

THE ANALYSIS STUDY OF EFFECTIVENESS AND SAFETY OF ORAL SILDENAFIL CITRATE FOR TREATMENT OF ERECTILE DYSFUNCTION : A COMPREHENSIVE SYSTEMATIC REVIEW

*¹Dhimas Mohammad Fajar Nugraha, ²Tsalitsa Laili Akmalia

¹*Sarkies Aisyiyah General Hospital, Kudus Regency, Central Java, Indonesia*

²*Faculty of Medicine, Sultan Agung Islamic University, Semarang City, Central Java, Indonesia*

Corresponding Author:
dhimasmfn2.27@gmail.com

To Cite This Article: Nugraha, D. M. F. ., & Akmalia, T. L. . (2024). THE ANALYSIS STUDY OF EFFECTIVENESS AND SAFETY OF ORAL SILDENAFIL CITRATE FOR TREATMENT OF ERECTILE DYSFUNCTION : A COMPREHENSIVE SYSTEMATIC REVIEW. *Journal of Advanced Research in Medical and Health Science* (ISSN 2208-2425), 10(7), 38-46. <https://doi.org/10.61841/qn44z039>

ABSTRACT

Background: Erectile dysfunction (ED) is a medical condition affecting men's sexual performance and well-being. Sildenafil citrate, a specific inhibitor of phosphodiesterase type 5, is approved for treating ED. The efficacy and safety of oral sildenafil citrate in treating ED are crucial for successful treatment procedures. Understanding the relationship between the efficacy and safety of oral sildenafil citrate can help develop successful treatment procedures for ED patients.

Methods: This systematic review adhered to the PRISMA 2020 guidelines and primarily examined entire English literature published between 2000 and 2024. Only editorials and review articles published in the same publication as the submission were accepted if they possessed a Digital Object Identifier (DOI). A variety of online platforms, including ScienceDirect, PubMed, and SagePub, were utilized to gather the relevant literature.

Result: The study analyzed more than 2000 papers from reputable sources such as Science Direct, SagePub, and PubMed. After deciding to subject eight publications to additional inspection, a thorough evaluation of the entire body of literature was carried out.

Conclusion: Sildenafil, a potent treatment for erectile dysfunction (ED), has been found to be effective in improving men's psychosocial aspects. It is an inhibitor of PDE5, a condition that affects men's emotional well-being. The study also found that the firmness of erections was linked to improvements in psychosocial aspects. Sildenafil can be used interchangeably with tablets, providing a convenient alternative for those with difficulty swallowing. However, follow-up for men with ED is often inadequate due to improper doses and lack of understanding.

Keyword: Erectile dysfunction, sildenafil citrate, efficacy, safety

INTRODUCTION

Erectile dysfunction (ED) is a medical condition characterized by the inability to achieve and/or sustain an erection that is enough for optimal sexual performance. It can be caused by both physical and psychological factors.¹ Global prevalence of erectile dysfunction is projected to reach 322 million patients by 2025.² According to Corona (2010), the prevalence of erectile dysfunction in men is estimated to be between 10% and 20% in the general population. The overall incidence of ED is reported to be 30% in the European Union and 18.4% in the United States.³ ED is prevalent among men in China, with a prevalence rate of up to 41% among individuals aged 40 years and older, as indicated by a population-based study done between 2010 and 2013.⁴ Research conducted by Chou has found that Asian males who experience ED are 2.2 times more likely to develop depression compared to men of the same age who do not have ED. The risk of depression is highest within the first year after receiving an ED diagnosis.⁵

ED greatly affects the overall well-being and satisfaction of patients. Studies have shown that men with ED experience reduced levels of physical activity, emotional fulfillment, and overall happiness. Additionally, they are shown to face constraints in their daily roles due to the negative influence it has on their mental well-being. ED significantly affects how men perceive themselves and their sexuality, and it also impairs their interactions with women or possible partners.⁶ Furthermore, it exerts a detrimental influence on their female counterparts, who express less sexual gratification and decreased sexual desire. Given that sexual satisfaction is widely recognized as a significant indicator of overall life satisfaction, addressing ED will probably enhance the quality of life for both affected persons and their partners.^{7,8}

There are multiple therapeutic choices for treating ED. One such choice is the use of pharmacotherapy based on phosphodiesterase type 5 (PDE5) inhibitors.⁹ Phosphodiesterase type 5 inhibitors are the initial choice of treatment for erectile dysfunction.¹⁰ Sildenafil citrate, marketed as Viagra by Pfizer Inc. in New York, is a specific and competitive inhibitor of phosphodiesterase type 5, which acts on cyclic guanosine monophosphate. It is approved for the treatment of ED. The approval for sildenafil citrate tablets includes doses of 25 mg, 50 mg, and 100 mg. However, the suggested dose for the majority of patients is 50 mg.^{11,12} Understanding the relationship between the efficacy and safety of oral sildenafil citrate as a treatment for erectile dysfunction can help in developing successful treatment procedures. This systematic literature review seeks to examine the relationship between the efficacy and safety of oral sildenafil citrate in patients with erectile dysfunction, based on research completed in the past two decades.

