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Author manuscript *J Sex Med.* Author manuscript; available in PMC 2022 October 12.

Published in final edited form as:

J Sex Med. 2019 June ; 16(6): 843–852. doi:10.1016/j.jsxm.2019.03.269.

## An Analysis of Popular Online Erectile Dysfunction Supplements

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## Abstract

**Introduction:** Erectile dysfunction supplements (ED-Ss) are featured on online marketplaces like Amazon.com, with dedicated pages and claims that they naturally treat ED. However, their efficacy and safety are largely unknown, limiting the ability to counsel patients regarding their use.

**Aim:** To evaluate the highest rated and most frequently reviewed ED-Ss on Amazon.com to facilitate patient counseling regarding marketing myths, ingredient profiles, and evidence for product efficacy and safety.

**Methods:** The Amazon marketplace was queried using the key term "erectile dysfunction" with default search settings and ranking items based on relevance. The top 6 ED-S products identified on September 29, 2018, were reviewed based on price, ratings, reviews, manufacturer, and ingredients. Consumer reviews were categorized using subtopics within the International Index

SUPPLEMENTARY DATA

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Supplementary data related to this article can be found at https://doi.org/10.1016/j.jsxm.2018.10.004.

of Erectile Function (IIEF) questionnaire to better understand ED-S efficacy and then reanalyzed following filtration of untrustworthy comments using ReviewMeta.com, a proprietary Amazon review analysis software.

Outcomes: Quantitative and qualitative evaluation of ED-S products sold on Amazon.com.

**Results:** The top 6 ED-Ss had an average of  $2,121 \pm 1,282$  reviews and a mean rating of  $3.92 \pm 0.42$  stars. A total of 21 ingredients were identified in these ED-Ss. Ginseng, horny goat weed, L-arginine, and tongkat ali were the most popular ingredients included in the analyzed products. Our literature review identified 413 studies involving the 21 identified ingredients, of which 59 (16%) involved human subjects. Among these 69 human studies, only 12 (17%) investigated supplement ingredients individually and reported improvement in ED. Analysis of top-ranked customer reviews from the first 2 pages of reviews for each supplement revealed differences in IIEF scores before and after ReviewMeta.com filtration. After filtration, we observed a 77% decrease in reviews reporting improved erection strength, an 83% decrease in reviews reporting increased sexual satisfaction, an 88% decrease in reviews reporting increased enjoyment with intercourse, and an 89% decrease in reviews reporting increased erection confidence.

**Strengths & Limitations:** Study strengths include a novel approach to ascertaining consumers' perceptions and satisfaction with ED-Ss and practical summary information that clinicians can provide to patients. Limitations include selection bias, the small number of supplements analyzed, and the proprietary nature of the Amazon review analysis software.

**Conclusions:** Our investigation revealed that human studies evaluating the efficacy of ED-S ingredients are limited and have yielded no definitive findings of the effects on ED. Patients considering ED-S use should receive appropriate counseling, given the prevalence of disingenuous reviews and the ready availability of Food and Drug Administration–approved drug therapies.

#### Keywords

Erectile Dysfunction; Supplements; Nutraceutical; Internet

## INTRODUCTION

Erectile dysfunction (ED) is defined as the inability to achieve or maintain an erection sufficient for satisfactory sexual performance.<sup>1</sup> ED is highly prevalent, affecting upward of 52% of men age 40–70 years in the United States alone.<sup>2</sup> The pharmacologic management of ED continues to evolve.<sup>3</sup> Following the approval of sildenafil in 1998, 2 other oral phosphodiesterase-5 (PDE-5) inhibitor medications, tadalafil and vardenafil, were introduced in 2003.

