When science meets culture: the prevention and management of erectile dysfunction in the 21st century

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Abstract

Traditionally, the term "impotence" has been used to signify a male's inability to attain and maintain an erection. Impotence, in most circumstances, is more precisely referred to as erectile dysfunction (ED). An estimated 10-20 million men suffer from the condition. However, this number is expected to increase dramatically, with an estimated figure of 322 million by 2025. Even though the prevalence of ED increases with age, it must be stressed that ageing itself is not a cause of ED as it is associated with metabolic syndrome, cardiovascular disease, diabetes mellitus and other noncommunicable diseases, such as obesity. Many patients self-medicate by resorting to local herbs and over-the-counter (OTC) preparations to manage ED. Because of the increasing number of men seeking treatment for ED, there is a need to assess the safety and biological plausibility of some of the readily available preparations (as well as food and drink) that reportedly enhance sexual desire or performance. For the purpose of this review, the aphrodisiacal qualities of freely available foods and natural OTC products will be reviewed and evaluated. These include oysters, alcoholic beverages, chocolate, chilli, *Epimedium* extract (horny goat weed), *Panax ginseng*, *Ginkgo biloba*, *Tribulis terrestris, Eriosema kraussianum* and Spanish fly (cantharides).

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Introduction

It is now well recognised that sexual health is important to overall health and well-being.[1] Sexual performance carries a sense of identity and self-esteem for men and results in anxiety when sexual ability declines.[2] Despite substantial progress in the treatment of erectile dysfunction (ED) and available treatment facilities throughout the world, low treatment-seeking behaviour could be attributed to the sensitivity and social stigma associated with ED,[3] as well as the cost, lack of availability and side-effects that are linked to pharmacological treatment.[4,5] It is estimated that the global prevalence of ED will be 322 million by the year 2025.[6,7] According to Fazio and Brock,[8] the ageing global population, decreasing social stigma associated with ED, and increasing availability of effective oral treatment, has increased the number of patients presenting with this condition.

In a study conducted on Ethiopian men with diabetes, 79% of patients never complained about ED.[9] However, it is a common secondary side-effect of a number of noncommunicable diseases. Motorsi et al[10] explain that ED exists approximately 39 months before cardiac events and the relationship between cardiovascular disease (CVD) and ED has been firmly established.[11-13] The presence of ED predicted the onset of CVD events in men with type 2 diabetes without clinically explicit CVD.[14]

Evidence generated by epidemiological studies found modifiable risk factors, such as physical activity and leanness, to be associated with a reduced risk for the development of ED. Obesity was found to be a risk factor for its development.[5] Logistical regression analysis indicated fasting blood glucose levels and waist circumference measurement to be the most important predictors of the development of ED. Therefore, it would seem that metabolic syndrome (MS) is an additional risk factor for the development of ED.[15-17] A review that documented the relationship between MS and ED confirmed a reciprocal relationship in that MS is associated with ED, while MS can be viewed as a risk factor for the development of ED.[18] The prevalence of ED in patients with diabetes varies, but can be as high as 90%, depending on the assessment method[19-21] as the risk of ED increases with the duration of the condition and with increasing levels of glycosylated haemoglobin.[20,22]

The prevalence of ED increases with age. The prevalence of complete or severe ED was 5% and moderate ED 17% in a large cross-sectional, community-based survey conducted on men aged 40-49 years of age.[23] The prevalence increased to 15% and 34% respectively, in older men aged 70-79 years of age. 9.6% of the subjects reported complete ED.[24] In 2000, the overall prevalence of ED in the same study population was re-estimated to be 44%.[25]

However, ED cannot be viewed as an inevitable result of ageing, as 54% of the healthy and 41% of the diseased men in the oldest age category of the study sample (65-70 years) did not complain of moderate or severe ED.[26]

Ischaemic strokes and smoking are associated with ED. (The prevalence of ED is twice as high in smokers as it is in non-smokers).[27] Prescription, as well as non-prescription medication, may also cause or contribute to ED in 25% of treatment-seeking men.[28] The medication in question may include diuretics, antihypertensive and cholesterol-lowering medication, antidepressants and tranquilisers.[8,29]

The risk factors for ED are multifactorial and complex, and in most instances inter-related to lifestyle.[27,30-32] In addition, not all risk factors follow the same mechanism of causation.[32] MS associated with a Western lifestyle, as well as endothelial dysfunction and downregulation of nitric oxide synthase on a biochemical level, is suspected to be a leading cause of ED.[31] CVD, in general, is also associated with possible endothelial dysfunction in penile vasculature.[32] Some of the risk factors associated with CVD are also linked to the onset of ED, such as smoking, that leads to possible endothelial dysfunction, associated atherosclerosis and sympathetic overactivity.[27] Diabetes mellitus promotes the onset of ED via vasculopathy from endothelial dysfunction and autonomic neuropathy.[32] Ischaemic strokes follow a different pathway, causing disruption of descending neural control of the proerectile processes.[32] The contribution of depression and stress, even though they are significant contributors, is not very well understood.[32]

