

Life Extension Magazine November 2009

## ON THE COVER

### A Natural Approach to Erectile Dysfunction that *Improves Vascular Health*

By Robert Haas, MS

Aging individuals become very enthusiastic when they discover something that produces an immediate result.

Life Extension® members often send us samples of dietary supplements they claim have enhanced their **sexual performance**. These members are elated that a purported “natural” product produces such striking **erection-inducing** benefits and want us to inform other members.



When we try these products, we find most of them do indeed work! After we assay these products, we disappointingly find out **why** they are so effective.

It turns out that unscrupulous supplement makers are spiking herbal preparations with **prescription drug** ingredients found in Viagra®, Levitra®, or Cialis®.

So when we started getting calls about another “natural” male sex product, we were skeptical. We were impressed that five different **clinical studies** documented the efficacy of the nutrient combination, but we wondered, is this just another drug-spiked product **pretending** to be a dietary supplement?

As expected, we observed the same remarkable benefits reported in the clinical studies. What amazed us, however, was that our assays did not detect any prescription drug residue in this supplement.

Based on its underlying mechanisms of action—backed by solid scientific data—it would appear that this nutrient combination not only produces a rapid **improvement** in male sexual function, but may also confer significant benefit to the **vascular system** as well.

Erectile dysfunction is often associated with coronary artery disease.<sup>1</sup>

A nutrient formula that improves male **erectile capability** may very well protect against heart attack and stroke as well. This article describes the science behind this **drug-free** male sex enhancer.

#### ERECTILE DYSFUNCTION ASSOCIATED WITH VASCULAR DISEASE

Mainstream doctors generally resort to one of three FDA-approved prescription drugs (Viagra®, Cialis®, or Levitra®) to treat patients suffering from mild erectile dysfunction (ED)—with mixed results. As Mayo Clinic professor of urology Dr. Ajay Nehra recently told the *New York Times*, “the medications do not work for about half of the men with ED.”<sup>2</sup>

Although these drugs may help some men with ED to achieve *temporary* erections sufficient for sexual activity, they do nothing to treat **chronic endothelial dysfunction**, one of ED’s stealth causes.

The unfortunate reality is that **many aging men remain unaware of the link between ED and vascular disease**. They go to their doctors seeking help for sexual dysfunction, get a prescription, and leave with no idea of the creeping health dangers that may lie in store for them.

These dangers are real. “Erectile problems may show up about three years before a cardiovascular event such as a heart attack or stroke,” Dr. Ira Sharlip reported in the same *New York Times* article.<sup>2</sup>

Prescription drugs for ED can cost as much as **\$15 per pill**.<sup>2</sup> They are often accompanied by an array of side effects ranging

from indigestion,<sup>3</sup> flushing,<sup>4</sup> blurred vision,<sup>5-7</sup> hearing loss,<sup>8,9</sup> congestion,<sup>10</sup> and headache<sup>11</sup> to more serious health problems, from neurologic disorders<sup>12</sup> to heart attacks.<sup>3,13</sup>

These drugs provide short-term relief to ED sufferers by relaxing the smooth muscles that line the arteries, thus increasing blood flow into arteries that supply the penis. In those instances when ED is the result of **plaque buildup** in penile arteries, these drugs offer no *long-term* benefit.

For men interested in achieving optimal health—including dynamic sexual health—a better option is now available.

## A UNIQUE STRATEGY TO SUPPORT ENDOTHELIAL HEALTH—AND RESTORE POTENCY

Researchers have developed a unique natural strategy for management of erectile dysfunction that includes a blend of **Pycnogenol®** (French maritime pine bark extract) and **L-arginine aspartate**, an amino acid chelate; combined with **icariin**, a flavonoid compound used in Chinese herbal medicine.

The interaction of these three ingredients creates a **unique strategy** that promises to tackle erectile dysfunction from multiple angles.

The nutrients' *underlying mechanisms of action* are innovative yet elegantly simple. Here's how it works: to get an erection, you need adequate blood flow. This requires the relaxation of the smooth muscle in the arteries of the penis. The chemical compound **nitric oxide** triggers this process of relaxation, increasing the blood flow to the penis required for an erection.



