Introduction

Erectile dysfunction (ED) is defined as the persistent inability to attain and maintain an erection that is sufficient to permit satisfactory sexual performance (1). The current pharmaco-therapeutic research in ED focuses on underlying endothelial dysfunction as the root cause for ED and introduction of phosphodiesterase type 5 inhibitors to potentiate nitric oxide (NO) action and cavernosal smooth muscle vasodilation, has revolutionized modern ED treatment over the past two decades (2). In contrast to Western Medicine, the traditional and complementary medicine (TCM) aims at restoration and better overall bodily regulation with medicine to invigorate qi (energy) in vital organs such as kidney, spleen and liver; to enhance physical fitness, increase sexual drive, stabilize the mind and improve the overall situation resulting in natural and harmonious sexual life (3).

While Western medicine emphases the link between cardiovascular function and ED, TCM places importance on liver and kidney ailments as causative factor for development of ED. Western medicine involves a step-wise approach by targeting the relevant organ systems to treat various clinical symptoms; but TCM focuses on restoring the balance between various organs to achieve harmony.
and holistic approach to inner sense (4). The following article reviews our current understanding regarding the philosophical approach, and evaluates the evidence surrounding various ED therapies between mainstream Western medicine and TCM (see Table 1).

### Western medicine

**Principle of treatment**

In Western medicine approach, health and disease are clearly divided entities. The emphasis is on protection of the individual body from disease or how to replace the body’s lost functions. Antibiotic therapy is used to combat harmful bacteria during infections, exogenous synthetic hormones are used to replace hormone-deficient individuals and artificial prostheses are applied when an organ loses its functions. This is very different from the holistic Eastern approach where the treatment entity is taken as a whole, and the objective is to seek harmony between different bodily systems.

When it comes to scientific development, in Western medicine, an analytic approach is often used to identify and resolve medical challenges. A hypothesis is first derived through general observations of a phenomenon. A research plan is then carefully designed and data collected. Once sufficient data is collected, critical statistical evaluations are done and conclusions are drawn (4). Every aspects of a disease entity are studied from macroscopic to microscopic views, down to the cellular and molecular levels. The deep understanding of the role of cGMP-specific phosphodiesterase type 5 enzymes in ED and the use of phosphodiesterase-5 inhibitors in treatment of ED exemplifies the success of this approach.

**Pharmacotherapy: oral or intracavernous vasoactive agents**

The development of PDE5-inhibitors is a clear example of how Western medicine approached the problem of ED differently from Eastern medicine. The erectogenic effect of sildenafil (Viagra®) was discovered by accident when patients undergoing heart clinical trials reported better erections as a side effect after taking sildenafil. This observation led to further elucidation of the NO/cGMP signalling pathway and development of PDE5-inhibitors as a first-line therapy in ED (5).

Currently, there are four PDE5-inhibitors namely sildenafil, tadalafil, vardenafil and avanafil are approved for use in United States, with more expected to join the market. Udenafil and microdenafil are PDE5-inhibitors developed in Korea and Lodenafil carbonate from Brazil (6).

For patients who failed oral medical therapy or unable to tolerate the side effects, intracavernosal injection of vasoactive agents can often provide effective alternative. Various vasoactive agents such as alprostadil, papaverine or phentolamine have been used either as single agent or combination agents to potentiate the NO release and cavernosal smooth muscle vasodilation. However,
intracavernosal injection therapy has high attrition rate and can be associated pain especially with alprostadil injection (2). The practice of isolating compounds and understanding its pharmacological attributes before using it as a drug therapy has been a strength of Western medicine.

Mechanical and device-related therapy

Various devices have been developed to enhance penile erection without the common side effects of systemic vasodilation associated with pharmacotherapy. In fact some of these devices have a longer history than modern ED medicine.

