The Use of Natural Products for the Treatment of Female Sexual Dysfunction: A Systematic Review of Randomized Clinical Trials

Ana Rosa Jurado¹,², Mirian Jouda-Benazouz¹, Loreto Mendoza-Huertas¹, Nicolás Mendoza¹*

¹Departament of Obstetrics and Gynecology, University of Granada, Granada, Spain
²Instituto Europeo de Sexologia, Marbella, Málaga, Spain

Email: anarosajuradolopez@gmail.com, mirianjouda7@gmail.com, *nicomendoza@telefonica.net, loretomendoza2@gmail.com

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Abstract

Female sexual dysfunction (FSD) affects 40% of the world’s females, most of which are disorders linked to desire or interest/excitement. Whilst all types of therapy that attempt to improve female sexual desire have long been established, the results are contradictory. Objective: To analyze all available evidence to validate the effectiveness of natural therapies in the treatment of FSD. Method: The study was registered at http://www.prospero.org (CRD42019127700). We searched the Institute for Scientific Information Web of Knowledge, MEDLINE, Pubmed, Scopus and Cochrane databases for all articles published in peer-reviewed journals in April 2019 (in any language). The PICOS standard is women with FSD; (intervention) of any type of Natural therapy; (outcome) primary outcome: frequency of changes, severity, and average mean scores on sexual symptoms measured with a validated instrument, secondary outcome: quality of life; (study design) and randomized clinical trial (RCT). Results: The literature search strategy identified 95 articles, 81 of which were excluded at the different search stages. Finally, we systematically reviewed 15 RCTs, 11 of which referred to primary FSD, and four of which analyzed women with drug-induced FSD (DFSD). Most of them analyzed hypoactive sexual desire disorder. Although differences related to placebo were found in most people, the majority of the studies are considered to be of poor quality and low external effectiveness. Conclusion: Although the quality of the evidence is not high, most natural product interventions appear to improve FSD, particularly hypoactive sexual desire disorders including those categorized as primary and drug-induced.

Keywords

Female Sexual Dysfunction, Drug-Induced Female Sexual Dysfunction, Sexual Health, Natural Therapies
1. Introduction

It is estimated that some type of sexual dysfunction affects 40% of females worldwide, with most being manifest as desire or interest/excitement disorders [1]. The majority of postmenopausal women report symptoms that affect their sexual health, which can either be secondary to vulvovaginal atrophy (VVA) or the result of disorders of desire, interest, or excitement [2]. In this regard, there is a close relationship between female sexual dysfunction (FSD) and poor quality of life, which is often associated with psycho-affective problems such as anxiety, melancholy, low self-esteem, or marital problems [3]. However, there are significant problems regarding the manner in which various studies have evaluated “sexual dysfunction” or distress in women, including the use of non-validated instruments [4].

Moreover, the use of any type of formulation that attempts to improve female sexual desire has long been established, although the results are contradictory. A recent meta-analysis has also indicated that placebo accounts for almost 70% of FSD treatment, meaning that any interventions studied to date have reached a lower level than placebo, which emphasizes the need for more treatments that are effective for any type of FSD [5]. However, certain biases are observed in the conclusions of this meta-analysis, such as that the different conditions and different treatments for FSD in this single meta-analysis, or that placebo rates are also high for other conditions or other treatments for women.

The purpose of this systematic review is to analyze all available evidence to validate the effectiveness of natural therapies in the treatment of FSD.

2. Methods

2.1. Selection of Studies

We searched the Institute for Scientific Information Web of Knowledge, MEDLINE, Pubmed, Scopus, and Cochrane databases for all articles (in any language) published in peer-reviewed journals in April 2019 using the search strategy described in Appendix. The search criteria were adjusted for each database as well as the database-specific filters available. Other publications were identified by manually searching through a reference list of papers identified by the search as well as key words, which were hand-searched to select additional publications. We also considered those that were in press in peer-reviewed journals and available online prior to publication.

