Abstract

Many women typically experience a significant reduction in sexual desire during the late perimenopausal and early postmenopausal stages, with the biggest decline in sexual desire occurring from three years prior to two years after the final menstrual period. Despite being a prevalent female complaint, currently no standard treatment for low sexual desire exists. Herbal medicines have been used therapeutically all around the world, and are an important component of Traditional and Complementary Medicine. There have been numerous trials and pharmacological studies of specific herbal preparations related to the treatment of low sexual desire. This article serves to provide a clinical review of the evidence relating to the herbal treatment options for this common condition.

Keywords: herbal medicines, low sexual desire, low libido, menopause, phytotherapy

1. Introduction

1.1 Problem Statement

Low sexual desire, or decreased libido, is one of the most prevalent sexual complaints in menopausal females. Many women find that their interest in sex as well as the intensity of their sexual desire gradually decrease with age. This is attributed to hormonal and physical changes, as well as sociopsychological factors (Kingsberg, 2010). Indeed, menopause is often associated with a variety of distressing symptoms such as irregular or heavier menses, hot flushes, night sweats, anxiety, depression, insomnia, fatigue, vaginal dryness, and urinary symptoms, all of which can contribute to low libido (Ashrafi *et al*., 2010; Hendrix, 2011). In some cases, the decrease or loss of sexual desire can be very distressing (Kingsberg, 2010), yet currently there is no standard treatment for low sexual desire in females. Available treatment options include psychological therapy and pharmacological drugs, but their efficacy remains to be proven (Basson, 2011). In addition, for many women, the risks associated with pharmacological treatments often outweigh the benefits (Hendrix, 2011). A systematic review on the use of complementary medicines (CMs) found that 50.5% of women worldwide reported that they used CMs specifically for their menopausal symptoms, with herbal medicines being the most popular (Posadzki *et al*., 2013). A large number of aphrodisiac herbal medicines have been studied with regards to male sexuality (Kotta *et al*., 2013), yet there is still a need for a review evaluating the efficacy of herbal medicines specifically for low sexual desire in menopausal women.

1.2 Aim

The aim of this article is to provide a clinical review of the medical literature related to the treatment of low sexual desire in menopausal women by means of herbal medicines, thus producing a comprehensive summary of the current perspectives related to this common condition.

1.3 Definition of key concepts

The concepts that are central to this study are defined as follows:

Low sexual desire can be defined as a loss of interest in sexual activity over a period of months (Heiman *et al*., 2011).

Sexual arousal is described as "a feeling that includes both physical and mental aspects of sexual excitement. It may include feelings of warmth or tingling in the genitals, lubrication, or muscle contractions" (Rosen *et al*., 2000).

Perimenopause includes the following stages: early menopausal transition (characterised by variability in the menstrual cycle); late menopausal transition (characterised by frequent anovulation and irregular menses); and the first 12 months of early postmenopause (Harlow *et al.*, 2012).

Menopause is defined as the physiological termination of menses due to a decrease in ovarian function (Hendrix, 2011).

Herbal medicine is the use of medicinal plants to prevent and treat diseases (Mosby's Medical Dictionary, n.d.), and makes use of herbs, herbal materials, preparations, and products that contain as active ingredients parts of plants, or other plant materials, or combinations thereof (WHO, 2016).

2. Methods

A search for the current medical literature related to low sexual desire in menopausal women was carried out between January to July 2016 by means of a multiple online database search, using the combined keywords of "low sexual desire", "libido", "menopause", "phytotherapy", "medicinal plants", and "herbal medicine". Once the relevant herbs were identified, these key words were then added to the search terms. Literature was explored and evaluated for relevance

by means of the title and abstract. The search was limited to studies, published in English, relating to the herbal medicine treatment of low sexual desire in menopausal women. The following databases were made use of: Science Direct, Ujoogle, Google Scholar, MEDLINE, Pubmed, Allied and Complementary Medicine, and the Cochrane Library. The review included full-text articles, abstracts and reports. A total of 305 articles were evaluated and, of these, 12 studies were found to be relevant to the topic (Table 2). Each relevant item was summarised and is discussed in the results section.