Vacuum constriction and erection devices

The vacuum device is approved by USA Food and Drug Administration (FDA) for treatment of ED since 1982. Vacuum therapy (VT) works by creating a negative pressure environment around the penis through the use of a cylindrical housing attached to a pump mechanism, which can be manually-operated or battery-operated. Vacuum draws mixed arterial and venous blood into the corporal bodies and distends the corporal sinusoids to create an erect penis. If a pre-loaded constriction band is applied over the base of the penis to prevent outflow of blood and maintain tumescence for intercourse, it is considered a vacuum constriction device (VCD). It is recommended that the constriction band be removed within 30 mins to return the penis to its flaccid state, as prolonged application of the constriction band can compromise both arterial and venous blood flow (7). Some minor side effects associated with VCD are penile discomfort, coldness, numbness, bruising and pain on ejaculation. Major side effects such as penile skin necrosis, gangrene, urethral injury and Peyronie’s disease are very rare (8).

The same device is considered a vacuum erectile device (VED), when it is used to increase inflow of the blood to the penis without a constriction band. Regular use of VED in post-prostatectomy patient increases penile oxygenation and is accepted as a valid option in penile rehabilitation. Recent study reported transient increase in oxygenation to the glans penis and corporal bodies were detected by oximetry after VED was applied, providing proof for possible role for VED to counter the early penile hypoxia, cavernosal fibrosis and long-term ED after radical prostatectomy (9).

Penile vibratory stimulation (PVS)

Penile vibratory stimulator is a battery operated device with oscillating discs that can provide excitation of afferent penile nerves at various regulated frequency and amplitudes. PVS has been utilised to activate the ejaculatory reflex for patients with spinal cord injury above T10 seeking to collect retrogradely ejaculated semen in fertility treatment (10). The Viberect is a vibratory stimulation handheld device approved by FDA for treatment of ED. It is clamp-shaped with two oscillating discs facing each other near the tips, and the glans penis is placed between the two oscillating discs to receive concurrent dorsal and ventral stimulation at adjustable frequencies and amplitudes.

In a study by Segal et al. (11), 4 out of 5 healthy individuals were able to achieve tumescence beyond 60% maximum rigidity when subjected to PVS using the Viberect® alone, with no other external visual sexual stimulation. In a randomized controlled study by Fode et al. (12) involving 68 men who underwent nerve-sparing radical prostatectomy, 30 men who received PVS to the frenulum daily for 6 weeks, using the Ferticare® vibrator, showed a trend towards better erections. After 1 year, 53% in the PVS group had an IIEF score ≥18 compared with 32% in the control group, although no statistical achievement was achieved. The role of PVS in penile rehabilitation is based on the postulation that PVS provides early activation of the parasympathetic erectile spinal centres at S2–S4 level, which result in early recovery of the neuropraxic cavernosal nerves.

Low intensity extracorporeal shock wave therapy (LIESWT)

The use of shock wave therapy has revolutionized the treatment of many aspects of medicine. High intensity extracorporeal shockwave therapy has been used for the treatment of nephro-urolithiasis while medium intensity shockwave therapy is used by orthopaedic surgeons to treat joint pain as well as tendinitis. Low intensity shockwaves therapy was first noted to improve ischaemia-induced myocardial dysfunction in animal studies when low intensity shockwaves were applied to porcine myocardium (13). Shockwaves induces a localized stress on cell membranes in the same way that shear stress affects endothelial cell membranes (14) and this triggers the release of angiogenic factors, such as increased NO production through increased activity of endothelial NO synthase (eNOS) and neuronal NO synthase (nNOS), platelet-derived growth factor (PDGF) and vascular endothelial growth factor (VEGF) (15). These shockwaves also cause membrane hyperpolarization (16), activation of the Ras signaling pathway, non-enzymatic synthesis of NO and induction of

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stress fibers and intercellular gaps (17).

The pilot study by Vardi et al. (18) showed that LIESWT was effective in treating men with ED, suggesting a physiologic impact of LIESWT on cavernosal hemodynamics. The LIESWT is an effective penile rehabilitation tool that improves erectile function and potentially reverses underlying ED. Recent meta-analysis (19) of 14 studies showed that LiESWT could significantly improve the International Index of Erectile Function (IIEF) [mean difference: 2.00; 95% confidence interval (CI), 0.99–3.00; P<0.0001] and Erection Hardness Score (EHS) (risk difference: 0.16; 95% CI, 0.04–0.29; P=0.01). In addition, the therapeutic efficacy was noted to last for at least 3 months. LiESWT has been cited to a potential cure for ED, unlike other well established non-surgical methods of treatment (i.e., PDE5i, ICI and VED) being on demand treatments.