The PICOS (Population, Intervention, Comparison, Outcomes, Study design) criteria are developed a priori to guide the scope of the review and the procedures, selection, and synthesis of the literature search. The selection criteria were as follows: (population) FSD female; (intervention) any type of natural therapy; (outcome) primary outcome: change in frequency, severity and average mean scores of sexual symptoms measured with a validated instrument; secondary outcome: Quality of life; (study design) randomized clinical trial (RCT). Complete articles that meet the inclusion criteria were reviewed in detail. Other related papers are

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for reference purposes only.

The exclusion criteria were: other etiologies for FSD and prevention (or treatment) of the FSD.

Key words: female sexual dysfunction, drug induced female sexual dysfunction, sexual health, natural therapies.

PICO question: Can natural products improve FSD, both primary and drug induced?

2.2. Data Extraction

Two independent reviewers (NM and MJ) extracted the data from the included studies using a specifically developed data extraction form based on the selection criteria. The extracted information includes a description of the study, participants, and findings based on the above results. Where there was no data (method or result) of interest in the published paper, we contacted the authors by email.

2.3. Assessment of Study Quality and Data Synthesis

We conducted a systematic review in accordance with PRISMA [6]. The authors (NM, MJ, and AR) conducted an independent search and screening studies to include, extract and examine data and synthesize the results. The authors (NM, MJ, AR and CN) independently determined the adequacy and primary methodological characteristics of the study design to determine the validity of the study. Any disagreements were resolved through discussion and consensus.

3. Results

As shown in Figure 1 (PRISMA flow diagram), the literature search strategy identified 96 articles, 81 of which were excluded at different stages of the search. Finally, we systematically reviewed 15 RCTs [7]-[21], 11 of which mentioned the primary FSD [8] [13] [15] [21] or hypoactive sexual desire disorders (HSDD) [7] [9] [10] [11] [12] [14] [20]. The other four RCTs analyzed women with DIFSD [16] [17] [18] [19]. A summary of the main features of the selected studies (population, intervention, comparison, outcomes, and study design) is displayed in Table 1.

Regarding the characteristics of the intervention, in FSD or HSDD, Tribulus terrestris was used for four studies [9] [12] [13] [14], visnadine (Ammi visnaga) was used for three [15] [20] [21], and ArginMax was used for one [7], red clover (Trifolium pratense) is used in one [8], Libifem (Trigonella foenum-graecum) in one [10], Elaeagnus angustifolia in one [11]. Ginkgo biloba leaves were used in one study [16], saffron (Crocus sativus) was used in one [17], and Rosa damascena oil was used in two studies [18] [19].

Placebo-related differences were found in 9 of the studies [7] [8] [9] [10] [15] [16] [17] [18] [19] [21]. One of the interventions with Tribulus terrestris (750 mg/day for 4 weeks), found placebo-related differences in terms of desire, arousal,
Table 1. Summary of findings in female sexual dysfunction.