Despite this considerable pharmacologic innovation, patients seeking treatment for ED continue to face notable barriers to care. Frederick et al<sup>4</sup> found that ED is undertreated in the United States in light of patients' reticence in discussing the condition with physicians, high medication costs, inadequate insurance coverage, and failure to respond to PDE-5 inhibitor therapy. Le et al<sup>5</sup> corroborated these findings, noting that reimbursement and insurance policies for ED lack transparency and impede patients from pursuing appropriate

Cui et al<sup>6</sup> recently reported that patients are using herbal and nutrient supplements to address various men's health issues, including ED. Erectile dysfunction supplements (ED-Ss) are composed of a heterogeneous array of ingredients, with popular ingredients including ginseng, maca, and epimedium, among others.<sup>7</sup> Pursuant to the Dietary Supplement Health and Education Act of 1994, the US Food and Drug Administration (FDA) does not regulate ED-S products or other supplements.<sup>8</sup> This policy has permitted ED-S products to gain traction without the scrutiny given to conventional pharmacotherapies. ED-S marketing materials often claim that these products can naturally improve erectile function as effectively as FDA-approved therapies, such as sildenafil.<sup>9</sup> While ED-S products are proliferating, investigations of these supplements have shown that these products are often mislabeled or adulterated with therapeutic doses of conventional PDE-5 inhibitors.<sup>9–13</sup>

Online marketplaces like Amazon.com are increasingly popular sources for acquiring health and nutritional supplements.<sup>14,15</sup> The popularity of electronic commerce (e-commerce) is projected to continue to grow owing to increasing consumer preference for the online marketplace over traditional physical retail stores.<sup>14,16</sup> ED-S products are prominently featured on Amazon, with numerous dedicated pages and claims that they can "naturally" improve ED. The presence of ED-Ss in the Amazon marketplace ensures their considerable visibility and ready consumer accessibility.<sup>14</sup>

Customers acquiring products online, including ED-Ss, often consult user reviews featured on product pages to validate product efficacy. This consumer behavior is promoted by the broader online phenomenon of social commerce, which encourages consumers to post online product reviews. These product reviews, often featured on Amazon, have come under increasing scrutiny owing to disingenuous behavior by vendors, including fake reviews generated by "collusive spammers," as well as paid reviews.<sup>17–24</sup> The impact of fake product reviews is notable given consumers' general high levels of trust in health-related information available from online portals.<sup>25</sup>

Physicians should be aware of the most popular ED-Ss, owing to these products' easy obtainability, the high consumer interest in these products, and frequent questions that arise during patient consultations. In the present study, we evaluated the most highly rated and frequently reviewed ED-S on Amazon.com to facilitate patient counseling regarding marketing myths, ED-S formulations, and evidence of efficacy of these supplements. Specifically, we aimed to evaluate the underlying evidence of the efficacy of ED-S ingredients and to determine whether ED-S product reviews are from actual users or as part of a digital marketing strategy.

## METHODS

#### Identification of the Top 6 ED-S Products

ED-Ss were identified by querying the Amazon.com website using the key term "erectile dysfunction" (Figure 1). The 6 highest-ranked supplements on Amazon, using default search settings that sort and present featured items, on September 29, 2018, were selected for further examination. Supplement information, ingredients, and comments from the initial 2 available pages of reviews were collected and stored offline to ensure consistency in data analysis, given the dynamic and routinely updated online marketplace. Amazon allows consumers to validate reviews via a "helpful" button under each submitted product review. Comments that receive the highest number of "helpful" clicks are presented on the first 2 pages of reviews. Reviews from these 2 pages were selected for analysis in this study, because other consumers have vouched for these comments. In addition, comments from the first 2 pages are automatically presented to consumers who browse product pages. 6 supplements were chosen to provide a holistic survey of popular ED-S products available in the Amazon marketplace.

#### Assurance of Organic Search Results

A new Amazon account was created to minimize bias from user profiling techniques, including third-party tracking and browser cookies.<sup>26</sup> Bias was further mitigated by using browser-based private mode features for all online data acquisition. Additional efforts to ensure the integrity of search results involved installing uBlock Origin (https://github.com/gorhill/uBlock), a third-party software that blocks advertising and query tracking.

#### Analysis of ED-S Ingredients

Supplement ingredients were aggregated and cataloged. Ingredients were classified into active ingredients versus filler or inactive ingredients formally known as excipients.<sup>27</sup> A PubMed search was performed for all active ingredients in conjunction with the key term "erectile dysfunction." A systematic review was undertaken to classify articles based on study population, including human studies, animal studies, in vitro studies, and other studies (eg, case reports, review articles). Human studies were further stratified into investigations that were not supplementation-oriented and studies in which the ingredient was combined with multiple other ingredients. The remaining identified studies that used the International Index of Erectile Function (IIEF) questionnaire were reviewed to assess the impact of each ingredient on erectile function.