Penile prosthesis implant
Penile prosthesis implant remains the most effective and permanent treatment for ED. Penile prosthesis implants can be broadly divided into malleable and inflatable prostheses (20). Malleable penile prosthesis, also known as semi-rigid prosthesis, does not allow for (physiological) flaccid state of the penis. The patient can bend the prosthesis upwards for sexual intercourse and downwards for concealment. Although the angle of prosthesis concealment has improved with recent devices, however due to the constant rigid state of the penis, they are still less comfortable compared to their inflatable counterparts, are more likely to cause social embarrassment and associated with higher risk of implant erosions (21). However, malleable prosthesis still has its place for the treatment of ED as these implants are easier to handle, easier to place and would benefit patients with impaired manual dexterity.

There are currently two models of the inflatable penile prosthesis (IPP), namely, the two-piece IPP vs. the three-piece IPP. The three-piece IPP consists of a pair of corporal cylinders, a scrotal pump and an abdominal reservoir filled with saline. Owing to the presence of the reservoir, the corporal cylinders can be completely deflated to give the patient the physiological flaccid state when not in use, and likewise a maximally turgid state when inflated (21). The two-piece IPP lacks an abdominal reservoir and is often offered in patients with whom placement of reservoir is challenging or not possible such as following radical cystoprostatectomy with orthotopic ileal neobladder creation, or patients who had previous open book fracture of the pelvis with metal implants. The concept of ectopic reservoir placement has allowed many of these men the option for three-piece IPP placement (22). Technological advances have improved mechanical reliability, reduced prosthesis infection risk and offered excellent patient and partner satisfaction rate (23).

Penile cast
The use of penile support device such as penile cast worn externally during intercourse has been tried to provide length and rigidity to the penis during erection (24). Each device can be customised to the patient’s penis size and provided an option for patients who are seeking non-pharmaceutical/non-invasive treatment, or have end-organ failure who may not be candidates for, or unable to afford, penile prosthesis implant.

Regenerative medicine
Following the breakthrough in ED treatment using PDE5-inhibitors, Western medicine has now moved on to a new frontier of regenerative medicine, with stem cell and gene therapy leading the way (25). There is a practical need for novel therapy as a significant portion of diabetic or post-prostatectomy ED patients do not respond to oral pharmacotherapy. To date, stem cells derived from different sites including adipose tissue-derived stem cells, bone marrow mesenchymal stem cells and muscle-derived stem cells have been investigated using animal models for ED, to study their effects on neural, vascular, endothelial or smooth muscle regeneration (25,26).

In a prospective human phase 1 open-label and single-arm study reported by Haahr et al. (27), 17 men with refractory post radical prostatectomy ED were given a single intracavernosal injection of autologous adipose-derived regenerative cells (ADRCs) freshly isolated after a liposuction. The procedures were well-tolerated and over a 6-month follow-up period, 8 of 17 men showed improvement of their erectile function.

In time to come, regenerative therapy with adjuncts may be a treatment option for patients with medical refractory ED.

Eastern medicine
Principle of treatment
Sexual dysfunction has been evaluated in ancient literature of TCM in terms of subjective sensation and the actual sexual performance (3). In TCM, methods and matters
related to direct sexual activity is described in terms of “ten motions”, “seven impairments” and “eight benefits”, which asserted that the ideal intensity and frequency of sexual activity should be moderate. TCM is all about balance, to achieve better overall regulation of the yin and the yang. The aim of treatment of ED using TCM is not for the end point of a penile erection but rather for a natural and harmonious sex life. TCM aims to achieve regulation in terms of the man’s anxiety, fatigability, changing hormonal levels, insomnia and gastroparesis. Medicine to invigorate qi can enhance physical fitness, and medicine to warm the kidneys can regulate sex hormones, increase libido, invigorate the spleen, regulate the stomach and improve general wellbeing (28). Medications used to treat a “stagnated liver” provide tranquilization and helps to stabilize the mind, hence improving mental processes and emotional wellness. As a result, the patient’s overall condition and quality of life is improved.

