Erectile dysfunction (ED) is a widespread problem affecting many men across all age groups and it is more than a serious quality of life problem for sexually active men. It is defined as the persistent inability to maintain or achieve a penile erection sufficient for satisfactory sexual performance.

ED concerns 52% of men between 40 and 70 years of age. Over 30 million men suffer from ED in the U.S and it is becoming a public health issue. The prevalence of ED is very high and is expected to raise considerably over the next 25 years, impacting more than 300 million men by 2025.

**Physiology of penile erection**

The penile erectile tissue, specifically the cavernous smooth musculature and the smooth muscles of the arterial walls, plays a key role in the erectile process. In the flaccid state, these smooth muscles are tonically contracted, allowing only a small amount of arterial flow. Sexual stimulation triggers release of neurotransmitters from cavernous cells. This results in relaxation of the smooth muscles (Fig. 1).

![Diagram of penile erection]

The importance of smooth muscle relaxation has been demonstrated in animal and human studies. Nowadays, it is well known that Nitric Oxide (NO) plays a critical role in erectile function as it is the cornerstone of vasodilation mechanism allowing penile erection. NO is formed from the precursor amino acid, L-arginine, by enzymatic action.

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**Enostim™: new natural solution for men's health**
of NOS, and more specifically endothelial NOS (eNOS). The NO pathway is thus the most targeted lever to help organic’s causes of erectile dysfunctions⁴.

**A new natural solution in sexual enhancement: Enostim™**

It has recently been demonstrated that some substances offered for sexual enhancement and labelled as “natural” or “herbal” can represent a challenge to the public health system as they can have important psychoactive properties that cause unwanted harm and addictive behaviours⁵.

Nexira developed a new natural and safe solution in sexual health: Enostim™ is a unique and proprietary formulation of active ingredients, apple and grape polyphenols, enriched with saffron. It has been specifically developed to offer a natural and safe solution for erectile dysfunction.

**Enostim™ offers three synergistic benefits:**

- **Stimulation of Nitric Oxide production**

  Preliminary studies (ex vivo and in vitro) have highlighted Nexira’s proprietary formulation (NPF) specific vasodilating properties. The first study conducted by Nexira showed NPF dilating effect on the endothelium in isolated rat aortas. In this ex vivo study, increasing concentrations of NPF were added to the isolated cross-sections of rat aortas. Results obtained showed that NPF exerted a dilating effect on the endothelium of isolated rat aorta up to 50% (Fig. 2).

![Figure 2: NPF stimulates endothelial-dependent vasodilation by nitric oxide synthesis.](image)

These vasodilating properties have been confirmed and demonstrated by two other studies in human umbilical vein endothelial cells (HUVEC), which show that the addition of NPF significantly boosts nitric oxide (NO) production by 24% and induces 43% endothelial nitric oxide synthase (eNOS) activation. The phosphorylation of the amino acid ‘Serine 1177’ was used as a specific marker of the eNOS activation.

- **Saffron benefits**

  Since antiquity, saffron (flower stigmas from Crocus sativus) has been used in traditional medicine. It was already consumed as an aphrodisiac by ancient Persians and Egyptians. More recently, saffron’s ability to prevent erectile dysfunction has been demonstrated in several clinical studies⁸,⁹.

  In Europe, saffron benefits from the pending claim (ID 2427): “Improves erection and relaxes muscles” (Styli cum Stigmatis Crocus sativus: 28 mg/day).

- **Protective effects**

  a, Nitric Oxide protection: NO has a short lifespan and can be degraded by superoxide free radical. EnoSTIM™ antioxidant molecules showed in a in vivo study¹⁰, its potential to specifically protect NO from oxidation decreasing oxidative stress by 74%.

  b, Vascular inflammatory protection: unlike other products, a clinical study⁹ have shown a preventive effect of polyphenols on inflammatory scores also implied in atherosclerosis

  ![Figure 3: summary of Enostim™ mechanism and studies results](image)

  ![Figure 4: Clinical study – anti-inflammatory effect](image)
(on blood sampling after 28 days, 34 people cross-over): -10\% inflammatory markers (chemokine* – p< 0.05) : see Fig. 4. Atherosclerosis could be the first risk factor of ED.

*Chemokines (MCP1, MIF) are a family of cytokines (inflammatory markers) specialized in guide the migration of immune cells through blood wall

Applications and dosage
Thanks to its efficient vasodilation properties and protective effects, Enostim™ is a natural and safe alternative in food supplements for sexual enhancement (tablets, capsules). The recommended dosage is from 300 to 600 mg/day.

References
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