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FILE: ■Erectile Dysfunction
■Botanicals: Erectile Dysfunction
■Dietary Supplements: Erectile Dysfunction

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RE: Review of the Use of Botanicals for Treating Erectile Dysfunction

MacKay D. Nutrients and botanicals for erectile dysfunction: examining the evidence. *Alt Med Rev.* 2004;9(1):4–16.

Introduction

Erectile dysfunction (ED), which is defined as "the inability to achieve or maintain an erection sufficient for satisfactory sexual function," affects roughly half of all U.S. men aged 40–70 years. The National Institutes of Health regards ED as an important public health problem. Furthermore, over the next 25 years, the prevalence of ED worldwide is expected to more than double. Although most men with ED do not seek medical treatment, the number seeking treatment has increased since 1998, when oral sildenafil (Viagra) became available as an efficacious treatment for ED. However, because sildenafil is expensive and its long-term benefits and risks have not been established, researchers have begun investigating the use of naturally occurring compounds for treatment of ED. The present review examines the efficacy of several of natural agents.

Physiology of Erection

An erection represents the complex interplay between excitatory and inhibitory forces and involves psychological, neural, and vascular responses. Excitatory signals caused by sexual stimulation lead to the release of nitric oxide (NO) gas from the axons of parasympathetic nerves. The released NO gas enters the smooth muscle cells that line the arteries of the spongy erectile tissue, the corpus cavernosum, and activates guanylate cyclase. The action of guanylate cyclase increases cyclic guanosine monophosphate concentrations in the muscle cells, which relaxes these muscles in the penile arteries and allows more blood to enter the penis. The subsequent engorgement of the corpus cavernosum with blood compresses the penile veins; as a result, blood becomes trapped in the corpus cavernosum, and an erection is produced. The penis is kept in the flaccid state by the activity of the sympathetic nervous system.

Testing Substances for Effects on Erectile Activity

There is no uniform method for testing substances for their erectile activity. In one common method, the relaxation response of isolated smooth muscle from the rodent corpus cavernosum is measured after the addition of a test substance. Other animal methods involve observing the copulatory behavior of rodents given different doses of a test substance. Animal models, however, are inadequate because the cerebral aspects of human sexual activity are not addressed. Randomized, controlled human trials are necessary to show that a test substance plays a causal role in erection.

Natural Agents for Treatment of ED

The natural agents discussed in the present review are arginine, yohimbine (from *Pausinystalia johimbe*), Asian ginseng (*Panax ginseng*), maca (*Lepidium meyenii*), ginkgo (*Ginkgo biloba*), dehydroepiandrosterone (DHEA), and tribulus (*Tribulus terrestris*). L-Arginine is the precursor of NO, and impairment of endothelial L-arginine–NO activity is common to both ED and atherosclerosis. About three-fourths of men with ischemic heart disease also have ED. The results of human clinical trials of L-arginine for treatment of ED are mixed, but most studies found positive results. Yohimbine (an alkaloid derived from the bark of the yohimbe tree *Pausinystalia johimbe*, and not to be confused with the crude herb) is an α -2-adrenergic receptor antagonist. Although few controlled human trials of yohimbine for treatment of ED have been conducted, a systematic review of the most rigorous trials concluded that yohimbine was safe, more effective than placebo, and an appealing therapeutic option because of its cost and oral administration. The results of studies on Asian ginseng suggest that it may improve erectile function by increasing NO concentrations. Maca is a root vegetable of the mustard family that is grown in the Peruvian Andes. Studies in rodents and a single human study, which was a randomized, double-blind trial, suggest that maca may enhance male sexual function. Although the results of studies on ginkgo are mixed, ginkgo appears to ameliorate sexual dysfunction induced by the use of antidepressants. Because an inverse relation between ED and serum DHEA concentrations was recently observed, the use of oral DHEA or of precursors of DHEA, such as protodioscin from tribulus, for treatment of ED has begun to be investigated. However, no well-controlled clinical trials have yet been conducted.

Conclusion

Although adequate clinical support for the use of these natural agents to treat ED is minimal, the available research suggests that they do have a modest effect. The author recommends that L-arginine, yohimbine, Asian ginseng, ginkgo, and maca be used as part of an overall program for managing ED.

—Darren Early

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