The treatment of ED using TCM ties in with the treatment of late-onset hypogonadism (LOH). LOH occurs due to the breakdown in coordination between the heart and the kidneys, deficiencies of the spleen and kidney (yang), deficiencies of the liver and kidney (yin) and deficiencies of the kidney (yin and yang). The endocrine function of the pituitary and gonads becomes disordered with age due to a depression of overall function. This results in accumulation of free radicals and other toxins that cannot be relieved solely with male hormone supplementation. Warmed yang can energize kidneys to benefit the body, remove toxins, invigorate qi and promote blood circulation. Free radicals are removed, blood fat regulated, cardio-cerebral blood flow improved and again the key here is to improve the function of the digestive, respiratory and endocrine systems, hence regulating the body in every aspect holistically (28).

In addition to TCM, aphrodisiacs have also been used for the treatment of ED. An aphrodisiac is defined as any food or drug that arouses the sexual instinct, induces venereal desire and increases pleasure and performance (29).

**Animal products**

In Eastern medicine, animal products are commonly used for their perceived health benefits. The philosophy “like nourishes like”, suggests that consuming the organ of an animal will bring benefits to the corresponding organ in one’s body is a common belief. Men seeking greater potency have turned to eating penises from goats, bull, deer, horses, seals and other mammals in the form of cooked dishes or herbal preparations. While there is no scientific evidence supporting this practice, the cultural beliefs remain strong and supplements containing extracts from animal penises are readily available in the form of capsules, often mixed with herbal compounds pitching similar erectogenic properties. A significant proportion of these potency-inducing supplements in Asia have been found to contain PDE5-inhibitors substrates such as tadalafil and sildenafil (30). However uncontrolled use of illicit PDE5-inhibitors under the guise of natural supplements remains a health threat to the general public.

Deer velvet is a covering found on the growing bone and cartilage of deer’s antlers. In Eastern medicine, deer velvet is sought after for its Chinese medicinal properties which include boosting one’s endurance and improving one’s immunity. People have also used deer velvet as an aphrodisiac or to treat ED. The randomized double-blind placebo-controlled study on deer velvet by Conaglen et al. (31), no benefit but this study was underpowered involving healthy participants with no sexual dysfunction.

**Insect and arthropod products**

Besides mammalian organs, insects and arthropods are also consumed as aphrodisiacs in Eastern medicine. These include scorpions, spiders, beetles, flies and other bugs (32). Penile erections can be observed following administration of neurotoxins as it causes repetitive firing of the somatic, sympathetic and parasympathetic neurons, resulting in autonomic and neuromuscular over-excitation. Scorpions are often used as an ingredient found in herbal wines. However, there is a general lack of literature regarding the consumption of scorpion neurotoxins for potency.

Diaclina (also known as Panzer’s Darkling Beetle), Korean bug are used as aphrodisiacs in China, Korea and Southeast Asia. These are consumed either whole or as compounds within capsules. It is felt that the aphrodisiac properties come by stimulating the urogenital structures. Flies have been studied for their aphrodisiac effects, including Spanish fly, Chinese cantharide, and Eastern-Indian cantharide (32). The active compound found in the dried and mashed up bodies of these flies is cantharidin, which is a pheromone produced in the accessory glands of the male flies’ genitals. Cantharidin, stimulates the urogenital tract, causing pelvic hyperemia and possibly erections. As cantharidin is toxic and its safety dose not well determined, its use cannot be recommended. Cantharidin is lethal at high doses and exposure can lead to gastrointestinal and urogenital hemorrhage as well as acute renal failure.
Herbal products

Yohimbine
Yohimbine is an indole alkaloid derived from the bark of the African yohimbe tree (33). Yohimbine has been noted to treat fatigue, depression, diabetes, and sexual dysfunction. A meta-analysis of seven placebo-controlled trials (34) deemed yohimbine superior to placebo for the treatment of ED with rare adverse events. The proposed mechanism of action (35) is via the inhibition of central alpha-2-adrenergic receptors, decreasing central inhibition of arousal, and increasing penile nerve stimulation resulting in increased NO. Common side effects include headache, sweating, agitation, hypertension and insomnia. Contraindications include patients on tricyclic antidepressants, anti-hypertensives and central nervous system stimulants.