| Authors            | Method     | Population | Intervention                  | Objective            | Main results                                                                 |
|--------------------|------------|------------|--------------------------------|----------------------|-----------------------------------------------------------------------------|
| Ito et al. 2006    | RCT        | 108 women  | ArginMax\(^a\) (n = 55)        | Efficacy on HSDD     | Improvement in postmenopausal women (p = 0.008)                              |
|                    |            | with HSDD  | Placebo (n = 53)               |                      |                                                                             |
|                    |            | Age: 22 - 73 | 8 weeks                       |                      |                                                                             |
| Chedraui et al. 2006 | Crossover RCT | 60 women | Red clover\(^b\), 80 mg/day (n = 30) | Efficacy on FSD      | Improvement in dyspareunia, vaginal dryness and decreased libido (p < 0.05) |
|                    |            | with FSD  | Placebo (n = 30)               |                      |                                                                             |
|                    |            | Age: >40  | 3 + 3 months                   |                      |                                                                             |
| Akhtari et al. 2014 | RCT        | 67 women  | Tribulus terrestris\(^c\), 750 mg/day (n = 33) | Efficacy on HSDD    | Improvement on total FSFI (p < 0.001), desire (p < 0.001), arousal (p = 0.037), lubrication (p < 0.001), satisfaction (p < 0.001) pain (p = 0.041) |
|                    |            | with HSDD | Placebo (n = 34)               |                      |                                                                             |
|                    |            | Average age: 36 | 4 weeks                       |                      |                                                                             |
| Rao et al. 2015    | RCT        | 80 women  | Trigonella foenum-graecum\(^d\) seed extract (Libifem) 600 mg/day (n = 40) | - Primary: efficacy on HSDD; Secondary: E2 and testosterone | Improvement in sexual desire and arousal vs placebo (p < 0.05)              |
|                    |            | with HSDD | Placebo (n = 40)               |                      |                                                                             |
|                    |            | Average Age: 34.9 (20 - 49) | 2 menstrual cycles |                      |                                                                             |
| Zeinalzadeh et al. 2016 | RCT        | 125 women  | Elaeagnus angustiflora\(^e\), 4.5 g (n = 41) | - Primary: efficacy on HSDD; Secondary: TSH and prolactin | Only sildenafil decreased anxiety resulting from sexual dysfunction |
|                    |            | with HSDD  | Sildenafil 50 mg (n = 42)       |                      |                                                                             |
|                    |            | Age: 18 - 40 | Placebo (n = 42)               |                      |                                                                             |
|                    |            |            | 4 weeks                        |                      |                                                                             |
| Postigo et al. 2016 | RCT        | 60 women  | Tribulus terrestris\(^f\), 750 mg/day (n = 30) | Efficacy on FSD      | Improvements in all domains but NO differences respecting placebo          |
|                    |            | with FSD. | Placebo (n = 30)               |                      |                                                                             |
|                    |            | Average age: 55 | 90 days                       |                      |                                                                             |

\(^a\)ArginMax: a NO donor and an antioxidant, \(^b\)Red clover: a natural estrogen, \(^c\)Tribulus terrestris: a spermatogenesis enhancer, \(^d\)Trigonella foenum-graecum: a seed extract, \(^e\)Elaeagnus angustiflora: an antioxidant, \(^f\)Tribulus terrestris: a spermatogenesis enhancer.
### Continued

| Study Authors       | Design     | Study Group | Participants | Intervention | Duration | Primary Outcomes                                      | Secondary Outcomes                                                                 |
|---------------------|------------|-------------|--------------|--------------|----------|-------------------------------------------------------|-------------------------------------------------------------------------------------|
| Souza et al. 2016   | RCT        | 45 women    | HSDD         | *Tribulus terrestris* 750 mg/day (n = 20) | 12 weeks | Improvements in total FSFI score and most domains, increase of free and bioavailable testosterone | NO differences respecting placebo                                                  |
| Vale et al. 2018    | RCT        | 40 women    | HSDD         | *Tribulus terrestris* 750 mg/day (n = 20) | 120 days | Improvements in total FSFI score and most domains, increase of free and bioavailable testosterone | NO differences respecting placebo                                                  |
| Bernorio et al. 2018| Pilot study| 60 women    | FSD          | Visnadine spray (n = 30) | 30 days | Efficacy on FSD                                        |                                                                                     |
| Caruso et al. 2018  | Crossover  | 38 women    | HSDD         | Visnadine spray on demand (n = 30) | 60 days  | Both improved HSDD (p < 0.001)                         |                                                                                     |
| Caputo et al. 2018  | Pilot study| 69 women    | FSD          | Visnadine oil (n = 30) | 8 weeks  | Improvements on FSFI (p < 0.05)                       |                                                                                     |
| Meston et al. 2008  | RCT        | 63 women    | DFSD (antidepressant) | *Ginkgo biloba* 300 mg/day (n = 19) | 8 weeks  | Ginkgo biloba + sex therapy increased desire respect placebo (p < 0.05), but not *Ginkgo biloba* alone | Sex therapy alone enhanced orgasm function respect placebo (p < 0.05).               |
| Kashani et al. 2013 | RCT        | 38 women    | DFSD (fluoxetine) | Saffron* 30 mg/day (n = 19) | 4 weeks  | Improvement in total FSFI (p < 0.001), arousal (p = 0.028), lubrication (p = 0.035), and pain (p = 0.016) but not in desire, satisfaction and orgasm. |                                                                                     |
| Farnia et al. 2015  | RCT        | 61 women    | DFSD (SSRI)  | *Rosa damascena* oil* 2 ml/day (n = 31) | 8 weeks  | No Improvements on FSFI compared to placebo            |                                                                                     |
| Farnia et al. 2017  | RCT        | 50 women    | DFSD (methadone) | *Rosa damascena* oil* 2 ml/day (n = 25) | 8 weeks  | Improvements on FSFI (p < 0.05) and sex hormones compared to placebo |                                                                                     |