METHODS PROTOCOL

The author of the work meticulously followed the Preferred Reporting Items for Systematic Review and Meta-Analysis (PRISMA) 2020 criteria to ensure complete adherence to all requirements. A rigorous and deliberate process was used to provide accurate and persuasive research findings.

CRITERIA FOR ELIGIBILITY

This article provides a thorough examination of the studies completed in the past ten years on the efficacy and safety of oral sildenafil citrate for the treatment of erectile dysfunction. The objective of this program is to clarify and enhance patient care techniques by doing comprehensive data analysis. The primary objective of this thesis is to elucidate significant themes that are present in a variety of literary compositions.

To ensure the accuracy of the data used in this research, strict criteria for inclusion and exclusion were implemented. Any work that has been formally published or made accessible in the English language between 2000 and 2024 is deemed eligible for inclusion. The exclusion criteria include published reviews, editorials, submissions without a DOI, and duplicate entries within the same journal.

SEARCH STRATEGY

The study's keywords include "erectile dysfunction, sildenafil citrate, effectiveness, safety, treatment, outcome, therapy, effect". For this research, the following Boolean MeSH keywords were entered into the databases: (((("erectile dysfunction"[MeSH Terms] OR "sildenafil citrate"[All Fields] AND "effectiveness"[All Fields]) OR ("erectile dysfunction"[MeSH Terms] OR "sildenafil citrate"[All Fields] AND "safety"[All Fields]) AND ("treatment"[MeSH Terms] OR "effectiveness"[All Fields] OR "safety"[All Fields] OR "outcome"[MeSH Subheading] OR "therapy"[All Fields] OR "effect"[All Fields])))).

DATA RETRIEVAL

Before initiating this extensive inquiry, the writers thoroughly evaluated the pertinence of each publication by scrutinizing its title and abstract. Only research that satisfied the objectives and met the criteria for inclusion in the article were given greater importance. A clear and consistent pattern emerged after completing multiple searches. Full-text submissions were restricted to English only. The screening process was comprehensive and yielded content that was highly pertinent to the study's subject matter and satisfied all predetermined inclusion criteria. Research that failed to meet these requirements was generally disregarded, and its conclusions were deemed insignificant. The assessment covered a wide range of data, including factors, titles, authors, publishing dates, venues, and study procedures.

QUALITY ASSESSMENT AND DATA SYNTHESIS

The authors themselves carefully scrutinize the abstract and title of each article to determine which ones require further research. Consequently, each document that was initially being considered had to undergo a thorough scrutiny. The assessment results affected the selection of the review papers. This criterion allowed for the quick selection of articles for further analysis, thereby providing a more thorough study of earlier research and the circumstances under which it was evaluated.