3. Theory

3.1 Female sexuality and menopause

Menopause is a time of biological, social, and psychological change, which may impact on various phases of the sexual response cycle and can lead to sexual dysfunction (Clayton & Harsh, 2016; Woods *et al.*, 2010). Low sexual desire is one of four defined components of female sexual dysfunction, and is the most prevalent complaint related to sexual function in women (Kingsberg & Rezaee, 2013; Reed *et al*., 2007). Although there are currently no South African statistics, one study has found that between 68% and 86.5% of menopausal women in the United States are affected (Ambler *et al*., 2012).

Low sexual desire may be associated with feelings of low self-esteem, discontent, anger, and depression. One European study found that clinicians are reluctant to discuss female sexual dysfunction, as they felt it might shift the focus of the consultation to a problem for which they had almost no useful treatment options (Goldstein *et al*., 2009). These findings emphasise the frustration experienced by both clinicians and patients and further highlight the need for safe and effective treatment options for female sexual dysfunction.

3.2 Biochemical factors regulating the female sexual response

The neurotransmitters norepinephrine (NE) and nitric oxide (NO) and the neuropeptide vasoactive intestinal peptide (VIP) are responsible for maintaining genital blood flow and muscle tone, and the sex hormones (oestradiol and testosterone) also play a significant role (Traish *et al*., 2010). The sexual excitation pathway is activated by the release of certain neurotransmitters within the brain. Dopamine and melanocortin stimulate sexual attention and desire, while sexual arousal is stimulated by NE and oxytocin (OT). This activation can be triggered internally, through the action of the sex hormones, while external triggers include sexual cues or certain drugs. Serotonin, opioids, and endocannabinoids inhibit these excitatory neurotransmitters; they are naturally released during an orgasm in order to produce sexual satiety, but they can also be

triggered by situational factors such as stress, or by drugs that enhance their action, such as selective serotonin reuptake inhibitors (SSRIs) (Pfaus, 2009).

3.3 The female sexual response cycle

Over the years, several different models to explain the female sexual response have been proposed. The linear or DEOR model describes four phases: desire, excitation, orgasm, and resolution (which refers to a general state of relaxation after orgasm), thus creating the expectation that a normal female sexual response cycle follows in a linear manner, from desire to resolution. In Basson's circular model, the female starts in a desire neutral state. She may initiate or become receptive to sexual cues if she perceives sufficient emotional intimacy between her and her partner, resulting in a state of arousal. Arousal and desire thus occur simultaneously and reinforce each other, which will then motivate her to move toward orgasm and sexual satisfaction (Wylie & Mimoun, 2009). According to Basson (2011), women frequently relate better to the linear model at the start of a relationship, but in long-term relationships, sexual desire tends to become a responsive rather than a spontaneous occurrence. The debate as to which of the models most accurately represents the female sexual response continues within scientific literature.

3.4 Diagnosing female sexual desire disorders

Hypoactive Sexual Desire Disorder (HSDD) was listed under the DSM-IV (Diagnostic and Statistical Manual of Mental Disorders, 4th edition); however, in the revised edition (DSM-V), sexual desire and arousal disorders have been combined into the Female Sexual Interest/Arousal Disorder (FSIAD) (see criteria in Table 1). For diagnosis of FSIAD, sexual dysfunction has to be present for a minimum of six months; occur in at least 75% of sexual encounters; and must cause clinically significant distress in the individual (American Psychiatric Association, 2013; Sungur & Gündüz, 2014). Not all women with low sexual desire will meet the diagnostic criteria for FSIAD, and should therefore rather be classified as experiencing a sexual difficulty as opposed to a sexual dysfunction (Hendrickx *et al.*, 2014).

3.5 Causes of low sexual desire in menopausal women

The most frequently reported causes include both physical and psychological factors (Reed *et al.*, 2007). Some of these factors will be addressed below, but it is important to note that separation between these factors is somewhat artificial, as they are usually inter-related (Basson, 2011).

3.5.1 Physical causes

Perimenopause is initially associated with large fluctuations in oestrogen levels, which are largely responsible for the myriad of symptoms seen (Hendrix, 2011). When menses cease due to ovarian failure, oestradiol levels drop, and oestrone (a weaker oestrogen) becomes the principal form of oestrogen (Brockie, 2013). Decreasing oestrogen levels lead to vaginal dryness and thinning of the mucosa, resulting in an increased risk of atrophic vaginitis and dyspareunia (Hendrix, 2011). Physiological and anatomical changes in the bladder and pelvic floor also occur, and many women experience a variety of urinary symptoms (Perry, 2012), which further exacerbate sexual dysfunction (Yih *et al*., 2013). During menopause, androgen (testosterone, androstenedione, dihydrotestosterone, and dehydroepiandrosterone) levels decline gradually to approximately half of premenopausal levels (Hendrix, 2011). Androgens are important for the maintenance of the female sex organs, and testosterone in particular has an effect on sexual desire; decreased levels of these hormones results in dramatic alterations in genital tissue structure and function (Hendrix, 2011; Traish *et al*., 2010). Other physical factors contributing to low sexual desire include sleep disturbances, chronic illness, and certain medications (Reed *et al.*, 2007).