#### Analysis of User Comments

All available Amazon reviews from the first 2 product review pages were aggregated for each product. The IIEF questionnaire (Supplementary Figure 1), a validated tool for identifying and classifying ED symptoms and assessing response to ED therapies, was used to analyze reviews for ED-S efficacy.<sup>28</sup> Two raters (A.B. and A.S.) coded all aggregated comments using the IIEF questionnaire. An qualitative analysis of an Amazon comment using the IIEF is diagrammedin Figure 2.The IIEFquestionnairewas usedas a checklist to grade each comment. As the comment was read, each reviewer analyzed whether

the comment's content was relevant to a particular IIEF domain. If, for example, the comment contained content related to erection frequency or erection strength, then the reviewer independently noted that the comment was pertinent to that IIEF domain. Interrater reliability was determined using the *k* statistic.<sup>29</sup> A third rater (N.T.) determined the final IIEF scoring of a comment if a difference between raters was observed.

#### **ReviewMeta Screen**

A proprietary web-based online review analyzing service, ReviewMeta, was used to analyze the integrity of review comments for each supplement. ReviewMeta analyzes products hosted on the Amazon marketplace using 11 filters: suspicious reviewers, reviewer ease, rating trend, unverified purchases, word count comparison, phrase repetition, overlapping review history, reviewer participation, brand repeats, incentivized reviews, and deleted reviews. ReviewMeta identifies the percentage of overall comments that are considered suspect. The ReviewMeta algorithm also assigns a score of "pass," "warn," or "fail" under each of the 11 domains to provide additional insight into patterns underlying suspicious reviews. Once the filtering process is complete, ReviewMeta produces a ranked list of the most trustworthy comments. After ReviewMeta filtering, the number of failed categories for each supplement was correlated with the percentage of eliminated untrustworthy comments using Pearson correlation. All trustworthy comments returned via ReviewMeta analysis were then analyzed using the IIEF questionnaire as detailed above.

## RESULTS

#### **ED-S Ingredients**

The top 6 ED-S products sold on Amazon on September 29, 2018, included Korean Panax Ginseng (NutraChamps, Toronto, ON, Canada), Leyzene with Royal Jelly (Natural Subsistence, Wadsworth, OH, USA), Horny Goat Weed Extract (Zhou Nutrition, Park City, UT, USA), Boost Elite (Zhou Nutrition), Extra Strength L-Arginine (Havasu Nutrition, Sunrise, FL, USA), and IncrediBULL (eSupplements, Vineyard, UT, USA). These supplements, including manufacturers, cost per unit, and ingredient profiles, are listed in Table 1. The top 6 ED-S products had an average of  $2,121 \pm 1,282$  reviews (range 37-3,728), and an average rating of  $3.92 \pm 0.42$  stars (range 3.4-4.5 stars).

All 6 ED-Ss were sold by 5 unique US-based manufacturers, and 3 were identified as being produced in "FDA registered" facilities. The average cost per bottle was  $23.83 \pm 7.56$  (range 1.5.17 to 34.50). The average suggested dose was 1.8 pills (range 1-3 pills), with an average cost per pill of  $1.12 \pm 1.40$  (range 0.18-3.45). One of the 6 supplements was designated as an Amazon Choice purchase. The packaging of all 6 ED-Ss reported quantities of individual ingredients. A total of 21 active and 6 inactive ingredients were identified across the 6 supplements, and the supplements had an average of  $8.2 \pm 4.3$  ingredients (range 2-13). Ginseng, L-arginine, tongkat ali, and horny goat weed were the 4 most commonly included active ingredients.

The 6 ED-Ss contained variable amounts of these ingredients per dose. Ginseng was present at an average of  $254 \pm 420$  mg per dose, with a range of 20-1,000 mg across

the 6 supplements. A similar degree of variability was seen for the other 3 most popular ingredients (Table 2).