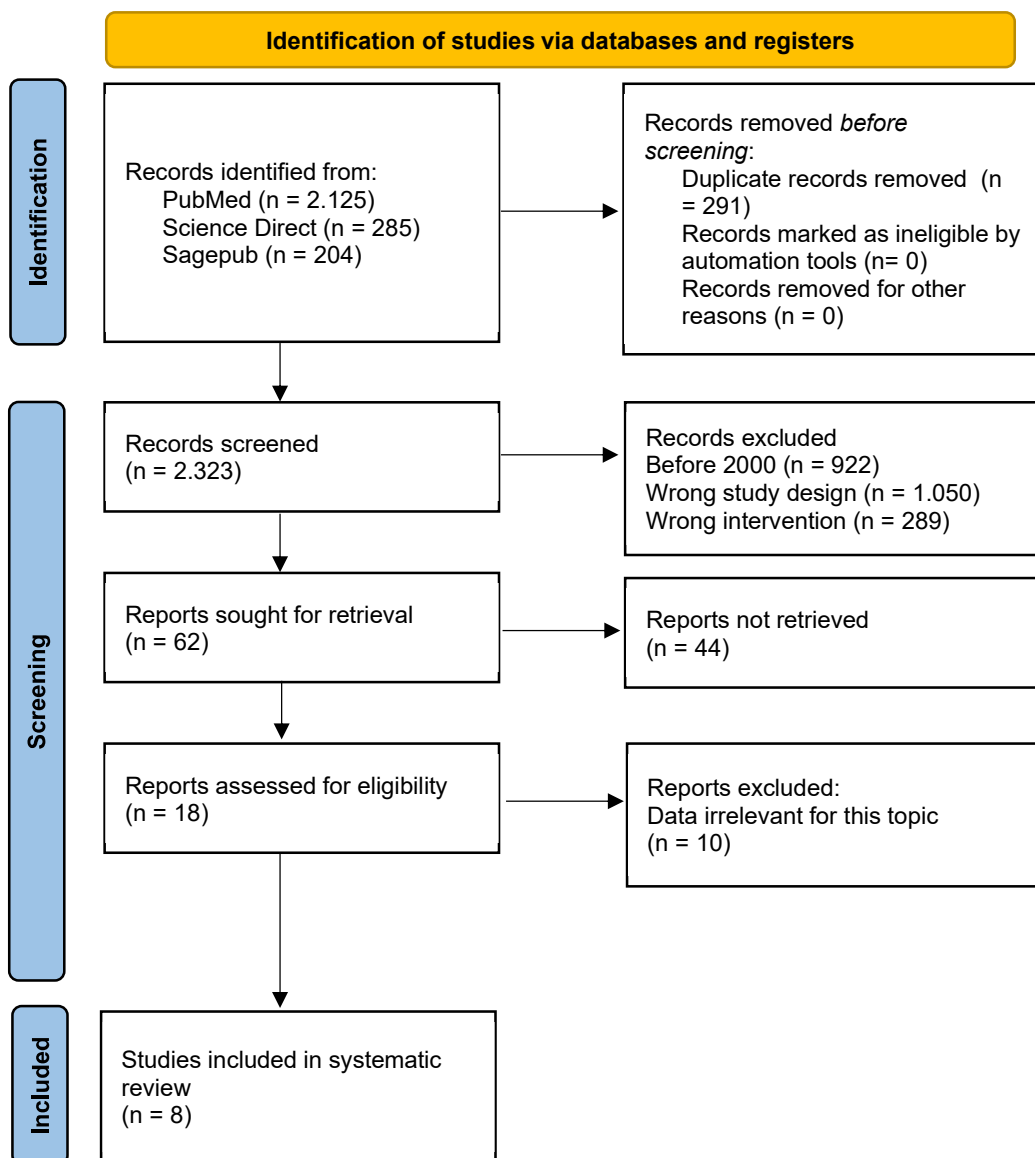


Figure 1. Article search flow chart

RESULT

In order to commence the investigation, our team meticulously collected a substantial array of documents from reliable sources such as Science Direct, PubMed, and SagePub. Following a comprehensive three-stage evaluation procedure, we have chosen eight papers that are deemed extremely pertinent to our current systematic investigation. Afterwards, we chose specific subjects to investigate in more detail and thoroughly assessed each report. To accelerate our investigation, we have provided a succinct overview of the assessed data in Table 1.

Table 1. The literature included in this study

Author	Origin	Method	Sample	Result
Fink et al.¹³ (2002)	USA	Meta Analysis	27 studies	Sildenafil significantly improved erectile function in all evaluated subgroups, with a higher percentage of successful intercourse attempts and at least one success during treatment compared to placebo. In parallel-group, flexible as-needed dosing trials, men randomized to receive sildenafil were less likely to drop out for any reason and no more likely to drop out due to an adverse event or laboratory abnormality. Sildenafil was not significantly associated with serious cardiovascular events or death.
Gomez et al.¹⁴ (2002)	Colombia	RCT	158 patients	The study assessed the efficacy and safety of sildenafil in patients with erectile dysfunction in Colombia, Ecuador, and Venezuela. Results showed that sildenafil increased patients' ability to achieve and maintain erections, with 77% of treated patients reporting improved erections. Intercourse attempts were successful, and sildenafil patients showed significant improvements in three IIEF functional domains.
Blonde, Lawrence¹⁵ (2006)	USA	Retrospective Study	11 studies	Sildenafil treatment significantly improved erections and successful sexual intercourse attempts in 974 men with DM and ED, compared to placebo. Adverse events were mild to moderate, including headache, flushing, and dyspepsia. The treatment was more effective than placebo, regardless of additional CV risk, and was more effective in men with ED.
King et al.¹⁶ (2007)	Australia	Retrospective Study	33 studies	Sildenafil, a medication used to treat erectile dysfunction,