3.5.2 Psychological factors

Depression affects as many as 70 – 90% of women, and a bi-directional association exists between depression and sexual dysfunction (Atlantis & Sullivan, 2012; Hendrix, 2011). The pathophysiology can be directly attributed to the changes in neurotransmitter levels that occur, particularly brain dopamine, which forms the core of the sexual excitatory pathway (Basson & Schultz, 2007; Hori & Kunugi, 2013; Pfaus, 2009). Indirect mechanisms such as sleep disturbances and low self-image also contribute to the prevalence of low sexual desire (Toffol *et al*., 2014). In addition, low sexual desire is a recognised side-effect of certain antidepressant medications, namely SSRIs and serotonin-norepinephrine reuptake inhibitors (SNRIs) (Fooladi *et al*., 2012). The use of SSRIs leads to increased levels of cortisol, prolactin, and serotonin, which negatively impact sexual function (Montgomery, 2008). Research suggests that bupropion and other newer antidepressants exhibit a more favourable sexual dysfunction profile (Clayton *et al*., 2014). Other psychological factors associated with low libido include anxiety (Kalmbach *et al*., 2014), chronic daily stress (Hamilton & Meston, 2013), negative body image (Weaver & Byers, 2013), and a history of sexual abuse (Zwickl & Merriman, 2011). Relationship factors also remain an important contributor to libido (Sims & Meana, 2010).

3.6 Treatment of low sexual desire

There is currently no standard treatment for low sexual desire in females. However, pharmacological treatment in conjunction with psychological therapy is often recommended (Katz-Bearnot, 2010).

3.6.1 Pharmacological Treatment

- *Hormone Replacement Therapy (HRT)*

Both oestradiol and testosterone have been reported to be critical for modulating sexual desire in women. Controlled trials have demonstrated that oestrogen-only therapies that produce periovulatory levels of circulating oestradiol increase sexual desire in postmenopausal women (Cappelletti & Wallen, 2016). Studies regarding testosterone therapy in women, however, have produced conflicting results (Davis & Braunstein, 2012; Gotmar *et al.*, 2008). Recent evidence suggests that testosterone therapy enhances the effectiveness of low-dose oestrogen therapies, which in turn improves low sexual desire; however, it remains unclear whether endogenous testosterone itself contributes to the modulation of women's sexual desire (Cappelletti & Wallen, 2016).

Moreover, HRT use is not without risk. Oestrogen therapy increases the incidence of deep venous thrombosis, pulmonary embolism, ischaemic stroke, breast cancer, dementia, and coronary artery disease (Hendrix, 2011). Furthermore, although the safety and efficacy data pertaining to the use of testosterone therapy in women is not yet conclusive (Guidozzi *et al*., 2014), the most common adverse effects experienced are hirsutism and acne. In addition, long-term use may negatively affect the cardiovascular system, as well as stimulate endometrial and breast tissue, possibly leading to the development of carcinoma (this may be dose-dependent) (Davis & Braunstein, 2012). It is worth noting at this point that Tibolone, a synthetic molecule with oestrogenic, progestogenic, and androgenic actions, appears to be effective for a variety of menopausal symptoms, including sexual well-being and libido, with fewer adverse effects than other HRT options (Genazzani *et al*., 2006; Nijland *et al*., 2008).

- *Flibanserin*

Flibanserin is a non-hormonal serotonin agonist/antagonist originally developed to treat depression, and was recently approved by the FDA specifically for the treatment of HSDD. Studies conducted in both pre- and postmenopausal women with HSDD have shown the efficacy of Flibanserin (Dhanuka & Simon, 2015; Katz *et al*., 2013). The drug regulates levels of the sexual excitatory neurotransmitters dopamine and NE in the brain, while producing a temporary decrease in serotonin. Common side effects include somnolence, dizziness, hypotension, and nausea (Dhanuka & Simon, 2015).

