great vision and leadership, as an organisation focused mainly on the provision of contemporary medical interventions against aging, and in also supporting the SENS Foundation's efforts to hasten the development of much more powerful future interventions."

**Marios Kyriazis** M.D., MSc, MBiol, CBiol

"All my working life I've been interested in anti-aging medicine. For much of that time I've known about and worked alongside IAS. Therefore, I am in a good position to tell you about their commitment to this field, not only to make the latest medicines, hormones and nutrition available, but also to help support and promote the science and organizations including the British Longevity Society, so that together we can make a real difference to the future of health care."



**JONATHAN WRIGHT** M.D.

"Every adult has the right to take care of his or her own personal health as he or she chooses. In the 20th and 21st centuries, this universal human right has been nearly obliterated by an ocean of nanny-state regulation and deliberate suppression of information by bureaucracies, with hidden and not-so-hidden agendas. International Antiaging Systems is a beacon of useful health care information and a literal island of freedom of health care product choice in our otherwise un-free health care world."

**NICHOLAS PERRICONE** M.D.

"IAS is an outstanding resource for the finest, most up-to-date news and information on healthy aging. They also offer products of the highest integrity and efficacy. In fact, IAS is the world's greatest source (often the only source) for the most cutting edge and advanced nutrients to ensure optimum healthspan and maximum life span."



**THIERRY HERTOGHE** M.D.

"IAS has a history of making throughout the world crucial, but difficultly accessible medications available to patients. IAS is one of the pioneering societies in antiaging medicine that has helped this new medical specialty move forward."

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## MAIL

Unfortunately personal checks and money orders cannot be accepted at this time.

Please contact our customer service team if you need any assistance in placing your order.

**note:** Our customer care team is available from 9am till 6pm GMT Monday-Friday. Outside of these times your call will be handled by our out-of-hours answering service or go to voicemail.

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**60ml liquid spray or dropper application.**

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These cutting edge growth factors: IGF-1, bFGF and caffeine, plus the DHT blocker azelaic acid, are the key combination that are delivered straight to the hair follicles, stimulating and kick-starting the follicles into growth mode that Minoxidil alone will not effectively accomplish.

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Restrictions may apply, please see IAS terms and conditions for full details. Offer valid until 1<sup>st</sup> March 2018

*All side effects and contraindications are available on the IAS website.*