Endothelial cells are responsible for **nitric oxide** production. They release *nitric oxide synthase*, an enzyme that catalyzes the production of **nitric oxide** from L-arginine. This process is essential to maintaining an erection. Dysfunctional endothelial cells, disabled by plaque buildup, can no longer produce enough of this enzyme.<sup>30</sup>

**Pycnogenol®** stimulates endothelial *nitric oxide synthase* to produce nitric oxide in the artery linings from the amino acid **L-arginine**, yielding sufficient bioactive nitric oxide to maintain an erection.<sup>31</sup> At the same time, **icariin** acts to *block* the enzyme responsible for causing erections to subside, known as phosphodiesterase-5 (PDE5).<sup>32</sup>

Interestingly, these nutrients not only promote erections, but also *enhance* male fertility and endo-thelial health. In other words, **numerous** distinct modes of action work together to produce a broad array of clinically proven health benefits. Meanwhile, prescription erectile dysfunction drugs such as

Viagra® support penile erection primarily by blocking the action of PDE5, without delivering any other benefit.

## PYCNOGENOL® AND L-ARGININE ASPARTATE: A CLINICALLY PROVEN, LONG-TERM ALTERNATIVE TO ED DRUGS

The efficacy of Pycnogenol® and L-arginine aspartate has been tested in **five independent clinical studies**. All of these studies showed that male sexual function was restored during supplementation with these ingredients.<sup>33-37</sup> Patients also reported an increase in sexual dreams and fantasies and more frequent morning erections. Their partners noted higher sexual interest and enhanced sexual performance.<sup>38</sup>

The first clinical trial to report successful treatment of erectile dysfunction with Pycnogenol® and L-arginine aspartate involved 40 men between 25 and 45 years of age suffering from mild ED. After treatment with arginyl aspartate (which provided the equivalent of 1.7 g L-arginine per day) for one month, only 2 patients (5% of all patients) experienced normal erections. **During a second month of treatment, 80 mg Pycnogenol® per day was added to the arginine regimen and yielded a significant improvement, with 32 patients (80%) enjoying normal erections.** A third month's treatment with L-arginine, together with an increased amount of Pycnogenol® (120 mg per day), further increased the number of patients with restored normal erectile function. At the end of the trial, 37 patients, equivalent to **92.5%** of all participants, achieved normal erectile function.<sup>35</sup>

- A blend of Pycnogenol® and L-arginine aspartate, combined with icariin, work together to restore healthy endothelial function and promote optimal sexual performance.
- This nutrient combination promotes healthy erections *without* the adverse side effects associated with drugs prescribed to treat erectile dysfunction.



- Prescription drugs can temporarily restore erectile function for some individuals, but they do *not* treat chronic endothelial dysfunction, an underlying cause of heart disease, peripheral artery disease, diabetes, and erectile dysfunction.
- **Five clinical studies** have found that Pycnogenol® and L-arginine aspartate work together to restore sexual function, enable erections, boost libido, performance, and sperm motility, viability, and quantity.
- Pycnogenol®, L-arginine aspartate, and icariin promote the synthesis of nitric oxide, which is essential for healthy vascular function, providing body-wide benefits.
- Icariin herbal extract act as a PDE5-inhibitor, the same mode of action as Viagra®, Cialis®, and Levitra®. Icariin has been shown to enhance the production of nitric oxide in human endothelial cell culture and in animal models, and exhibits testosterone-like activity.

## WHAT YOU NEED TO KNOW: A NATURAL APPROACH TO ERECTILE DYSFUNCTION

A second clinical study examined 50 middle-aged men with low testosterone levels who suffered from ED as well as from poor fertility due to impaired sperm motility and morphology.<sup>36</sup> Men were given 3 g L-arginine aspartate and 120 mg Pycnogenol® plus 120 mg testosterone undecanoate over a period of 11 months. A statistically significant **76%** of men achieved **normal sexual function** and this effect was **sustained** during the entire treatment period. The researchers found that this treatment improved sperm quality and quantity at the end of the 1-year treatment and an astounding **40%** (20 of 50 patients) achieved fertilization.