#### Ingredient Analysis

A PubMed analysis as detailed in Methods was undertaken for the 21 active ingredients used across all supplements (Table 2). The number of studies examining each of these ingredients was determined, and studies were grouped based on in vivo human and animal studies, in vitro studies, and other types of studies. The PubMed search, which included the ingredients as well as the term "erectile dysfunction," yielded 413 studies mentioning these active ingredients, of which 68 (16%) involved human subjects, 181 (44%) involved animal models, 45 (11%) were in vitro studies, and 119 (29%) were other types of studies (eg, case reports, review articles). There was no uniform distribution of articles among the most common ingredients. An average of  $19.7 \pm 55.0$  articles were identified per ingredient (range 0–256), with no published studies for 8 of the 21 ingredients (38%). The most extensively studied ingredient was L-arginine, with 256 articles, including 36 studies in humans. Ginseng had 41 human studies, and zinc had 32 human studies. Among the analyzed ingredients with a minimum of 5 associated studies, saw palmetto berry had the highest ratio of human studies to total studies (33%; 5 of 15).

Among the 69 human studies, only 26 (38%) investigated ingredients individually, and of these, 16 (62%) used pre- and post-IIEF measurements to monitor response to ingredients. Among these studies, 12 (75%) observed an improvement in ED, none reported a negative effect, 3 (19%) reported no effect, and 1 (6%) had indeterminate data. Accurate comparisons among the 68 human studies were not possible, given the nonuniform dosing and sampling timelines. The study designs, demographics, and inclusion criteria of these studies are summarized in Supplementary Table 1.

#### Analysis of Supplement Comments Before ReviewMeta Filtration

User comments on Amazon were evaluated to gain insight into the benefits and efficacy of the ED-S products. All reviews from the top 2 pages of comments were collected for each supplement, resulting in a total of 90 reviews, and analyzed using the IIEF questionnaire as described in Methods. The *k* statistic for interrater reliability was 0.94, indicating strong agreement among our raters before a third rater addressed any discrepancies.<sup>30</sup> Results from the qualitative analysis of comments via IIEF from the first 2 product pages before ReviewMeta filtration are summarized in Table 3 and graphically presented in Figure 3. We found that many reviewers reported improved erection strength (36%), improved ability to maintain an erection overall (29%), increased satisfaction (32%), increased enjoyment with sexual intercourse (27%), increased satisfaction with sex life (27%), and improved erection confidence (31%). 53 of 90 comments (58%) from the first 2 pages of reviews did not contain content relevant to any IIEF questions or domains.

#### Analysis of Supplement Comments Following ReviewMeta Filtration

All supplements were filtered using the proprietary ReviewMeta service as detailed in Methods to analyze malicious review trends and eliminate untrustworthy comments. As described previously, the algorithm uses 11 categories as described in Methods and

determines whether reviews of a product "pass," "warn," or "fail" under each domain. We correlated the number of "fail" results with the number of comments that were removed and found a positive correlation (R = 0.8484; P < .05), indicating that the more "fail" results a supplement had, the greater the likelihood that it had questionable reviews (Supplementary Figure 2). There were a total of 12,840 reviews for the 6 ED-S products, of which 48% were considered untrustworthy by ReviewMeta filtration and excluded from our analysis. 37 of 60 comments (61%) following ReviewMeta filtration did not contain content relevant to any IIEF questions or domains.

After filtration, 60 user comments were reevaluated using the IIEF questionnaire to semiquantitatively determine the effects of individual ED-S products on quality of life. The k statistic was 0.96, indicating very high interrater agreement before resolution of disagreements by a third rater.<sup>30</sup> Results from the qualitative analysis of comments filtered by ReviewMeta via IIEF are summarized in Table 3 and graphically presented in Figure 3. After filtering supplement reviews using the ReviewMeta service, considerable differences in both overall and the popular IIEF categories identified before filtration were observed. We identified a 77% decrease in users reporting improvements in erection strength and an 83% decrease in users reporting improvements in ability to maintain an erection overall. Similarly, we observed a 90% decrease in users reporting increased sexual satisfaction and an 88% decrease in users noting increased enjoyment with sexual intercourse. Furthermore, we observed an 88% decrease in users noting increased satisfaction with their sex life and an 89% decrease in users reporting increased erection confidence. 21 of the 60 filtered comments (35%) explicitly mentioned negative side effects associated with the ED-S products, most commonly a lack of response (86%; n = 18), headache (14%; n = 3), increased blood pressure (9.5%; n = 2), nausea (9.5%; n = 2), dizziness (5%; n = 1), anxiety (5%; n = 1), and heartburn (5%; n = 1).

