

Combining a Nitric Oxide Boosting Dietary Supplement with Sildenafil Improves Nighttime Erections more than Sildenafil alone

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ABSTRACT

Objective: This study investigated whether ingesting a NO-boosting dietary supplement with Sildenafil one hour before sleep can improve nighttime erectile function compared to Sildenafil alone, using the TechRing by FirmTech to measure penile pressure while sleeping.

Methods: Twenty-two men (mean age 55, mean SHIM score 18.1) participated in the study. Participants wore the FirmTech TechRing, a validated device that measures erectile firmness and duration, over four nights. Following a two-day washout period without ejaculation or ED-related medications/substances, participants recorded baseline erectile activity after ingesting 40 mg Sildenafil one hour before sleep for two nights, then ingested two tablets of a nitric oxide-boosting supplement (containing L-citrulline, red beet root extract, *Panax ginseng*, and Muira Puama) in addition to the 40 mg Sildenafil one hour before sleep for two subsequent nights. Erectile quality was quantified as the area under the curve per hour of sleep (AUC/hr).

Results: AUC/hr significantly increased from a mean of 87 (baseline) to 117 (with supplements) with a mean difference of 30 and a p-value of 0.00004 ($t=5.219$). The number of nightly erections showed a significant increase from 3.25 to 3.87 with a mean difference of 0.62 and a p-value of 0.034 ($t=2.285$). No significant side effects were reported.

Conclusion: The combination of Sildenafil and a NO-boosting dietary supplement increased the intensity, duration and number of nighttime erections compared to Sildenafil alone without side effects. This study supports the use of a dual-therapy approach to ED treatment that minimizes side effects from high PDE5i doses.

Keywords: Erectile dysfunction; Nighttime erections; Nitric oxide boosters; L-citrulline; AFFIRM; TechRing; Beet root extract; *Panax ginseng* root extract; Muira Puama extract; PDE5 inhibitors; PDE5i; Sildenafil

INTRODUCTION

Erectile Dysfunction (ED) negatively impacts mental, emotional and sexual health [1]. Treatment for ED can enhance quality of life and adequate circulation is essential for erectile function. Nitric Oxide (NO) is critical for arterial vasodilation and adequate levels are required to maintain erectile function [2]. However, NO levels decline with age, contributing to increased ED prevalence [3]. In mammals, NO is generated *via* the citrulline/arginine pathway and the nitrate/nitrite/NO pathway [4,5]. Through the NO-cGMP signaling pathway, NO elevates cyclic Guanosine Monophosphate (cGMP) levels, initiating a

cascade that results in arterial dilation [6,7]. This vasodilation facilitates oxygen and nutrient delivery to muscle tissues, boosting energy, enhancing exercise performance and improving recovery post-exercise [8].

NO-boosting supplements such as L-citrulline, *Panax ginseng* root extract, beetroot extract and Muira puama extract enhance NO bioavailability and support cardiovascular health by lowering blood pressure and improving circulation. L-citrulline and *Panax ginseng* act through the citrulline/arginine pathway [9,10], while beetroot increases NO via the nitrate/nitrite/NO pathway. Muira puama is believed to influence the NO-cGMP pathway.

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Phosphodiesterase type 5 (PDE5), highly expressed in penile tissue, degrades cGMP. PDE5 inhibitors (PDE5i) maintain cGMP levels by selectively inhibiting PDE5 activity.

First-line ED therapies, including PDE5i and NO boosters, are typically administered orally and are preferred over second and third-line therapies [11]. Our previous research [12] supported the use of NO boosters as potential standalone treatments for ED. There is a growing body of literature that investigates the synergistic effects of NO and PDE5i [13-18], but there is a lack of studies that investigate their combined effects in human subjects using objective measurements. Most ED research relies on subjective instruments, such as the International Index of Erectile Function (IIEF), the Sexual Health Inventory for Men (SHIM) and the Erection Hardness Score (EHS). Objective tools, such as Nocturnal Penile Tumescence (NPT) assessments, are less commonly used. Subjective evaluations may be influenced by emotions, memory and interpretation, suggesting an incomplete picture of erectile health. In contrast, objective measures allow for the unbiased assessment of treatment efficacy and differentiation between psychogenic and non-psychogenic ED causes [1]. Combining both approaches may offer a more comprehensive understanding of ED.

AFFIRM is a commercially available NO-boosting supplement produced by AFFIRM Science, containing L-citrulline, Muira puama extract, red beetroot extract and *Panax ginseng* root extract. NPTs or nighttime erections, occur spontaneously during sleep and are used as indicators of erectile health [19]. The TechRing, a smart wearable developed by FirmTech, is a validated, non-invasive tool that uses two sensors and an AI interface to objectively monitor NPT by measuring erection firmness and duration [20-24]. The present study aimed to determine whether ingesting two AFFIRM tablets one hour before sleep improves NPT as measured by the TechRing.