Ginseng
Ginseng is the most common ingredient among top-selling supplements for men's sexual health (36). The English word ginseng derives from the Chinese term renshen. Ren means “person” and shen means “plant root”. This plant has been named in this manner as its roots resemble the lower limbs of a human, Traditionally, ginseng has been used to restore and enhance the normal well-being of the body. The effects are due to ginseng's reactions with the central nervous system, metabolism, immune function and cardiovascular system. The principal active compounds are triterpene saponins known as ginsenosides. Animal studies have suggested that specific ginsenosides may be responsible for ginseng-mediated effects on copulatory behavior (37). Ginsenoside induces smooth muscle relaxation by hyperpolarizing the smooth muscle membrane via activation of large-conductance KCa channels (38).

In contrast to Chinese ginseng, Korean ginseng is divided into three types, depending on how it is processed. Red Ginseng is harvested at the sixth year of cultivation and is steamed and dried. In addition to the effects mentioned regarding the effects of ginsenoside, red ginseng has been reported to improve erectile function in a rat model of metabolic syndrome and it was also found to inhibit fibrosis of the corpus cavernosum of the penis (39). As with most herbal medicines, the concentration of ginsenoside are distributed unevenly throughout the ginseng plant and the concentrations in individual supplements can vary. Common side effects include headaches, insomnia, gastric upset, rash and constipation.

Tribulus terrestris
Tribulus terrestris is a dicotyledonous herbal plant of the Zygophyllaceae family, used to increase serum testosterone levels, which has only been shown in animal studies (40). A prospective, randomized, double blind study of 30 men showed that Tribulus terrestris was not more effective than placebo on improving IIEF scores or serum total testosterone (41). Two accounts of hepatotoxicity have been reported in young men who ingested high doses of this herbal medication (42,43).

Horny Goat Weed (Epimedium spp)
The Epimedium plant is a flowering perennial found throughout Asia and parts of the Mediterranean. Horny Goat Weed's active ingredient is icariin, a falvonol glycoside and reputed to improve cardiovascular function, hormone regulation, modulation of immunological function and antitumor activity (44). Icariin has also been shown to have a PDE5i effect. Animal studies have been carried out showing improvements in penile hemodynamic parameters. There is one report of tachyarrhythmia and hypomania with the use of this herb (45).

Tongkat Ali (Eurycoma longifolia Jack)
Tongkat Ali is a well-known herb in Malaysia and Singapore and is commonly used especially by the Malay ethnic group for treating diseases and enhancing general health and sexual health (29). It is a flowering plant of the family Simaroubaceae.

Quassinoids isolated from Tongkat Ali have been reputed to be anti-tumor, anti-malarial, anti-amoebic and anti-inflammatory. Its leaves are used for washing itches, its fruits for the treatment of dysentery, its bark used as a vermifuge, the taproots used for treatment of hypertension and the root bark for treatment of diarrhea and fever. The roots extracts are used for sexual dysfunction, aging, malaria, cancer, diabetes, anxiety, aches, constipation, exercise recovery, fever, increased energy, increased strength, leukemia, osteoporosis, stress and syphilis. Animal studies done on middle age sex rats showed enhancement of the sexual qualities in terms of hesitation time among middle aged rats (46).

Ginkgo Biloba
Ginkgo Biloba is promoted to treat conditions ranging from hypertension to Alzheimer's dementia. There is evidence
that shows improvement of memory enhancements in the geriatric population (47), improvement in terms of cognitive function via effect on cerebral vasculature (48), improvement of claudication distance and cutaneous ulcers in patients with peripheral vascular disease (49). Ginkgo Biloba extract is proposed to induce NO in endothelial cells and thus causing relaxation of vascular smooth muscles. Animal studies have reported relaxation of rabbit corpus cavernosal smooth muscle cells with the use of Ginkgo Biloba (50). Adverse effects include headaches, major bleeding (in patient who are taking warfarin concurrently) and seizures with reported fatality (36).