A third study—this one a randomized, double-blind, placebo-controlled, crossover study—evaluated the effects of Pycnogenol® and L-arginine aspartate on spermatozoa parameters in 50 middle-aged men diagnosed with infertility.<sup>37</sup> Investigators found improvement of sperm quality in all participants, with better results in younger men. Study results confirmed that **this treatment improved sperm parameters in men with infertility.**

A fourth clinical study, which used a randomly allocated, double-blind, placebo-controlled, crossover design, examined 50 middle-aged men with mild to moderate erectile dysfunction who were treated for one month with placebo or with Pycnogenol® and L-arginine aspartate.<sup>33</sup> Study participants recorded their sexual function/dysfunction in diaries. Investigators monitored testosterone levels and endothelial nitric oxide synthase levels along with routine clinical chemistry. Treatment with Pycnogenol® and L-arginine aspartate for one month restored erectile function to normal, and intercourse frequency doubled. Investigators found that **endothelial nitric oxide synthase in spermatozoa and testosterone levels in blood increased significantly**, while blood cholesterol levels and blood pressure were lowered.

The fifth clinical study used a randomly allocated, double-blind, placebo-controlled, crossover design.<sup>34</sup> It examined 50 infertile men who were treated for one month with placebo or Pycnogenol® and L-arginine aspartate. Investigators tested semen samples at four-week intervals and found that **treatment with this formula significantly increased semen volume, concentration of spermatozoa, percentage of motile spermatozoa, and percentage of spermatozoa with normal morphology compared with placebo treatment.** Intake of Pycnogenol® and L-arginine aspartate for one month restored the fertility index to normal values. After treatment, the fertility index decreased again to infertile status. No adverse events were reported.

Researchers believe that improving the quality of spermatozoa from infertile status to a normal fertility index could be caused by two mechanisms: the first is that Pycnogenol® in combination with L-arginine aspartate inhibits the peroxidation of the lipid membrane of spermatozoa, thereby improving the morphology and motility of spermatozoa. The second action could be that these ingredients enhance sperm motility and function by stimulating the activity of endothelial *nitric oxide synthase*. Both mechanisms, perhaps acting simultaneously, have been shown to improve the quality of spermatozoa.

## ERECTILE DYSFUNCTION LINKED TO *ENDOTHELIAL* DYSFUNCTION AND AGE

The vascular endothelium is the thin layer of cells lining the interior surface of blood vessels throughout the entire circulatory system. Endothelial cells are involved in many aspects of vascular function.



Endothelial *dysfunction* leads to constriction of blood vessels, inflammation, and increased tendency toward blood clotting. It is associated with the major forms of **cardiovascular disease**, **peripheral artery disease**, **diabetes**, **chronic renal failure**, and **erectile dysfunction**.<sup>14,15</sup>

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The aging process leads to physiological changes in male sexual activity, including **erectile dysfunction (ED)**, **reduced libido**, and **loss of fertility**.<sup>16</sup> A remarkable **52%** of men between the ages of 40 and 70 suffer some degree of erectile dysfunction. The likelihood of erectile dysfunction increases with age, and older men are more likely to suffer from more serious erectile dysfunction.<sup>17-19</sup>

**Changes in blood flow** to and from the penis are thought to be the most frequent cause of male erectile dysfunction.<sup>20</sup> Alterations of penile arterial endothelial cell function relate to arterial risk factors such as atherosclerosis and hypertension—health problems that occur more frequently as men age.

Normal endothelial function depends on nitric oxide (NO) release by endothelial cells.<sup>21</sup> With age, arterial production and availability of NO declines.<sup>22</sup> One reason may be that an altered form of the amino acid arginine, called **ADMA** (asymmetric dimethylarginine) competes with L-arginine, the precursor of nitric oxide, thus inhibiting NO production and leading to **endothelial dysfunction** and **atherosclerotic disease**.<sup>23,24</sup> This makes adequate ingestion of arginine all the more important as we age.