MATERIALS AND METHODS

Twenty-two men (mean age 55, mean SHIM score 18.1) completed the study. A single tablet of the NO-boosting dietary

supplement contains 750 mg L-Citrulline, 65 mg Muira Puama extract 4:1, red beet root extract 45 mg 4:1 and *Panax ginseng* root extract 35 mg 4:1. This supplement is commercially available as AFFIRM. Sildenafil was administered as two 20 mg tablets.

Participants wore the TechRing during sleep to measure nighttime erectile function. The TechRing uses two sensors and an artificial intelligence interface to measure the firmness and duration of erections.

The research protocol involved a 2-day washout period with no ejaculation, ED medications or supplements. On days 1 and 2, participants ingested 40 mg Sildenafil one hour before sleep and wore the TechRing while sleeping. On days 3 and 4, participants ingested two AFFIRM supplement tablets and 40 mg Sildenafil one hour before sleep and wore the TechRing while sleeping. Data from the TechRing was uploaded from the FirmTech mobile app. To standardize results between patients and between days, the Area Under the Curve per hour of sleep (AUC/hr) was calculated from the TechRing data as a measure of erectile activity.

RESULTS

Participants taking 40 mg Sildenafil without AFFIRM supplements on days 1 and 2 had a mean AUC/hr of 87 and a mean of 3.25 nightly erections. Participants taking 40 mg Sildenafil with AFFIRM supplements on days 3 and 4 had a mean AUC/hr of 117 and a mean of 3.87 nightly erections. The difference in means was 30 (34% increase) with a p-value of 0.00004 ($t=5.219$). The difference in means of nightly erections was 0.62 (19% increase) with a p-value of 0.034 ($t=2.285$). No side effects were self-reported from taking AFFIRM supplements or 40 mg Sildenafil before sleep (Table 1).

Table 1: Comparison of AUC/hr and number of erections between Sildenafil 40 mg and Sildenafil 40 mg with AFFIRM treatment.

	AUC/hr mean	AUC/hr median	Number of erections
Sildenafil 40 mg	87	88	3.25
Sildenafil 40 mg and AFFIRM	117	110	3.87
Mean difference	30	23	0.52
Percentage difference	34%	26%	19%

DISCUSSION

The present study aimed to determine if ingesting 2 AFFIRM tablets with 40 mg Sildenafil one hour before sleep can improve nighttime erections by using the TechRing to measure mean NPT and the mean number of nightly erections. It was found that AFFIRM, consisting of NO boosters L-citrulline, Muira puama extract, red beet root extract, and *Panax ginseng* root extract, improves erectile quality (p-value=0.00004) without side

effects as measured by the area under the curve per hour. There was also a significant increase in nightly erections (p-value=0.034). These results support the synergistic effects between NO boosters and PDE5i in treating ED.

As men age, they experience an increase in erectile dysfunction. One way to improve erectile function is by enhancing the vascularity of the penis through focused shockwave therapy and platelet-rich plasma injections. Less-invasive methods include

strengthening the nitric oxide signal, which leads to an increase in cyclic GMP and dilates blood vessels and blocking the breakdown of cGMP. Our previous research [12] has shown that ingesting nitric oxide boosters like AFFIRM is a safe way to amplify the NO signal in men. PDE5 inhibitors, such as Sildenafil, block the enzyme that breaks down cGMP, resulting in elevated cGMP levels and improved erectile function.

The combination of 40 mg Sildenafil and a NO-boosting dietary supplement increased the duration, intensity and number of nighttime erections compared to 40 mg Sildenafil alone as measured by the TechRing. This NO-boosting dietary supplement improves genital circulation at night. This NO-boosting supplement may also be synergistic with Sildenafil and improve genital circulation during awake sexual activity. Many men who take PDE5i will get side effects. Taking a NO-boosting dietary supplement may boost the effectiveness of a PDE5i without generating side effects that can limit the dose.

CONCLUSION

This study provides evidence for the synergy between NO boosters and PDE5i in treating ED, contributing to the growing body of literature on the topic. The lack of reported side effects from this treatment protocol supports the use of this dual-therapy approach to ED treatment that minimizes side effects from high PDE5i doses.

DISCLOSURE

This study is sponsored by BrandeisMD. Judson Brandeis, MD, is president of AFFIRM Science, and Elliot Justin, MD is president of FirmTech.

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