## DISCUSSION

The psychosocial burdens of ED can lead men to experience feelings of shame, guilt, or stigma.<sup>31,32</sup> These associated stressors may contribute to patients' reluctance to discuss ED symptoms and management with providers.<sup>4,33</sup> Although efforts such as the "process of care" model are routinely updated in an effort to standardize ED diagnosis and management, similar initiatives have not been undertaken for Internet content focused on ED.<sup>34</sup> This lack of oversight is critical, given that people are increasingly receiving health care information via the Internet.<sup>35</sup> Globally, Zhang et al<sup>36</sup> reported that younger Chinese patients are using the Internet as their default location to learn about ED specifically. Read et al<sup>37</sup> and Amber et al<sup>38</sup> have demonstrated that online information about ED is often biased. As e-commerce becomes the most popular avenue for obtaining goods for American consumers, investigations of the information presented on ED-S product pages are warranted, given the generally high level of trust in online information.<sup>14,16,25</sup> The increasing influence of the Internet, along with the ready availability of supplements oriented toward ED, underscore the importance of understanding ED-S products sold on Amazon.com.

In this study, the top 6 ED-S products listed on Amazon.com on September 29, 2018, were identified and found to be manufactured by 5 unique US manufacturers. Of note, quantities

of each ingredient were transparently indicated on the labels of each supplement despite flexible reporting regulations.<sup>39</sup> This information enabled us to determine that each ED-S had a heterogeneous ingredient composition. The variability in doses of popular ingredients, such as ginseng, L-arginine, horny goat weed, and tongkat ali extract, raises the question of why specific combinations of ingredients were chosen for each supplement.

We also found that only one-half of these supplements were marketed as being assembled in "FDA-registered" facilities. Although this labeling should be viewed with caution, given that the FDA does not formally review supplements, the lack of any statement regarding standardized manufacturing practices in the remaining ED-S products raises concerns about actual supplement composition. This is particularly significant given a string of recent investigations revealing that some "natural" supplements contain active pharmaceutical ingredients.<sup>13,40–43</sup> Patients should also be counseled that these ingredient concerns are not unique to herbal or natural supplements targeted at ED. Chiang et al<sup>10</sup> reported that even compounded PDE-5 inhibitors have been counterfeited, even though they are subject to more stringent regulations related to drug manufacturing. Taken together, these findings support the importance of healthcare practitioners counseling patients to obtain ED treatment from reputable sources.

A review of the literature examining ED-S highlights the limited amount of available efficacy data. We observed that only 69 of the 413 studies that we identified (17%) were undertaken in human subjects. Of these 69 human studies, only 26 (38%) investigated these active ingredients individually, whereas 25 (36%) evaluated a combination of active ingredients. Patients should be counseled that the current body of evidence examining the efficacy of ED-S product ingredients is derived from studies using heterogeneous supplementation protocols. The lack of uniformity across these studies highlights concerns about the variable ingredient profiles and online customer reviews claiming that these supplements can dramatically improve ED symptoms.

Nearly 50% of the reviews of the top 6 ED-S products were excluded following filtration using the ReviewMeta.com software. The removal of nearly one-half of all reviews associated with these products raises concerns about the veracity of comments linked to these products. The positive linear correlation that we identified between the number of fails per category and untrustworthy comments as determined by ReviewMeta.com further suggests that product reviews hosted on online marketplaces like Amazon.com should be interpreted with caution, and that product reviews might artificially overinflate supplement efficacy.