				has been shown to improve erection hardness and other outcomes in men. Studies have shown that optimal erection hardness, correlated with emotional well-being and satisfaction, suggests that sildenafil 100mg may be the most appropriate dosage for most men with ED, potentially reducing the need for more invasive treatments.
Buvat et al.¹⁷ (2008)	France	RCT	492 patients	Clinical trials of sildenafil show that men with erectile dysfunction (ED) are interested in improving their erectile function. Most participants completed the studies, and most participants continued taking sildenafil through open-label extension phases. Patients titrated to 100 mg showed greater improvement, with headache, flushing, and hot flushes being common adverse events.
Guiliano et al.¹⁸ (2010)	France	Review	67 studies	Sildenafil, a medication used in treating ED, is well-tolerated in men aged 65-75 years. No causal link or new safety risks were found. The safety profile was similar in men with moderate renal or hepatic function impairment. Overdose was rare in the ED population, and no new safety issues or adverse reactions were identified.
Scaglione et al.⁹ (2017)	Italy	Literature Review	9 studies	Sildenafil, a medication used to treat ED, is effective in oral PDE5 inhibitors, with low occurrence of serious adverse effects. It is well-tolerated and has mild adverse reactions like headache, flushing, dyspepsia, and nasal congestion. Both film-coated tablets and ODT formulations have equivalent systemic exposure, making it an advantageous alternative for patients with ED.
Lv et al.¹² (2020)	China	Experimental	36 patients	Sildenafil citrate treatment sequences were tested on healthy Chinese male subjects, demonstrating bioequivalence and well-tolerance. Both formulations were well tolerated, with

				90% CIs for AUClast, Cmax, and AUCinf.
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Fink's systematic review and meta-analysis indicates that sildenafil significantly improves erectile function and is well tolerated by men with ED. However, further research is needed to determine its efficacy and safety over time. Longer-term trials are needed to determine its effectiveness in black and Hispanic patients, men with a history of radical prostatectomy, peripheral vascular disease, or depression, and in men at increased risk for cardiovascular events.¹³

Gomez's study reveals sildenafil as an effective oral treatment for South American patients with mixed organic and psychogenic ED, improving erectile function, intercourse satisfaction, overall sexual life satisfaction, and successful intercourse attempts.¹⁴

Blonde's retrospective analysis of pooled data from men with DM and ED found that treatment with sildenafil was generally well-tolerated and improved erections, erectile function, and successful sexual intercourse attempts, regardless of additional cardiovascular risk factors.¹⁵

King's study on men with ED found that sildenafil treatment improved outcomes assessing erection hardness, intercourse enjoyment, sexual satisfaction, emotional well-being, and satisfaction with the ED treatment. The possible dose-response relationship for fully hard and rigid erections suggests that 100mg may be the most appropriate dose for most men. This suggests that completely hard and rigid erections may be the appropriate goal of ED treatment.¹⁶

Buvat et al.'s study revealed that patients with ED responded well to initial treatment with 50 mg sildenafil, and titration to 100 mg improved efficacy and satisfaction without increasing AEs. Therefore, titration to 100 mg sildenafil should be considered for optimal ED therapy.¹⁷

Giuliano's data review reveals that sildenafil is well-tolerated in men aged 65-75 years, with no causal link to cardiovascular events. The safety profile is similar to men with ED, with no impairment of renal or hepatic function. The safety risk from drug interactions is low.¹⁸

Scaglione's study highlights sildenafil as a well-tolerated option for treating ED, demonstrating its effectiveness and well-tolerated treatment outcomes. The rapid disintegration of sildenafil in the mouth offers an alternative to solid tablets, improving treatment adherence and enhancing sexual health.⁹

Lv et al. found that sildenafil citrate ODT, a safe alternative to commercial formulations, is bioequivalent to or meets bioequivalence criteria in healthy Chinese men.¹²

DISCUSSION

The administration of sildenafil for the treatment of ED is of utmost importance for the emotional well-being and overall mental health of men. A comprehensive analysis of 33 trials including the use of Sildenafil revealed a significant association between the firmness of erections and favorable enhancements in many psychosocial aspects. The present study evaluated the quality of erections using the QEQ, and there was a substantial improvement in the overall score among males who were given a dosage of 100 mg.¹⁷ Sildenafil, a highly effective inhibitor of PDE5, has demonstrated considerable effectiveness in the treatment of erectile dysfunction (ED) as measured by several indices.⁹ A meta-analysis revealed that sildenafil, vardenafil, and tadalafil demonstrated comparable efficacy at the highest prescribed levels, with no significant variations. The adverse events linked to PDE5 inhibitors were generally modest and encompassed flushing, headache, dyspepsia, and myalgia.^{19,20}

