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Systematic Review

Effectiveness of Korean Ginseng in Men with Erectile Dysfunction

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Abstract

Erectile dysfunction (ED) is a common condition that has a substantial impact on quality of life. It is described as the continuous inability to develop or maintain sufficient stiffness of the penis to allow satisfactory sexual performance. Early detection and treatment of ED and comorbidities associated with ED, such as hypertension, diabetes mellitus, and hyperlipidemia, can significantly improve the quality of life for men and their partners. About 35.6% of Indonesian adults have ED. The bulk of ED treatments now on the market are pharmacological and surgical procedures. Even though there has been substantial progress, it seems that the aforementioned treatment has a high dropout rate due to cultural restrictions and taboos. These patients would then look for herbal nutritional supplements like ginseng as an alternative. This systematic review evaluates the current evidence for the effectiveness of red ginseng in managing erectile dysfunction. We performed systematic review conducted from MEDLINE, ScienceDirect, ProQuest. The authors screened the articles based on inclusion criteria : (1) Mild-to-moderate erectile dysfunction; (2) Ginseng as interventional therapy; (3) Human studies that have IIEF score as an outcome; (4) Written in English. Four randomized control trials (RCT) using keywords "((Erectile Dysfunction) AND (Korean Ginseng) AND (Ginseng))" were included. Three randomized control trials (RCT) study involving 454 male patients with mild to moderate erectile dysfunction, aged from 20 to 70 years old. Our findings support that the mean in International Index of Erectile Function scores were significantly higher in patients treated with Korean ginseng than in those who received placebo. Korean ginseng could be an effective alternative treatment for male erectile dysfunction if more research with larger-scale clinical trials and higher standards is done in the future on the safety and effectiveness of ginseng.

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1. Introduction

Erectile dysfunction (ED) is defined as the consistent or recurrent inability to attain and/or maintain penile erection sufficient for sexual satisfaction, including satisfactory sexual performance.[1]

prevalence ranges between 1-10% in men younger than 40 years (*International Consultation Committee for Sexual Medicine*). The prevalence increases with age in a range from 2% to 9% in men between the ages of 40 and 49 years, 20-40% in men aged 60-69 years and > 50% in men older than 70 years. Erectile function can be divided into a central component that influences the sympathetic outflow from the thoracolumbar region of the spinal cord and a peripheral reflexogenic erectile function mediated by nitrergic nerves that project from the sacral region of the spinal cord. The severity of ED is commonly diagnosed using the

blurred vision, and may have dangerous interactions with other medications.

To avoid the risks of potential side effects associated with drugs, people often turn to dietary supplements or phytotherapy. Panax ginseng is particularly common and widely used in oriental countries, because of its property of boosting the immune system, as well as providing vigor and enhancing sexual activity.[7] It contains medicinal ingredients, including saponin, polysaccharide, polyacetylene, phenols, gomisin, acidic peptide.

as an adaptogen, include restoring and enhancing normal wellbeing. Red ginseng is used medicinally, and one of its claims is that it improves sexual performance.

This review was carried out to update, complete, and evaluate the RCT data supporting or against red ginseng's efficacy in treating ED patients.

2. Method

Search Strategy and Selection Criteria

We performed systematic review in accordance with Preferred Reporting Items for Systematic Reviews and Meta-Analyses

Erectile dysfunction (ED) has been identified as the most common sexual problem, with high prevalence and incidence worldwide, that affects the *quality of life* (QoL) of patients and their partner's are estimated that about 322 million men would suffer from ED global by the year 2025. ED primarily affects men older than 40 years of age. ED

International Index of Erectile Function questionnaire (IIEF).[2] ED onset contributes several environmental and lifestyle risk factors such as diabetes mellitus, hypertension, hyperlipidemia, obesity, metabolic syndrome, depression, smoking and limited or absence of physical exercise.[2,3,4,5]

The first line of treatment is oral medication therapy; specifically, 5-phosphodiesterase (PDE) inhibitors such as sildenafil, tadalafil and vardenafil are generally prescribed by andrologist to treat ED.[6] However, these substances can produce negative side effects, including headache, gastrointestinal disorder, muscle pain and