In most instances, the treatment of ED relies on lifestyle interventions, such as diet, exercise and weight loss in the case of MS, cessation of smoking, counselling, and appropriate glycaemic control through diet.[27,30-32] In other instances, ED is treated in combination with drugs, such as the cautious use of phosphodiesterase type 5 (PDE5) inhibitor in patients who suffer from vascular disease.[29]

An estimated 34.8% of men aged 40-70 years have moderate to complete ED.[33,34] A modern lifestyle and environmental factors, such as pollution, have resulted in an increase in male infertility in almost every part of the world.[35] In South Africa, male infertility accounts for 40% of total infertility or failure to conceive.[36]

In a feature published in the popular magazine, *Men's Health*, male readers were educated on how to assess their risk of developing ED. Readers were referred to a case study of a man aged 31 years who did not have ED problems yet, but a suggestion was made that his "poor diet, sedentary lifestyle and family history would eventually catch up with him", and if he didn't start exercising or eating properly his "sex life expectancy" would be an estimated 10 years.[37] The concept of sexual well-being used to focus on sexually transmitted disease and reproductive anxieties, but has broadened to (and has perhaps become primarily fixated on) a concern with the maintenance and enhancement of sexual desire and performance.[38]

Pharmacological management

The most commonly used therapy for the treatment of ED includes oral therapy with PDE5 inhibitors, such as sidenafil (Viagra®). However, some patients may not be able to tolerate PDE5 or may require a lower dose because of side-effects relating to vasodilation. As a result, oral therapy has the potential to induce hypotension, cause headaches, flushing, dyspepsia, gastrointestinal symptoms and nasal congestion, blurred vision, a rash and back pain.[5,8,29,39] An additional concern, when considering the frequent coexistence of ED and CVD, is that PDE5 may result in coronary ischaemia.[39]

Nutritional and lifestyle prevention and management

The Health Professional's Follow-up study[6] found several modifiable lifestyle factors, such as physical activity and leanness, to be associated with the maintenance of good erectile function. For example, men with a body mass index (BMI) of more than 28.7 kg/m^2 were likely to have a 30% increased risk of developing ED, as opposed to those with a BMI of 25 or lower.

Cross-sectional studies[40] have also found higher levels of physical activity to be associated with a significant reduction in the prevalence of ED, and that the prevalence of ED directly relates to overweight and obesity. A baseline BMI $\geq$ 28 kg/m^2 significantly predicted the development of ED in the long term, while initially overweight subjects remained at a high risk of developing ED, despite follow-up weight loss.[30] A large population-based survey conducted in Brazil[26] found that the prevalence of ED was inversely related to the level of physical activity.

Subjects with cholesterol- and fat-rich diets have been found to be more likely to develop ED during follow-up than those with more balanced diets. In addition, a lower intake of vegetables, fruit and nuts and a lower ratio of monounsaturated to saturated fats was evident in men with ED.[41] Food intake that is more likely to be associated with an increased risk of the development of CVD tends to be higher in men with ED, whereas the intake of foods that are associated with a decreased risk of CVD tends to be lower.[42]

Although epidemiological evidence supports the role of lifestyle factors, limited data are available to suggest that the treatment of underlying risk factors and coexisting illness through weight loss, exercise, stress reduction and smoking cessation may improve erectile function.[27,30] A randomised trial on 110 obese men with moderate ED[31] which compared intensive lifestyle changes with an educational control, found that approximately a third of the subjects in the intervention group recovered normal erectile function during the course of the study, compared to less than 10% in the control group. Of a sample of middle-aged men with hypertension, those who achieved the highest levels of fitness and a reduction in blood pressure level were also more likely to show an improvement in sexual function. Therefore, these studies indicate that significant improvements in sexual function can be expected in patients who implement intensive lifestyle changes, including weight loss and rigorous exercise, and that are associated with positive changes in weight, fitness levels and other markers for cardiovascular health.[43]

Esposito et al[42] also assessed the effect of changes in lifestyle on subjects with ED or who were at an increased risk of developing ED. Men who were randomly assigned to the intervention group (n = 104) received detailed advice on how to reduce body weight, improve their dietary quality and increase physical activity, while men in the control group (n = 105) were given general information about healthy food choices, and general advice on how to increase their level of physical activity. The outcome was that there was a statistically significant improvement in erectile function score in the intervention group (p-value = 0.015). The effect of the intervention was that the restoration of erectile function was most pronounced in subjects who implemented comprehensive lifestyle changes. In addition, there was a strong correlation between the success score and the restoration of erectile function, thereby leading the authors to conclude that it is possible to achieve an improvement in erectile function in men at risk by means of a nonpharmacological intervention that targets weight loss and increased physical activity.[42]

The promotion of specific foods and traditional and herbal remedies that combat erectile dysfunction

Many patients self-medicate by resorting to local herbs and OTC preparations based on anecdotal evidence in an attempt to manage their ED.[2] Traditional remedies have been used to treat male reproductive disorders in South African men for many years.[44] In addition, alternative remedies, such as rhinoceros horn,[2,35,45] are a major cause for concern.[46] Because of the increasing number of men seeking treatment for ED, there is a need to assess the safety and biological plausibility of some of the OTC preparations, as well as food and drinks, that reportedly enhance sexual desire and/or performance.