3.6.2 Psychological Treatment

Both cognitive-behavioural and mindfulness based therapies have shown to be useful for HSDD sufferers, particularly those suffering from depression or anxiety. However, more research is needed in these areas to evaluate efficacy (Brotto and Basson, 2014; Staccini, 2015). Women with sexual dysfunction associated with relationship problems may benefit from couples therapy (Basson, 2011).

4. Results and findings

Numerous studies have been conducted on the use of herbal medicines for menopausal symptoms. However, only limited studies could be found evaluating their efficacy for the treatment of low libido specifically. These are discussed below, and summarised in Table 2.

4.1 Phytoestrogens

Phytoestrogens are nonsteroidal plant compounds that have a weak oestrogenic activity, and are a commonly used alternative to HRT. In the low oestrogen setting encountered in peri- and postmenopause, phytoestrogens act as selective oestrogen receptor modulators (SERMs). They appear to have a greater affinity for beta oestrogen receptors, exerting their effects on skin, bone, and blood vessels and on the central nervous system without stimulating breast or uterine tissue, thereby reducing the undesired effect oestrogen can have on these body systems (Lethaby *et al*., 2013).

4.1.1 Red clover (*Trifolium pratense*)

Red clover is a phytoestrogen that contains dadzein, irilone, and genistein; however, it is also rich in methylized precursors (biochanin A, formononetin, prunetin, and glycitein) (Lutter *et al*., 2014). Clinical research supports the positive effects of red clover isoflavones in menopausal women on vasomotor symptoms, as well as vaginal and sexual health (Chedrui *et al*., 2006; Ghazanfarpour *et al*., 2016; Lethaby *et al*., 2013; Lipovac *et al*., 2011; Shakeri *et al*., 2015). The isoflavones in red clover are deemed safe for women to use and do not promote the growth of cancer cells (Reiter *et al*., 2011).

4.1.2 Hops (*Humulus lupulus*)

Hops is a commonly used supplement for insomnia and menopausal symptoms. It contains various bio-active compounds such as 6-prenylnarigenin (6-PN) and 8-prenylnarigenin (8-PN), the latter being considered a powerful phytoestrogen. Hops is non-toxic and appears to play a

protective role against breast cancer by modulating oestrogen metabolism as well the chemical oestrogen carcinogenesis pathway (Depypere & Comhaire, 2014; Wang *et al*., 2016). While animal studies have shown hops to have aphrodisiac effects (Di Viesti *et al*., 2011; Zanoli *et al*., 2009), there are very few clinical studies conducted on the use of hops for sexual disorders. According to one study conducted on postmenopausal women, topical application of a gel containing hops extract, hyaluronic acid, liposomes, and Vitamin E proved effective in reducing vaginal dryness and atrophic vaginitis (Morali *et al*., 2006; Van Die, 2011). Sparavigna *et al*. (2013) conducted a similar study on the same gel and found its moisturising effects to be quick-acting and long-lasting. The authors of a review on medicinal plants for female sexual dysfunction suggest that hops may help with desire disorders; however, there is a need for further clinical studies to be conducted (Mazaro-Costa *et al*., 2010).

4.1.3 Maca (*Lepidium meyenii*)

Maca, a plant of the mustard family, has been shown to reduce vasomotor menopausal symptoms by increasing oestrogen production while simultaneously lowering cortisol levels (Depypere & Comhaire, 2014; Murray, 2015). Several in vivo studies have shown that maca may improve sexual behaviour and enhance androgen-like effects in rats (Shin *et al*., 2010). A systematic review conducted by Shin *et al*. (2010) found only limited evidence available, and only one study relating to sexual dysfunction in postmenopausal women. This study revealed maca to be effective in improving sexual desire as well as psychological symptoms of anxiety and depression after six weeks of use (Brooks *et al*., 2008). Maca has also been shown to be helpful in alleviating SSRI-related sexual dysfunction; however, this result appears to be a dose-related effect (Dording *et al*., 2008). Further large scale studies need to be conducted to confirm these findings.