Depending on how it is used, the ginseng grown in Korea is divided into three categories: fresh (less than 4 years old), white (4-6 years old and dried after peeling), and red (more than 4 years old) (harvested when 6 years old, steamed and dried). Before being heated, steamed, or in any other way, and then dried, red ginseng is not skinned. Ginseng starch is gelatinized during the steaming process, increasing the saponin content.[8] Traditional uses of red ginseng, which is frequently referred to

(PRISMA) guideline and the Strengthening the Reporting of Observational studies in Epidemiology (STROBE) statement.[9]

The authors screened the articles based on inclusion criteria: (1) Mild-to-moderate erectile dysfunction; (2) Ginseng as interventional therapy; (3) Human studies that have IIEF score as an outcome; (4) Written in English. 4 randomized control trials (RCT). Review articles, unpublished articles, abstract-only, and irrelevant articles were excluded from this study. The literature search was carried out by authors through the databases (MEDLINE, ScienceDirect, and ProQuest) using keywords "((Erectile Dysfunction) AND (Korean Ginseng) AND (Ginseng))" were included.

PRISMA 2020 flow diagram for new systematic reviews which included searches of databases, registers and other sources

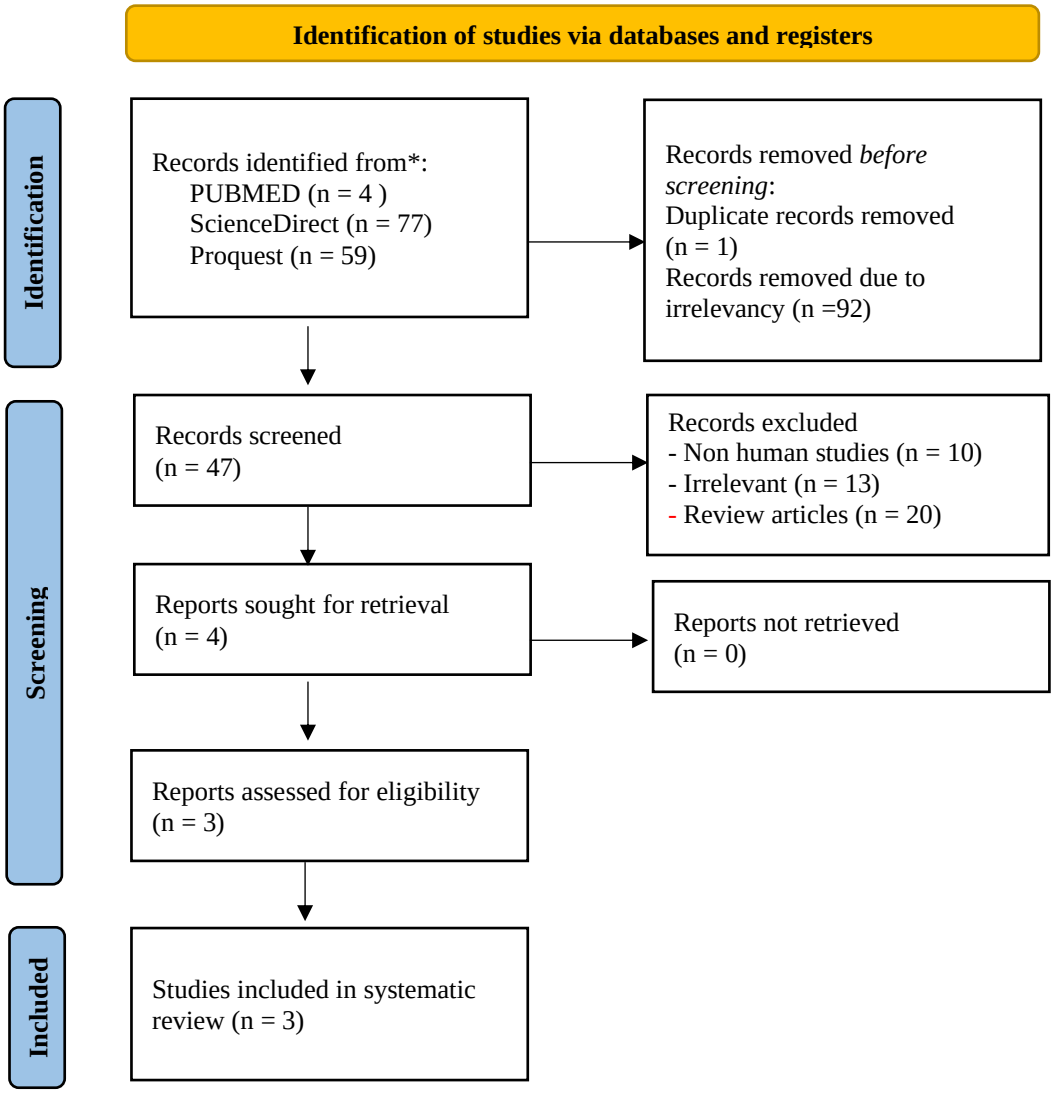

Figure 1. PRISMA Flow

Data Extraction and Quality Assessment

The authors extracted data from selected studies into the evidence table. We evaluated the information including first authors' names and publication year, study design, sample size, patient age, ginseng intervention, and IIEF score. The other authors examined the table evidence based and cleared up any confusion. Discrepancies were resolved through discussion between two authors (please include the initial name here (FYA) and if needed, by seeking the opinion of a third reviewer (EE).

Data synthesis

First study in 2004 which ginsengs and placebos were given to 192 patients, second study 119 patients were recruited between May 2010 and January 2011, and the last study in 2010 total of 143 patients participated on third study. All Participants were evaluated using IIEF score.

Extracted data from included studies in which methods and parameters varied were descriptively synthesized as systematic review.

3. Results

Endpoints

Table 1. Result Based on IIEF Score at The End of The Treatment.

Study name	Study type	Population	Outcome	Comparison	Ginseng dose	Parameter	IIEF score 8 weeks
Enrico, et al. 2007	Randomized clinical trial	Mild-to-Moderate Erectile Dysfunction	IIEF-5 score	Placebo	1000mg	IIEF-5	21.0 ± 6.3 (P 0.0003)