**Abbreviations:** DFSD: Drug-induced Female Sexual Dysfunction; FSFI: Female Sex Function Index; HSDD: Hypoactive Sexual Desire Disorder; RCT: Randomized Control Trial; Sexual Function Questionnaire; SFI: Sexual Function Index; SQ-F: Sexual Quotient-female; SSRI: Selective Serotonin Reuptake Inhibitor; TSH: Thyroid Stimulating Hormone.

*ArginMax contains L-arginine, ginseng, ginkgo, damiana, multivitamins and minerals; *red clover extract (MF11RCE) 80 mg isoflavones; *ethanol extract (60% amyrine); *equivalent to 9.9 g dry herb, standardised to a minimum 50% saponin glycosides; *flowers extract; *standardized *G. biloba* extract EGb761; *ethanolic stigma’s extract (3.5 mg of crocin); *8.5 mg of citronellol/2 ml of *R. damascena* essential oil.
lubrication, satisfaction and pain, along with Female Sexual Function Index (FSFI) total score [9]. The remaining interventions with *Tribulus terrestris* proved scores in all domains, but failed to obtain differences with respect to placebo.

Visadine is a local treatment applied to the vulvar area 10 min before sexual stimulation. The 3 Visadine interventions are applied in different ways: One of them evaluated the use of spray on demand [15], another evaluated both on demand and daily use, without placebo group [20], whilst a further study assessed the use of Visnadine oil [21]. Both spray and oil produced differences in the FSFI score with respect to placebo [15] [21], although the oil intervention was a pilot study. The other study found results to indicate the efficacy of both daily and on-demand use in women with HSDD [20].

ArginMax was tested in pre, peri, and postmenopausal women, and was found to produce differences with respect to placebo in postmenopausal women with HSDD [7]. Red clover oral supplement, administered at a dose of 80 mg/day for 3 months, improved \( p < 0.05 \) dyspareunia, vaginal dryness, and libido when evaluating women aged over 40 years with FSD [8]. With regard to younger women (20 - 49) with HSDD, the use of Libifem for two menstrual cycles improved sexual desire and arousal when compared with placebo [10].

Studies evaluating the efficacy on DIFSD were concerned with interventions using *Ginko biloba* [16], Saffron [17], and *Rosa damascene* [18] [19]. DIFSD was a result of antidepressant medication in three of the studies [16] [17] [18]. Only *Ginkgo Biloba* and Saffron were found to increase sexual function with respect to placebo in these interventions. The intervention with *Ginko biloba* consisted of evaluating four groups [16]: one group received 300 mg/day alone, another group received the same dose along with sexual therapy, a further group received sexual therapy alone and a final group were given placebo. Significant differences were found for the *Ginkgo biloba* + sexual therapy group vs placebo, but not for the group given *Ginkgo biloba* alone, in terms of increasing sexual desire. The Saffron intervention (30 mg/day for 4 weeks) improved sexual function by increasing arousal, lubrication, and reducing pain, but had no effect on sexual desire, satisfaction and orgasm in women with DIFSD due to Fluoxetine [17].