We observed that many reviews did not explicitly state the supplementation regimen associated with ED-S products. The lack of specificity regarding dosages is important, given the variable ingredient compositions of the supplements. We also found that many comments did not include any mention of lifestyle modifications or patient comorbidities. Emerging research linking ED to systemic conditions, such as cardiovascular disease and diabetes, underscores the importance of a thorough evaluation before using any supplement or drug.<sup>44,45</sup>

After filtration by ReviewMeta.com, the online comments were more tempered in their praise for these supplements. Although there were significant reductions in touted benefits across all IIEF categories, 8.3% of product reviews continued to report improvements in erection strength after filtering. This finding can help healthcare practitioners understand patients' subjective assessment of product efficacy and tailor future counseling efforts about the true impact of these ingredients on erection strength. Previous ED studies have also demonstrated that treatment of ED with oral placebos can elicit clinical effects and improve ED symptoms.<sup>46</sup> The positive placebo effect on erectile function and quality of erection should also be considered when interpreting purported benefits of ED-S products.

This study has several limitations that should be acknowledged. First, this analysis was limited to 6 ED-S products hosted on Amazon.com that were yielded the top results from a single search query on a single day. Although many other ED-Ss are available in the Amazon marketplace, these products did not rank sufficiently high to be considered for the present study. Even though these other ED-Ss are likely relevant in a discussion of ED-Ss on Amazon, we believe that our supplement selection is warranted, given that customers often consider only the most highly rated products. In addition, we believe that the findings gleaned from the products included in this study are applicable for other, less highly ranked products as well. Second, we acknowledge that the proprietary nature of the ReviewMeta algorithm limits the transparency with which we and others can report results. Although validation of the review results obtained via the ReviewMeta tool is desirable, no other comparable services are available. Third, we recognize that we have limited information about whether users submitting reviews on these product pages have ED or are using ED-S for self enhancement. Furthermore, we acknowledge that for users who actually did have ED, we had no information on the severity of their ED symptoms to evaluate whether ED-S use resulted in clinically significant improvements.

## CONCLUSION

ED-S products are readily accessible from online marketplaces such as Amazon.com and are used by numerous patients with ED. Physicians must be aware of the ingredients in these supplements to better counsel patients about the efficacy of these supplements. Although consumer reviews hosted on ED-S online product pages prominently tout product efficacy, primary evidence supporting positive effects of these products on ED symptoms is lacking. The present study revealed a lack of consistency in supplementation protocols used in human studies evaluating the efficacy of ED-S ingredients. In the absence of more definitive human data, patients should be cautioned before considering ED-S use, particularly in light of the availability of highly effective FDA-approved drugs and increasingly affordable therapeutic options.

## Supplementary Material

Refer to Web version on PubMed Central for supplementary material.

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## Funding:

A.W.P. is a National Institutes of Health K08 Scholar supported by a Mentored Career Development Award (K08DK115835-01) from the National Institute of Diabetes and Digestive and Kidney Diseases. This work is supported in part through a Urology Care Foundation Rising Stars in Urology Award (to A.W.P.) and National Institutes of Health Grant K12 DK0083014 and a Multidisciplinary K12 Urologic Research Career Development Program from the National Institute of Kidney and Digestive Diseases (to D.J.L.). N.T. is a K12 Scholar. The content is solely the responsibility of the authors and does not necessarily represent the official views of the National Institutes of Health.

#### Conflicts of interest:

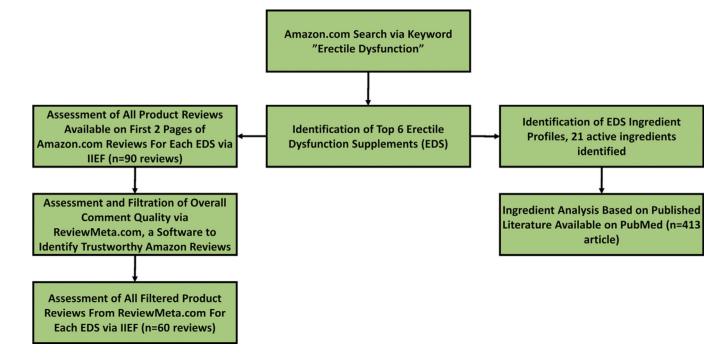
Dr. Pastuszak: Endo Pharmaceuticals: advisor, consultant, speaker; Boston Scientific, advisor; Antares Pharamaceuticals, advisor. Dr. Lipshultz: American Medical Systems, speaker; AbbVie, consultant; Lipocine, consultant; Aytu Bioscience, consultant; Endo Pharmaceuticals, speaker/consultant. Dr. Hotaling: Endo pharmaceuticals, educational/research grant; Boston Scientific, educational/research grant; Streamdx; Andro360; Nanonc-Equity.