Kim, et al. 2021	Randomized clinical trial	Mild-to-Moderate Erectile Dysfunction	IIEF-5 score	Placebo 1000mg BID	1000mg BID	IIEF-15	15.34 ± 6.13 (P<0.00)
Choi, et al. 2012	Randomized clinical trial	Mild-to-Moderate Erectile Dysfunction	IIEF-5 score	Placebo	350mg	IIEF-15	46.19±12.69 (P 0.002)

Search Results

The search results identified 140 articles. One article were removed due to duplicates. We screened 139 articles from abstracts and titles. Fourty three studies were excluded due to non-human studies, irrelevant, and article reviews. The screening results obtained 3 studies that were assessed for eligibility and were included in this systematic review.

Quality of included studies

We assessed the quality of all our randomized trial studies with the Cochrane risk-of-bias tool[10], resulting all three studies showing low risk of bias.

Included studies' characteristics

This systematic review included a total of 454 male patients. There were 167 (51.54%) patients received Korean ginseng and 154 (48.46%) patients received placebo. Participant age range was 20 to 70 years old.

These studies enrolled mild-to-moderate ED patients who had the disease for 3 months or longer. Diagnosis of erectile dysfunction includes using validated questionnaires (such as the International Index of Erectile Function-5 [IIEF-5]), obtaining a psychological, medical and sexual history, physical exam, blood tests (testosterone), nocturnal erection test, and injection test.[11] The index uses five domains to evaluate erectile function (6 items), orgasmic function (2 items), sexual desire (2 items), intercourse satisfaction (3 items), and overall satisfaction (2 items). A short version composed of five items the IIEF-5, was developed to allow for the evaluation of ED specifically, according to the criteria established by the National Institutes of Health.[12]

The dosage of Korean ginseng used 1000 mg twice a day compared to placebo, tissue cultured mountain ginseng extract used 350 mg four times a day compared to placebo, and *panax ginseng* CA Meyer both placebo used 1000 mg twice a day. Patients visited the hospital on weeks 4 and 8 in order to be checked for effects of the medication, including changes in erectile function and sexual satisfaction.[13]

This systematic review demonstrated the endpoints that were commonly used in measuring the success of erectile dysfunction therapy, measured using the erectile function domain of the International Index of Erectile Function (IIEF)-15 questionnaire or the total score of the IIEF-5 questionnaire.