4.2 Black cohosh (*Cimicifuga racemosa*)

Black cohosh is one of the most commonly used herbal treatments for symptoms associated with menopause. Its effects are thought to be due to a variety of compounds, in particular triterpene glycosides that have serotoninergic, noradrenergic, dopaminergic, and GABAergic actions on the hypothalamus. Extracts from the rhizome do not appear to have an oestrogenic effect; in fact, use is associated with a reduced risk of developing breast cancer (Eden, 2016). This herb is therefore thought to be safe for use in breast cancer patients (Seidlova-Wuttke *et al*., 2013). Efficacy studies on black cohosh for menopausal symptoms have produced mixed results (Leach & Moore, 2012). Remifemin, a standardised pharmaceutical preparation of black cohosh, has

shown efficacy for menopausal symptoms in at least four RCTs, one of which showed equivalence with an oestradiol HRT patch (Eden, 2016). However, only one RCT could be found that specifically evaluated sexual symptoms, and showed that black cohosh use over an eight-week period produced significant improvements in this sphere, amongst others. Black cohosh appears to be well tolerated and is generally considered safe. Minor side effects such as nausea, vomiting, and headaches, and dizziness have occasionally been reported (Mohammad-Alizadeh-Charandabi *et al*., 2013).

4.3 Maritime pine bark (Pycnogenol®)

Pycnogenol® is produced from the outer bark of *Pinus pinaster* Aiton subsp. *atlantica*. It has strong antioxidant and anti-inflammatory properties and has been found to significantly reduce vasomotor symptoms and improve the quality of life of menopausal females (Errichi *et al*., 2011). Pycnogenol® contains more than 40 functional components, including bioflavonoids. Based on its constituents, it is unlikely that Pycnogenol® exerts a hormonal effect by acting as a phytoestrogen, and the positive results observed are rather thought to be due to the beneficial effect it has on neurons and blood vessels, as well as its antioxidant effects (Depypere & Comhaire, 2014; Yang *et al*., 2007). According to Yang *et al*. (2007), the active compounds stimulate endothelial NO production, which increases genital blood flow. Their study showed that Pycnogenol® ameliorated all symptoms associated with menopause, including sexual symptoms, in a group of perimenopausal females. Pycnogenol® has GRAS (generally recognized as safe) status, based on data obtained from 70 clinical studies (Oliff, n.d.).

4.4 Tribulus *(Tribulus terrestris)*

Tribulus has shown beneficial aphrodisiac effects in a number of animal and human studies. The chemical substance protodioscin, derived from this plant, is converted into the androgen dehydroepiandrosterone (DHEA). Evidence shows that improvement in sexual symptoms is accompanied by a significant increase in DHEA levels, without causing an increase in testosterone levels (Gama *et al*., 2014). One recent three-month RCT was conducted on the effects of Tribulus in postmenopausal women with sexual dysfunction. The herb produced a statistically significant improvement in a variety of sexual problems, including sexual desire, with no significant adverse effects reported (Postigo *et al*., 2016). Other studies conducted in premenopausal women with HSDD also showed efficacy (Akhtari *et al.*, 2014; Gama *et al.*, 2014). Tribulus extract is reported to be safe and effective in the treatment of female sexual dysfunction (Gama *et al*., 2014). Possible side effects include mild gastrointestinal symptoms (Akhtari *et al*., 2014).

4.5 Gingko *(Ginkgo biloba)*

Gingko has been used for thousands of years for its medicinal properties, and is widely available. *Ginkgo biloba* extract (GBE) enhances blood flow and NO production, and also promotes smooth muscle relaxation, all of which are important components of proper female sexual function. Studies investigating the effect of GBE on female sexual desire have, however, produced conflicting results (Pebdani *et al*., 2014). Meston *et al*. (2008) and Kang *et al*. (2002) found no beneficial effects, while Cohen and Bartlik (1998) found that GBE was 84% effective in treating sexual dysfunction resulting from antidepressant drugs. The clinical trial conducted by Pebdani *et al.* (2014) showed that GBE significantly improves sexual desire in menopausal women. The authors concluded that GBE has weak oestrogenic properties, and suggested that it can be considered a safe means of improving sexual function in menopausal women.

4.6 Korean red ginseng *(Panax ginseng)*

Korean red ginseng (KRG) is an herb of the Araliaceae family and contains triterpene saponins called ginsenosides, which are believed to be responsible for its various pharmacological effects, including those on sexual function. Animal studies have reported that KRG has a relaxing effect on the clitoral cavernosal muscle and vaginal smooth muscles, and may have phytoestrogenic effects (Chung *et al*., 2015). Kim *et al*. (2013) conducted a systematic review on the use of ginseng for managing menopausal symptoms. The review only identified a small number of relevant RCTs; three of these studies compared the effects of KRG to placebo with favourable results. Of these, Oh *et al*. (2010) specifically studied its effects on sexual arousal in menopausal women. They found that KRG extracts induce a statistically significant improvement in sexual arousal, with no severe adverse events reported. The authors of the review did, however, conclude that there are an insufficient number of trials from which to draw definitive conclusions (Kim *et al*., 2013).