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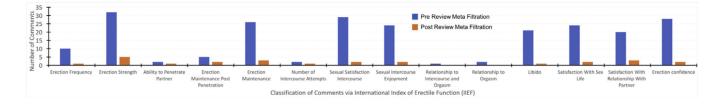
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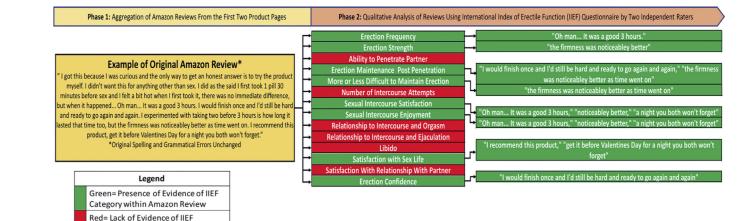


**Figure 1.** Overview of the investigative method.



### Figure 2.

Breakdown of qualitative analysis of Amazon reviews using the International Index of Erectile Function (IIEF) questionnaire.



#### Figure 3.

Category within Amazon Review

Comparison of the International Index of Erectile Function (IIEF) comments between preand post-ReviewMeta filter analysis.

Parameter	Korean Panax Ginseng (NutraChamps) (NutraChamps)	Leyzene with Royal Jelly (Natural Subsistence)	Horny Goat Weed Extract (Zhou Nutrition)	Boost Elite (Zhou Nutrition)	Extra Strength L Arginine (Havasu Nutrition)	IncrediBULL (eSupplements)
Cost per pill, \$	0.18	2.2	0.25	0.35	0.3	3.45
Active ingredients						
AAKG					х	
Piperine		Х				
Capsicum annuum			x		х	
Diindolylmethane				х		
Epimedium						х
Fenugreek seed				х		
Ginseng (panax ginseng, ginsenosides)	x	х	х	х		x
Gluconolactone		х				
Horny goat weed		х	х	х		
L-arginine		Х	х		х	
L-citrulline malate					х	
Maca root			х	Х		
Muira puama			х			х
Polypodium vulgare			х			
Rehmannia root						х
Royal jelly		Х				
Saw palmetto berry			х			
Tongkat ali			х	х		х
Tribulus terrestris			х	Х		
Yohimbe bark				х		
Zinc				х		
Inactive ingredients						
Gelatin		Х				

J Sex Med. Author manuscript; available in PMC 2022 October 12.

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Table 1.

Cost and ingredient profile of the top 6 ED-S products

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Parameter	Korean Panax Ginseng (NutraChamps) (NutraChamps)	Leyzene with Royal Jelly (Natural Subsistence)	Horny Goat Weed Extract (Zhou Nutrition)	Boost Elite (Zhou Nutrition)	Extra Strength L Arginine (Havasu Nutrition)	IncrediBULL (eSupplements)
Rice flour	Х		x	x	х	
Silica				Х	Х	
Vegetable cellulose			х	х		х
Vegetable magnesium stearate		х	Х	Х		
Total ingredients	2	8	13	13	7	6
Active ingredients	1	6	10	6	4	5
Inactive ingredients	1	2	ŝ	4	ε	1

AAKG = (L-arginine-alpha-ketoglutarate).