*Rosa damascena* oil (2 ml/day for 8 weeks) failed to increase sexual function when DIFSD was the result of antidepressant medication [18], but it increased FSFI with respect to placebo when DIFSD was due to methadone [19].

In the majority of the works, FSD (predominantly HSDD) was analyzed as the primary goal of the study. The results were mainly reported with regard to FSFI. In terms of the quality of the studies, most are considered to be of medium to low quality (Table 2), mainly due to the risk of bias, heterogeneity, and small sample size. In addition, the external validity of the studies are very low, since many natural products have been tested in eastern countries where volunteers must be heterosexual and married, and in many cases, the husband has signed a consent form.
Table 2. Quality of studies.

| Authors             | Random | Allocation | Double-blind | FSD       | FSFI     | Drop out (%) | Adverse effects               |
|--------------------|--------|------------|--------------|-----------|----------|--------------|------------------------------|
| Ito et al. 2006    | −      | −          | +            | HSDD      | FSFI modified | 0            | No significant difference in adverse effects |
| Chedraui et al. 2006 | −      | −          | +            | +         | KI       | 11.7         | Not described |
| Akhtari et al. 2014 | +      | +          | +            | HSDD      | +        | 10.4         | Only one patient reported grade 1 abdominal cramp. |
| Rao et al. 2015     | +      | +          | +            | HSSD      | +        | 0            | No significant difference in adverse effects |
| Zeinalzadeh et al. 2016 | +      | +          | +            | HSSD      | +        | 10.7         | Not described |
| Postigo et al. 2016 | −      | −          | +            | FSD       | SQ-F, FIEI | 0            | No significant difference in adverse effects |
| De Souza et al. 2016 | +      | −          | +            | HSSD      | +        | 20           | Not described |
| Vale et al. 2017    | −      | −          | +            | HSSD      | +        | 37.5         | Not described |
| Bernorio et al. 2018 | +      | +          | +            | FSD       | +        | 3.3          | Both products were very well tolerated |
| Caruso et al. 2018  | +      | −          | −            | HSDD      | +        | 26.9         | Not described |
| Caputo et al. 2018  | −      | −          | +            | FSD       | +        | 3.3          | Not described |

**DRUG-INDUCED FSD (DIFSD)**

| Authors             | Random | Allocation | Double-blind | FSD       | DIFSD    | Drop out (%) | Adverse effects               |
|--------------------|--------|------------|--------------|-----------|----------|--------------|------------------------------|
| Meston et al. 2008 | −      | −          | +            | FSD + DIFSD | +        | 19.1         | Not described |
| Kashani et al. 2012 | −      | −          | +            | DIFSD     | +        | 10.5         | Described with no differences |
| Farnia et al. 2015 | +      | −          | +            | DIFSD     | +        | 0            | No side effects |
| Farnia et al. 2017 | +      | −          | +            | DIFSD     | +        | 0            | Not described |

**Abbreviations:** DIFSD: Drug-induced Female Sexual Dysfunction; FIEI: Female Intervention Efficacy Index; FSD: Female Sexual Dysfunction; FSFI: Female Sexual Function Index; HSDD: Hypoactive Sexual Desire Disorder; SQ-F: Sexual Quotient-female.

4. Discussion

FSD can affect most women of any age and condition, and when it does, it worsens the quality of their lives. In all of these cases, the predominance of desire disorder is marked by its frequency. An international consensus on the incidence and prevalence of sexual dysfunction shows that there are fewer data available on female dysfunctions than those of males, and FSD increases with age, most commonly with desire disorders, although they are often presented together. Trying to combine data is difficult because it is very different, but the case closest to our environment provides data to indicate an incidence of 20% in women under the age of 25% and 80% in women over 55 years of age [22].