Physical exercise

Low levels of physical exercise can be associated with ejaculatory and erectile disorders. And higher levels of physical exercise have been shown to improve erectile function in hypogonadal men undergoing testosterone replacement therapy (51). There are however, no proven physical exercises that can improve erections directly.

Jelqing exercise

Jelqing is penile massage technique of ancient Arabic origin (52). Men who practise jelqing will stretch their penises while in a semi-erected state and repeatedly milk their penises from base to glans, with their thumb and index finger touching to form an “OK” hand sign around their penile shaft. This massage can be done daily with the aim to achieve greater penile length and harder erections. Unwanted side effects of bruising, pain and fibrosis had been reported. No studies have been done to evaluate the efficacy of jelqing objectively.

Qigong

Qigong is a form of breathing exercises commonly practised in Asia to maintain health (53). In a cross-sectional population-based comparison study in Taiwan, individuals practising Qigong demonstrate higher SF-36 scores in the domains of physical functioning, role limitations due to physical problems, bodily pain, general health and vitality (54). Techniques to concentrate the energy or qi in the pelvis or genitals are regularly practised, but the effects of Qigong on ED have not been studied.

Acupuncture

In TCM, the meridian system is thought to represent a path through which the life energy qi flows and as discussed in earlier section, the “Jing” (kidney) qi plays an important role in penile erection. Acupuncture helps to correct the imbalances to relieve physical symptoms by stimulating various meridian points. The Shensu (BL23), Zusanli (ST36) and Neiguan (PC6) points represents important acupoints for penis stimulation and thus has a positive homeostatic effect on the autonomic nervous system, and potentially modulate NO release (55,56). While some studies have showed up to a third of patients reported improvement in penile erection and sexual activity, systematic review showed insufficient data to conclude that acupuncture is an effective intervention for treating ED (56,57). Therefore, further scientific research is required to investigate whether there are specific benefits of acupuncture for men with ED before acupuncture can be accepted as evidence-based practice.

Conclusions

Since time immemorial, TCM has been adopted by many cultures and is widely practiced in Asian countries despite paucity of level 1 clinical evidence and limited published safety records. TCM is more congruent with Asian values, beliefs and philosophical orientation to health, simple administration, readily available and ease of access or procurement, and general belief that TCM is safer. While Asian males are clearly different from their Western counterparts with respect to biology, culture and beliefs, the practice of TCM appears to be adopted by many Western nations lately. Many men seek TCM to avoid embarrassing visits to physicians and potential side effects of pharmaceutical drugs, or after becoming frustrated with the outcome of modern medicine. Patients are choosing to take more responsibility for their health by exploring a variety of non-pharmaceutical drugs and wellness practices. Furthermore, TCM such as herbal medicine does not address a specific organ/system only and is meant to restore and realign the vital energy within the body, which is responsible for ageing, clinical diseases and the deterioration of bodily function; while in Western medicine, each pill is intended for a specific organ/system and that a patient may need a collection of pills to treat multiple comorbidities, rendering modern medicine less attractive to TCM.

Clinical practice in TCM has been an exemplary case of customized treatment with holism epitomizes the essence of TCM. TCM encompasses these aspects, taking a holistic approach to patient’s problem and these methods combine body, mind and spirit, and healings are achieved.
via the concept of energy rather than matter, as in modern medicine. Compared to the complexity of modern science, which is the basis of Western medicine, this concept is easily understood and comprehended, and is readily accepted because of its holistic approach.

Eastern medicine should be fully exploited, and integrated with modern medicine to combine the advantages of both TCM and Western medicine. More research should be conducted into the efficacy and safety of TCM, and integration of TCM and Western medicine may provide promising breakthroughs in future clinical treatment. This strategy may allow for the development of new therapeutic strategies based on concepts of TCM and integrated medicine. There is a need for multimodal therapy and holistic approach to treat men (and their partners) with ED through complementary use of herbal supplements and modern drug to optimize underlying medical comorbidities; acupuncture, exercise or massage to reduce stress and strengthen the body; introduction and escalation of various medical therapy with use of mechanical therapy to further enhance penile erection; and lastly surgical intervention in suboptimal or refractory ED cases.

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Footnote
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