5. Discussion

Herbal medicines are reported to be the most commonly used CM modality amongst menopausal women (Posadski *et al*., 2013). Green *et al*. (2007) conducted a 24-week pilot study to assess the effectiveness of professional herbal practice in the treatment of menopausal symptoms. They found that those women who made use of herbal medicines experienced a significant improvement in menopausal symptoms, including libido. This study offers supportive evidence for herbal medicine as a possible treatment choice.

Although certain herbs are widely used and commonly self-prescribed, herbal medicines should fulfil the basic requirements of being safe and effective before being recommended for use. Currently, the general public, and even medical practitioners, may have a poor understanding of the effects of herbal medicines. Indeed, while herbal medicines are often considered safer alternatives, they also may produce adverse effects and potentially cause drug interactions (Kunle *et al*., 2012). Herbal medicines made by reputable companies that ensure good manufacturing procedures (GMP) are thus recommended, and their use should be monitored by a qualified practitioner.

Clinical trials related to herbal medicines for sexual desire in menopausal women are limited. The majority of studies available relate to the vasomotor symptoms of menopause, rather than sexual symptoms specifically. A variety of symptom rating scales are used, and an aspect of sexual function is usually included as a small subsection in these scales. Future studies should thus make use of standardised scales to evaluate sexual function, such as the Female Sexual Function Index (FSFI). There are also many considerations when reviewing research related to herbal medicines. Eden (2016) explains that it is difficult to conduct meta-analysis on these studies due to heterogeneity – not only of the studies themselves, but also of the preparation methods and dosages. From the limited evidence available, phytoestrogens (red clover, hops, maca), black cohosh and Pycnogenol® appear to have beneficial effects not only on vasomotor symptoms, but on libido as well. Gingko, tribulus and Korean red ginseng show promising results in the treatment of low sexual desire, but the evidence is limited. Further studies need to be conducted before any definitive conclusions can be made regarding the use of these herbs for treating low sexual desire in menopausal women.

6. Conclusion

Low sexual desire is a common complaint amongst menopausal women, and this can have a significant impact on quality of life. There are very few conventional treatment options for low sexual desire, and the pharmacological options are associated with adverse effects. Many women turn to herbal medicines as a therapeutic alternative. This review highlights the clinical evidence related to the most commonly used herbal medicines indicated for low sexual desire. Tribulus, black cohosh, Gingko biloba, Pycnogenol®, Korean red ginseng, and the phytoestrogens red clover, hops, and maca all show positive benefits for low sexual desire, yet there is limited evidence available to definitively recommend their use for treating low sexual desire. Further clinical RCTs should be conducted to evaluate the safety and efficacy of these herbal medicines.

Conflict of interest: None

Acknowledgements: This work was financed and supported by the University of Johannesburg. The contents of this work are solely the responsibility of the authors and do not represent the official views of UJ.

References

Akhtari, E., Raisi, F., Keshavarz, M., Hosseini, H., Sohrabvand, F., Bioos, S., Kamalinejad, M., & Ghobadi, A. (2014). *Tribulus terrestris* for treatment of sexual dysfunction in women: randomized double-blind placebo-controlled study. *DARU Journal of Pharmaceutical Sciences*, 22, 40.

Ambler, D. R., Bieber, E. J., & Diamond, M. P. (2012). sexual function in elderly women: a review of current literature. *Review of Obstetric Gynecology*, 5(1), 16–27.

American Psychiatric Association. (2013). *Highlights of changes from DSM-IV-TR to DSM-V.* American Psychiatric Publishing. http://www.dsm5.org/Documents/ changes%20from%20dsm-iv-tr%20to%20dsm-5.pdf Accessed 25.07.2016.

Ashrafi, M., Ashtiani, S. K., Malekzadeh, F., Amirchaghmaghi, E., Kashfi, F., Eshrati, B., & Shabani, F. (2010). Symptoms of natural menopause among Iranian women living in Tehran, Iran. *Iranian Journal of Reproductive Medicine*, 8(1), 29–32.