4.1. Why Was It Important to Conduct This Systematic Review?

Despite the growing importance of FSD, there is a lack of research that can assess the efficacy of treatments. In addition, treatment of FSD usually does not include intervention using natural products. This systematic review included only RCTs for the natural intervention of FSD or DIFSD, but not for their prevention.
4.2. Strength

This systematic review presents the state-of-the-art regarding evidence on the effectiveness of FSD natural product interventions. Our search identified 15 studies involving 1000 FSD patients and 880 with HSDD as the primary symptom of FSD (185 of them were DIFSD). The strength of this evaluation is the systematic approach to identifying and assessing existing evidence of FSD-specific sexual intervention.

4.3. What Is New about Other Similar Reviews?

Our review is the first to systematically approach research into the FSD treatments. Two narrative reviews have provided updates on pharmacological treatments [23] and Chinese herbal medicine [24] and conducted a meta-analysis to assess the placebo effect of interventions for female sexual desire [5]. In our systematic review, we also included a study to assess the effectiveness of DIFSD treatment. The participants included 201 FSDs in women with depression as a result of medication.

4.4. Limitations

It was not possible to conduct a meta-analysis due to the heterogeneity of the research and the fundamental design and interventions used.

The studies included in this systematic review differed in design; whilst some studies included a comparison group without additional support for FSD, others compared intervention groups with an active control. Other important limitations to be noted are the small sample size of most studies, dropouts, and follow-up failures, along with the beneficial effects of placebo in many settings [5]. All studies except one [7] were highly biased because they included samples of less than 50 participants per trial. The trial differed not only in the content of the intervention but also in terms of the measurement of the outcome, which limited the joint analysis. In addition, the study lacked safety data. In general, the quality of evidence was lower for most of the included studies (see Table 2).

Regarding the diagnosis of FSD, all studies included heterosexual patients, mostly married couples. We suspect that in some studies, the diagnosis of FSD depends on the husband’s opinion. In fact, this is one of the reasons why we did not accept some studies [25].

Women could suffer from DIFSD for a variety of reasons. However, none of the studies indicate whether the problems existed previously or whether they occur because of drugs, other emotional causes, stress, or whether aging itself could be the underlying cause of FSD. All these matters could be considered bias of our study.

4.5. About the Strategies

Generally, there are few RCTs that evaluate the natural treatment of FSD, while those that do exist include small sample sizes and report mixed results.
The *Tribulus terrestris* extract contains protodioscin. Improvements in sexual function may be due to an increase in serum testosterone levels, particularly bioavailability and freeness, as this leads to an increase in the level of dehydroepiandrosterone (DHEA) in the human body. According to the results observed in [26], *Tribulus terrestris* may be an alternative to FSD in premenopausal and postmenopausal women, although it did not generate improvements with respect to placebo in three of the studies analyzed in this systematic review.

*Turnera diffusa*, commonly known as “Damiana”, is a plant used as an aphrodisiac in Latin America, mainly in Mexico [27] showing experimental effects on nitric oxide and anxiolytic pathways. In the RCTs collected in our review, Damiana was mixed with L-arginine, ginkgo, and ginseng, and thus the improvement in FSFI values may be due to the combined effects of these agents.

Saffron (*Crocus sativus*) has anti-inflammatory, anti-oxidant, neuroprotective and anti-depressant pharmacological effects. Its effect on opioid receptors could explain the reduction of pain during sexual intercourse [28], and an increase in dopamine levels is evidence of an improvement in sexual arousal [29].

Visnadine is an active ingredient of *Ammi visnaga* fruit, traditionally used for cardiovascular disorders, and has been thought to improve VVA [30].

*Turnera diffusa* and *Ginkgo biloba* appear to improve sexual desire by increasing free testosterone and improving vaginal vasodilation.

In traditional medicine, *Turnera diffusa* has been used to promote digestion, reduce inflammation and fight infections, treat sinusitis, and clear lung congestion. In addition, it is used as a galactogogue, which is associated with an increase in the size of the mother [31].

*Ginkgo biloba* has been used as a traditional Chinese herbal medicine with vascular protective function and has been proposed as a treatment for improving the sexual health of women over 50 years of age [32]. In the only article we have included in this systematic review, the effects of Gingko biloba alone on arousal did not differ from placebo [16].