The word "aphrodisiac" derives from the word "Aphrodite", the Greek goddess of beauty, fertility and love, while an aphrodisiac refers to any food, drink or drug that increases sexual desire or arouses sexual response.[47] The two main types of aphrodisiacs include psychophysiological stimuli, such as visual, tactile, olfactory and aural, as well as preparations that include food, alcoholic drinks and love potions. Historically, many natural substances have been known to possess aphrodisiac powers or qualities, and have been widely used in Africa and Europe.[45] These include *Panax ginseng* (ginseng), *Epimedium* extract (horny goat weed), the dried remains of the Mediterranean cantharides beetle (Spanish fly) and oysters.[2,48] In the USA, the only Food and Drug Administration (FDA)-approved natural product for erectile dysfunction is yohimbine, an alkaloid isolated from the bark of the yohimbe tree (*Pausinystalia yohimbe*)

For the purpose of this review, the aphrodisiac qualities of foods and commercially available products in South Africa, such as alcoholic beverages, chilli, chocolate, oysters, cantharides, *Epimedium* extract, *Ginkgo biloba, Panax ginseng and Tribulis terrestris* will be reviewed and evaluated. The foods and products are summarised in Table I.

Table I: Freely available foods and over-the-counter natural ingredients that are touted to have aphrodisiac properties

Product	Description	Mechanism	Dosage
Alcohol consumption	Although not promoted as an aphrodisiac, alcohol is known to reduce inhibitions, thereby promoting sexual intercourse.[49] Male alcoholics often report ED after the acute ingestion of large amounts alcohol, while in ED sufferers, alcohol is a frequent phenomenon.[50]	The pharmacological management of ED with PDE5 inhibitors centres around a mechanism whereby levels of PDE5 inhibitors and nitric oxide are increased. These effects result in relaxation of the smooth muscle in the corpus cavernosum of the penis.[8,27,39] Research conducted by Wallerath et al[51] revealed that the increase in eNOS expression and activity brought about by red wine from France (and probably other regions), may contribute to the beneficial effects of this beverage on the cardiovascular system.	N/A
Cantharides (Spanish fly)	Spanish fly (also referred to as cantharides) is the common name for a variety of blister beetles that are usually black or bronze green in colour.[52]	The beetles release an irritating substance, cantharidin, that acts as a powerful mucosal irritant and vesicant (blister inducing),[52] causing irritation of the urethra, with resultant vascular congestion and inflammation of the erectile tissue.[53]	Toxic. Not considered to be safe in any quantity[54]
Capsicum frutescens (chilli)	Chillies are the fruit of the plant *Capsicum frutescens* and are touted to have aphrodisiac qualities.[55,56] The spiciness of chillies is measured in Scoville heat units, which are indicative of the amount of capsicum present.[45]	This alkaloid stimulates chemoreceptor nerve endings in the skin, especially the mucous membranes.[55,57]	N/A
Chocolate	Cocoa and chocolate are referred to as an aphrodisiac,[58-61] Dillinger et al[61] cites Diaz del Castillo (1590), a Spanish conquistador who landed on the east coast of Mexico after Hernandos Cotéz (1519): "from time to time Montezuma's (ruler of the Aztecs) guard brought him, in cups of pure gold, a drink made from the cocoa plant, which they said he took before visiting his wives".	Bioactive substances in chocolate that may influence behaviour include tyramine and phenylethylamine,[59,62] which are similar to amphetamine.[62] The unsaturated N-acylethanolamines in chocolate, which may activate cannabinoid receptors or increase endocannabinoid levels, are associated with increased sensitivity and euphoria.[60,63] In addition, the taste and fatty nature of chocolate is reported to stimulate the hypothalamus, thereby resulting in pleasurable sensations and increasing brain serotonin (5-hydroxytrytrytamine) levels.[60,63]	N/A