Numerous conditions aside from endothelial dysfunction can also contribute to erectile dysfunction. Such conditions include: diabetes,<sup>25</sup> prostate disease,<sup>26</sup> prescription drug use,<sup>27</sup> smoking,<sup>28</sup> and psychological and physical stress.<sup>29</sup>

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### ICARIIN: SUSTAINING ERECTILE FUNCTION

Icariin is a flavonoid compound extracted from plants in the *Epimedium* family, which are also known as Yin Yang Huo. Chinese medicine practitioners claim that these plants produce aphrodisiac effects and help restore erectile function.

Researchers agree there is good evidence that icariin is the primary active component of *Epimedium* extracts. Like Viagra®, Cialis®, and Levitra®, icariin blocks the action of PDE5, the enzyme that causes erections to subside.<sup>32,39-41</sup>

Icariin enhances the production of nitric oxide in human endothelial cell culture and in animal models.<sup>42-44</sup> Additionally, scientists have noted that icariin behaves similarly to testosterone—a significant feature, since testosterone is crucial for healthy sexual function.<sup>45</sup> Animal research has shown that administration of *Epimedium* extracts improves erectile function in aged rats.<sup>46</sup>

Together, these multiple mechanisms of action suggest that icariin can help support healthy erectile function.

**THE ROLE OF NITRIC OXIDE IN PENILE ERECTION AND VASCULAR HEALTH**

- Promote a healthy immune system.<sup>55</sup>
- Play a critical role in blood clotting through its modulation of vascular tone, coagulation, fibrinolysis, and overall endothelial and vascular smooth muscle function.<sup>56</sup>

Nitric oxide can't be taken in supplement form because it is a gas. However, nutritional ingredients such as Pycnogenol®, Larginine aspartate, and icariin can together increase production of nitric oxide in the endothelium, and in doing so, may promote general health as well as improved erections, libido, performance, and male fertility.

Nitric oxide (NO) is a short-lived gas that acts as a signaling molecule in the body. Among its many other functions, NO acts in concert with acetylcholine and prostaglandins as a neurotransmitter for sexual stimulation and to dilate the small arteries in the penis that support erection.<sup>47</sup>



In addition to its role in erectile function, scientists now believe that **NO deficiency may contribute to numerous degenerative diseases such as cardiovascular disease.**

The arterial endothelium uses NO to signal surrounding smooth muscle cells to relax, thus dilating arteries, increasing blood flow, and maintaining normal blood pressure. NO, among its many roles, performs the following functions:

- Relax and widen blood vessels.<sup>48</sup>
- Facilitates the development and maintenance of erectile function.<sup>49</sup>
- Acts as a neurotransmitter that is involved in long-term memory.<sup>50-52</sup>
- Modulates the release of neurotransmitters.<sup>53</sup>
- Maintain blood pressure within the normal range.<sup>54</sup>

## CONCLUSION

Erectile dysfunction not only compromises intimate relationships; it can *also* be a harbinger of serious and potentially deadly cardiovascular disease.

Scientists have found that certain nutrients not only restore **erectile performance** but also improve **endothelial function** caused by **oxidative stress** and diminished levels of nitric oxide. Studies and clinical trials have shown that these nutrients can potentially reduce the risk of cardiovascular disease and erectile dysfunction.

In addition to their ability to correct erectile dysfunction, these nutrients have been shown to **improve libido** and **boost sperm viability, quantity, and motility**, all of which significantly increase male fertility. Drugs prescribed to treat ED have no positive effect on fertility.

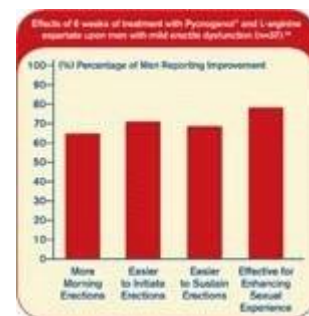
Individually and collectively, these nutrients promote systemic endothelial health and provide a consistent supply of compounds that can prevent and reverse erectile dysfunction. An estimated

Image

**330 million men** worldwide will be facing vascular disease and erectile dysfunction in the near future. These clinically proven nutrients offer welcome benefits of vascular health and improved sexual function to millions of men and their partners.

*If you have any questions on the scientific content of this article, please call a Life Extension® Health Advisor at 1-866-8643027.*

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