The study shows that the sildenafil citrate orally disintegrating tablet (ODT) formulation, when taken with or without water, is similar to the traditional sildenafil citrate tablet. Both formulations are generally well tolerated in healthy Chinese males, with the occurrence of modest treatment-emergent side effects. The study indicates that sildenafil citrate orally disintegrating tablets (ODT) and tablets can be used interchangeably, offering a valuable alternative to traditional tablets for individuals with difficulty swallowing (dysphagia).^{12,21}

The safety profile of sildenafil, a medicine prescribed for ED, has remained consistent with the initial regulatory filings made around a decade ago. The most frequent negative effects experienced by men who received sildenafil were directly linked to the pharmacological action of inhibiting PDE5, including headache, vasodilation, and face flushing.²² The postmarketing safety database primarily consisted of known adverse drug reactions related to sildenafil, with a higher occurrence of adverse events observed with a total daily dose of 50 mg compared to a total daily dose of 100 mg.^{18,23}

Men who receive sildenafil treatment express a desire to continue with the treatment beyond the trial. However, the follow-up of men with ED after the initial prescription is frequently inadequate, characterized by improper doses and a lack of understanding regarding sexual stimulation as prevalent factors.²⁴ Through dose modifications or re-education, the majority of men who were initially unsatisfied with sildenafil were able to attain treatment satisfaction and obtain successful outcomes.²⁴⁻²⁶ During the single-blind treatment phase of the current research, males who received a dosage of 50 mg of sildenafil experienced notable enhancements in EF (erectile function) and pleasure. Patients who were gradually increased to a dosage of 100 mg experienced a more significant improvement in effectiveness and contentment.¹⁷

Administration of Sildenafil has demonstrated notable enhancement in erectile function among males diagnosed with diabetes mellitus (DM), including individuals with hypertension, dyslipidemia, or a history of smoking.¹⁵ Historically, the efficacy of sildenafil has been reduced in males with diabetes mellitus (DM), resulting in a lesser proportion of individuals who respond positively to the medication and successfully engage in sexual intercourse. Poorer effectiveness outcomes in diabetic individuals with ED can be attributed to several factors. These include compromised blood flow to the penile arteries, decreased generation of nitric oxide and cyclic guanosine monophosphate, as well as altered neurogenic and endothelium-dependent relaxation of the penile arteries.²⁷

The research conducted by Montorsi et al. discovered a favorable correlation between enhancements in erectile function and erection hardness and the results of certain evaluations measuring sexual satisfaction, emotional well-being, and satisfaction with erectile dysfunction treatment.²⁸ The present findings indicate that individuals with erectile dysfunction experienced enhanced erection firmness across many measures following treatment with sildenafil. The administration of sildenafil resulted in equivalent or improved rigidity compared to the state before the onset of the man's erectile dysfunction. Positive correlations support the connection between outcomes evaluating emotional well-being, contentment, and erection hardness in men who have been treated with sildenafil for ED. The post-treatment results of assessments measuring pleasure during sexual intercourse, satisfaction with sexual experiences, mental state, and satisfaction with the therapy for ED were found to have a positive correlation with the evaluation of the erection's naturalness in terms of its hardness.¹⁶

CONCLUSION

Sildenafil is a highly effective treatment for erectile dysfunction (ED), a condition that affects men's emotional well-being and mental health. A study found that the firmness of erections was significantly associated with improvements in psychosocial aspects. Sildenafil, a highly effective inhibitor of PDE5, has shown considerable effectiveness in treating ED, with comparable efficacy at the highest prescribed levels. The safety profile of sildenafil remains consistent with initial regulatory filings, with frequent adverse effects linked to the pharmacological action of inhibiting PDE5. The study also found that the dosage of sildenafil citrate orally disintegrating tablet (ODT) and tablets can be used interchangeably, offering a valuable alternative for individuals with difficulty swallowing. However, follow-up for men with ED is often inadequate, characterized by improper doses and a lack of understanding regarding sexual stimulation. Sildenafil has also shown notable enhancement in erectile function among males diagnosed with diabetes mellitus (DM), including those with hypertension, dyslipidemia, or a history of smoking.

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