Epimedium extract (horny goat weed)	There are approximately 52 *Epimedium* species of herbaceous flowering plants, also known as rowdy lamb herb, bishop's hat or horny goat weed,[64] that have been used to treat ED for over 2 000 years.[65]	Icariin, the active ingredient,[66] increases levels of nitric oxide and PDE5 activity. This relaxes the smooth muscle in the corpus cavernosum[67] as icariin is able to inhibit PDE5 and PDE4 in vitro.[66] Liu et al[68] found that oral treatment with icariin elevated intracavernosal pressure,[69,70] while Ma et al[65] reported that *Epimedium* may have the potential to treat ED as icariin has been screened for pharmacological activity in vivo and vitro.[65] It has also been reported that *Epimedium* may increase testosterone levels and thyroid hormone levels. However, to date, no human studies have been conducted.[65]	200-400 mg extract/day[65]
Eriosema kraussianum ("African viagra")	Zulu traditional health practitioners have claimed that the roots of *Eriosema kraussianum* and other *Eriosema* species (Zulu indigenous umbrella name of *uBangalala)* are effective in treating ED.[47]	Isolation of five pyrano-isoflavones from *Eriosema kraussianum* found that the most active of the compounds had an activity equal to 75% of that found in Viagra® when tested in rabbit models.[47]	300 mg/day[47]
Ginkgo biloba	**Ginkgo biloba** is one of the oldest living tree species and its leaves are among the most extensively studied herbs in use today.[71-75]	*Gingko biloba* contains flavonoid glycosides (myricetin and quercetin), as well as terpenoids that have been used pharmaceutically.[71] Properties include the exhibition of reversible, nonselective monoamine oxidase inhibition, as well as the inhibition of reuptake at the serotonin, dopamine and norepinephrine transporters.[72] Despite conflicting results, *Ginkgo biloba* extracts may improve blood circulation, including microcirculation in small capillaries.[73-75]	120 mg/day in divided doses[74,75]
Oysters	Oysters are propagated as being an excellent aphrodisiac as they are a rich source of taurine which has a cardioprotective effect and also plays a role in nerve transmission.[2]	The reason for its classification as an aphrodisiac is not very clear.[76] Some authors[34,35,45,48] argue that the alkaloids in oysters stimulate the reproductive system and that they are a good source of zinc which is involved in the male reproductive system.	N/A
Panax ginseng (ginseng)	*Panax ginseng* is an adaptogenic herb, propagated as having the ability to serve as a source of energy, increasing testosterone levels and enhancing libido.[2,77]	The most commonly used type is Chinese ginseng *(Panax ginseng),* which contains steroids, peptides and triterpenoidal D-glucosides (specifically panaxsapogenin), and active ingredients referred to as tetracyclic triterpenoid saponins (ginsenosides).[64,77] *Panax ginseng* has been shown to induce relaxation of the corpus cavernosum in male rabbits[7,76,78,79] because of mediation by the release and/or modification of nitric oxide.[64,80] Jang et al[81] reported that the therapeutic efficacy alluded to by RCTs relates to an improvement in ED when compared to a placebo. Side-effects include insomnia, dermatitis and gastrointestinal disturbances.[76]	1-3 g/day[76]
Tribulis terrestris (puncture vine)	*Tribulis terrestris* extract has been used to treat ED in China and India for centuries.[82]	The benefits of the active ingredient, protodioscin, include the ability to act as a precursor of testosterone. The increase in intracavernosal pressure which confirms the proerectile property of *Tribulis terrestris* can be attributed to an increase in testosterone levels and the subsequent release of nitric oxide from the nerve endings in the corpus cavernosum.[82]	85-250 mg three times a day[82]

ED: erectile dysfunction, eNOS: endothelial nitric oxide synthase, N/A: not applicable, PDE5: phosphodiesterase type 5

which is native to tropical West Africa. Yohimbine hydrochloride increases libido, but its primary action is to increase blood flow to erectile tissue. Contrary to popular misconception, yohimbine has no effect on testosterone levels. Although FDA-approved, yohimbe has numerous side-effects and contraindications, including psychological disorders.

Conclusion

Globally, consumers are taking a more proactive role in their own health or disease management. A large proportion of consumers embrace alternative "holistic" treatments, particularly herbal or phytopharmaceutical products to treat a variety of conditions. There is a dearth of systematic scientific evidence of their efficacy and safety, when compared to synthesised chemical medicines. Standards have yet to be established by regulatory authorities with respect to the use of herbal medicines. Therefore, there is an urgent need for systematic research to assess the effect of these medicines in order to benefit both current users of herbal products and to contribute to the development of new therapeutic agents for the prevention and management of disease. In addition, there

is an urgent need for the protection of human health through the implementation of properly validated and analytical state-of-the-art, instrument-based methodologies which can chemically characterise and quantify the chief chemical constituents of the "remedy", as well as assure its quality and safety. Yet, it is clear from the body of scientific evidence that natural ingredients and some freely available foods can make a contribution to the traditional, nonpharmacological management of ED. However, in many instances, further research involving human subjects is required.

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