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Table 2.	Summary of systematic PubMed literature review for the 10 most common ED-S ingredients

		Inclusion	Inclusion in PubMe	ed Searchable Studies	ble Studie		Impact on Erectile Dysfunction in Human Studies	Dysfunction i	n Human St	udies				
Ingredients	Number of supplements included	Human studies	Animal studies	In vitro studies	Other	Total	Not supplementation oriented	Combined with other ingredients	Studies using non- IIEF outcomes	Pre-/post- intervention IIEF score measured	Positive effect	Negative effect	No effect	Indeterminate
Ginseng (panax ginseng, ginsenosides)	S	Q	6	2	24	41	0	-	_	Ś	ŝ	0	0	0
L-arginine	3	36	144	37	39	256	15	14	3	4	4	0	0	0
Tongkat ali	3	0	3	1	9	10	0	0	0	0	0	0	0	0
Horny goat weed	3	0	1	1	1	3	0	0	0	0	0	0	0	0
Tribulus terrestris	2	Ζ	S	1	11	24	0	3	0	4	2	0	-	1
Maca root	2	1	0	1	5	7	0	0	0	1	1	0	0	0
Muira puama	2	1	2	0	0	3	0	1	0	0	0	0	0	0
Capsicum annuum	5	0	0	0	0	0	0	0	0	0	0	0	0	0
Zinc	1	8	6	1	17	32	2	1	5	0	0	0	0	0
Epimedium	1	2	8	1	9	17	0	2	0	0	0	0	0	0
Saw palmetto berry	1	S	33	0	7	15	1	3	0	1	0	0	-	0
Fenugreek seed	1	1	0	0	1	2	0	0	1	0	0	0	0	0
Yohimbe bark	1	0	0	0	2	2	0	0	0	0	0	0	0	0
Diindolylmethane	1	1	0	0	0	1	0	0	0	1	0	0	1	0
AAKG	1	0	0	0	0	0	0	0	0	0	0	0	0	0
Piperine	1	0	0	0	0	0	0	0	0	0	0	0	0	0
Gluconolactone	1	0	0	0	0	0	0	0	0	0	0	0	0	0
L-citrulline malate	1	0	0	0	0	0	0	0	0	0	0	0	0	0
Polypodium vulgare	1	0	0	0	0	0	0	0	0	0	0	0	0	0
Rehmannia root	1	0	0	0	0	0	0	0	0	0	0	0	0	0
Royal jelly	1	0	0	0	0	0	0	0	0	0	0	0	0	0

		Inclusion	nclusion in PubMee	d Searchable Studies	ole Studie	s	Impact on Erectile Dysfunction in Human Studies	Dysfunction	in Human St	udies				
Ingredients	Number of supplements included	Human studies	Animal studies	In vitro studies	Other Total	Total	Not supplementation oriented	Combined with other ingredients	Studies using non- IIEF outcomes	Pre-/post- intervention IIEF score measured	Positive effect	Negative effect	No effect	Negative No effect Indeterminate
	Total	69	181	45	119 413 18	413	18	25	10	16	12	0	ю	1

AAKG = (L-arginine-alpha-ketoglutarate).

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IIEF category	Comments before ReviewMeta filtration, % (n/N)	Comments after ReviewMeta filtration, % (n/N)	Difference between pre- and post-ReviewMeta filtration, %
Improvement in erection frequency	(11.11 (10/90)	1.67 (1/60)	85.0
Improvement in erection strength	35.56 (32/90)	8.33 (5/60)	76.6
Improvement in ability to penetrate partner	2.22 (2/90)	1.67 (1/60)	24.8
Improvement in ability to maintain erection after penetration	5.56 (5/90)	3.33 (2/60)	40.1
Improvement in ability to maintain erection overall	28.89 (26/90)	5 (3/60)	82.7
Number of intercourse attempts	2.22 (2/90)	1.67 (1/60)	24.8
Increased sexual satisfaction	32.22 (29/90)	3.33 (2/60)	89.7
Increased enjoyment with sexual intercourse	26.67 (24/90)	3.33 (2/60)	87.5
Improved ability to ejaculate on stimulation or intercourse	1.11 (1/90)	0 (0/60)	100.0
Improved ability to orgasm on stimulation or intercourse	2.22 (2/90)	0 (0/60)	100.0
Increase in sexual desire (libido)	23.33 (21/90)	1.67 (1/60)	92.8
Increased satisfaction with sex life	26.67 (24/90)	3.33 (2/60)	87.5
Increased satisfaction with relationship with partner	22.22 (20/90)	5 (3/60)	77.5
Increased erection confidence	31.11 (28/90)	3.33 (2/60)	89.3