4. Discussion

Ginseng, a popular root, has been used for various conditions in East Asian countries for at least two to five thousand years[14,15] and is currently consumed in 35 countries around the world.[16] Ginseng belongs to the genus *Panax* and includes *Panax ginseng (P. ginseng,* Korean ginseng), *Panaxquinquefolius* (*P.quinquefolius,*Americanginseng)and *Panax notoginseng* (*P. notoginseng,* Sanchi ginseng).[17] Ginseng is generally classified in three different ways, depending on how it is processed: fresh

ginseng (less than four years old); white ginseng (four to six years old and dried after peeling); and red ginseng (harvested when six years old, steamed and dried).[17]

Ginseng is a herb that contains various chemical compounds such as ginsenosides (a class of steroid glycosides and triterpene saponins). To date, about 150 different ginsenosides have been identified from the roots, leaves and stems, fruits and flower heads of ginseng.[18] Recent results of studies in ginseng and ginsenosides show that they have beneficial effects on cardiac and vascular diseases, control of vasomotor function, adjustment of blood pressure and improvement in cardiac function.[13] In the case of *P ginseng*, ginsenosides (a class of steroid glycosides and triterpene saponins) are reported as the most important active components. The mechanisms underlying the effect of ginseng in treating erectile dysfunction are thought to be related to multiple pathways.[19] First, ginseng and ginsenosides promote endothelial nitric oxide (NO) release, resulting in improved penile hemodynamics of impaired endothelial L-arginine-NO activity, which exerts a direct effect on erectile dysfunction through triggering erections mediated by relaxation of the smooth muscles of the corpus cavernosum.[20,21] Second, ginseng has the potential benefit of improved cardiovascular risk factors that include hypertension, hyperglycemia, hyperlipidemia, adjusted blood pressure, anti-fatigue and anti-stress effects, improved climacteric disorder and sexual functions, which are regarded to be important risk factors of erectile dysfunction.[22,23,24] Ginseng's effect might be related to central humoral regulation, which is involved in sexual arousal as well as physical energy enhancement through ginseng's alleged anti-fatigue effect.[19]

Interpretation of documented adverse effects and drug interactions can be difficult because of the variety of available ginseng formulations, and because the exact amount of ginseng may not be identified. Korean ginseng *(Panax ginseng)* generally is well tolerated, and its adverse effects are mild and reversible. Associated adverse effects include nausea, diarrhea, euphoria, insomnia, headaches, hypertension, hypotension, mastalgia, and vaginal bleeding. Korean ginseng may interact with caffeine to cause hypertension, and it may lower blood alcohol concentrations. It also may decrease the effectiveness of warfarin (Coumadin). Concomitant use of Korean ginseng and the monoamine oxidase inhibitor phenelzine (Nardil) may result in manic like symptoms

The main treatment options for ED can be divided into pharmacological and surgical interventions.[25] Examples of pharmacotherapy include oral phosphodiesterase type 5(PDE5) inhibitors (sildenafil, tadalafil, vardenafil), and the surgical interventions, namely intraurethral or intracavernosal alprostadil, vacuum devices, and penile prosthesis.[26,27] PDE5-inhibitors act as a first-line therapy as they have favourable safety profiles and are highly effective.[28] Most of the patients respond well to the drug reactions.[29] These drugs prevent cyclic GMP from being neutralised by PDE5 enzyme, thus lengthening the penile erection.[29,30]

Our review has a number of important limitations. Although strong efforts were made to retrieve all RCTs on the subject, we did not find any relevant studies comparing ginseng or ginseng plus conventional treatment (namely, phosphodiesterase inhibitors) to placebo or conventional treatment. In addition, we were unable to analyse in detail due to lack of relevant data. For these reasons more scientific studies are necessary concerning this subject in pursuance of further knowledge.

5. Conclusion

As a result of the satisfaction scores in the five domains of the IIEF, the findings of our systematic review offer suggestive evidence for the efficacy of red ginseng in treating ED. The total sample size, average methodological quality, and number of RCTs that could be included in this analysis were all too low to allow for the drawing of firm conclusions. To determine whether red ginseng has a place in the treatment of ED, more high-quality studies are required.

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Conflict Of Interest

The authors declare that there is no conflict of interest to disclose.

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