*Rosa damascena* Mill is one of the most famous ornamental plants in the world, and is used primarily in the perfume industry. Traditionally it has been used as an astringent, analgesic, cardiac and intestinal supplement [33]. Farnia et al. found that this treatment improved male and female drug-induced sexual dysfunctions [34].

Libifem (*Trigonella foenum-graecum*) is a botanical extract rich in steroidal saponins, which has been found to have estrogenic and androgenic effects and generate improvements in male sexual function [35].

With respect to ArginMax (which contains L-arginine, ginseng, ginkgo, damiana, multivitamins and minerals), the Ito *et al.* study [7] used a 9-item scale, some items of which are similar to those in the 19-item FSFI and some of which are not, but none of which have been validated. This study also indicates that only 3 of the 9 items showed more success with the supplement than with placebo, and that the 3 differentiating items varied between the 3 subsets analyzed (premeno-
pausal, perimenopausal, and postmenopausal women). Therefore, the Ito study failed to establish a primary endpoint and concluded success, even though no consistent pattern of success was evident either across subpopulations or across the majority of endpoints.

4.6. Future Research

Our systematic review has identified important areas for future research, particularly interventions that increase the impact of several natural products found in this review. In particular, a larger double-blind study should be conducted over a longer follow-up period to assess different treatment strategies for HSDD.

5. Conclusion

Although the quality of the evidence is not high, most natural product interventions appear to improve FSD, particularly HSDD, including primary and drug-induced forms of the disorder.

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Conflicts of Interest

The authors declare no conflicts of interest regarding the publication of this paper.

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Appendix

SEARCH STRATEGY

((“arousal” [MeSH Terms] OR “arousal” [All Fields]) AND (“disease” [MeSH Terms] OR “disease” [All Fields] OR “disorder” [All Fields])) OR ((“hypokinesia” [MeSH Terms] OR “hypokinesia” [All Fields] OR “hypoactive” [All Fields]) AND (“libido” [MeSH Terms] OR “libido” [All Fields] OR (“sexual” [All Fields] AND “desire” [All Fields]) OR “sexual desire” [All Fields]))) OR ((“female” [MeSH Terms] OR “female” [All Fields]) AND (“sexual behavior” [MeSH Terms] OR (“sexual” [All Fields] AND “behavior” [All Fields]) OR “sexual behavior” [All Fields] OR “sexual” [All Fields])) AND (“physiopathology” [Subheading] OR “physiopathology” [All Fields] OR “dysfunction” [All Fields]) AND (((“biological products” [MeSH Terms] OR (“biological” [All Fields] AND “products” [All Fields]) OR “biological products” [All Fields] OR (“natural”[All Fields] AND “products” [All Fields]) OR “natural products” [All Fields]) OR (soy[All Fields] AND (“oestrogen” [All Fields] OR “estrogens” [Pharmacological Action] OR “estrogens” [MeSH Terms] OR “estrogens” [All Fields] OR “estrogen” [All Fields]))) OR (soy[All Fields] AND (“phytotherapy” [MeSH Terms] OR “phytotherapy” [All Fields]))) OR (“phytotherapy” [MeSH Terms] OR “phytotherapy” [All Fields]) AND (randomized controlled trial [pt] OR controlled clinical trial [pt] OR randomized controlled trials [mh] OR random allocation [mh] OR double-blind method [mh] OR single-blind method [mh] OR clinical trial [pt] OR clinical trials [mh] OR (“clinical trial [tw] OR (singl* [tw] OR blind* [tw])) OR (“latin square” [tw] OR placebo [mh]) OR placebos [mh] OR placebo* [tw] OR random* [tw] OR research design [mh:noexp] OR comparative study [mh] OR evaluation studies [mh] OR follow-up studies [mh] OR prospective studies [mh] OR cross-over studies [mh] OR control* [tw] OR prospective* [tw] OR volunteer* [tw] NOT (animal [mh] NOT human [mh])).