Atlantis, E., & Sullivan, T. (2012). Bidirectional association between depression and sexual dysfunction: a systematic review and meta-analysis. *Journal of Sexual Medicine*, 9, 1497–1507.

Basson, R. (2011). Gynecology and obstetrics: sexual dysfunction in women. In R. S. Porter, & J. L. Kaplan (Eds), *The Merck Manual*, 19th edition (pp. 2521–2525). New Jersey: Merck Sharp & Dohme Corp.

Basson, R., & Schultz, W. W. (2007). Sexual dysfunction 1. Sexual sequelae of general medical disorders. *The Lancet*, 369(9559), 409–424.

Brockie, J. (2013). Managing menopausal symptoms: hot flushes and night sweats. *Nursing Standard*, 28(12), 48–53.

Brooks, N. A., Wilcox, G., Walker, K. Z., Ashton, J. F., Cox, M. B., & Stojanovska, L. (2008). Beneficial effects of *Lepidium meyenii* (Maca) on psychological symptoms and measures of sexual dysfunction in postmenopausal women are not related to estrogen or androgen content. *Menopause*, 15(6), 1157–1162.

Brotto, L. A., & Basson, R. (2014). Group mindfulness-based therapy significantly improves sexual desire in women. *Behaviour Research and Therapy*, 57, 43–54.

Cappelletti, M., & Wallen, K. (2016). Increasing women's sexual desire: the comparative effectiveness of estrogens and androgens. *Hormones and Behavior*; 78, 178–93.

Chedraui, P., Hidalgo, L., San Miguel, G., Morocho, N., & Ross S. (2006). Red clover extract (MF11RCE) supplementation and postmenopausal vaginal and sexual health. *International Journal of Gynaecological Obstetrics*, 95(3), 296–7.

Chung, H. S., Hwang, I., Oh, K. J., Lee, M. N., & Park, K. (2015). The effect of Korean red ginseng on sexual function in premenopausal women: placebo-controlled, double-blind, crossover clinical trial. *Evidence-Based Complementary and Alternative Medicine*, 2015 (2015), Article ID 913158, 5 pages.

Clayton, A. H., El Haddad, S., Iluonakhamhe, J. P., Ponce Martinez, C., & Schuck, A. E. (2014). Sexual dysfunction associated with major depressive disorder and antidepressant treatment. *Expert Opinion on Drug Safety*, 13(10), 1361–74.

Clayton, A. H., & Harsh, V. (2016). Sexual function across aging. *Current Psychiatry Reports*, 18(3), 28.

Cohen, A. J., & Bartlik, B. (1998). Gingko biloba for antidepressant-induced sexual dysfunction. *Journal of Sex & Marital Therapy*, 24(2), 139–43.

Davis, S. R., & Braunstein, G. D. (2012). Efficacy and safety of testosterone in the management of hypoactive sexual desire disorder in postmenopausal women. *Journal of Sexual Medicine,* 9, 1134–1148.

Depypere, H. T., & Comhaire, F. H. (2014). Herbal preparations for the menopause: beyond isoflavones and black cohosh. *Maturitas*, 77, 191–194.

Dhanuka, I., & Simon, J. A. (2015). Flibanserin for the treatment of hypoactive sexual desire disorder in premenopausal women. *Expert Opinion on Pharmacotherapy*, 16(16), 2523–2529.

Di Viesti, V., Carnevale, G., Zavatti, M., Benelli, A., & Zanoli, P. (2011). Increased sexual motivation in female rats treated with *Humulus lupulus L*. extract. *Journal of Ethnopharmacology*, 134(2), 514–517.

Dording, C. M., Fisher, L., Papakostas, G., Farabaugh, A., Sonawalla, S., Fava, M., & Mischoulon, D. (2008). A double-blind, randomized, pilot dose-finding study of maca root (*L. meyenii*) for the management of SSRI-induced sexual dysfunction. *CNS Neuroscience Therapy*, 14(3), 182–191.

Eden J. (2016). Endocrine dilemma: managing menopausal symptoms after breast cancer. *European Journal of Endocrinology*, 174(3), R71–7.

Errichi, S., Bottari, A., Belcaro, G., Cesarone, M. R., Hosoi, M., Cornelli, U., Dugall, M., Ledda, A., & Feragalli, B. (2011). Supplementation with Pycnogenol® improves signs and symptoms of menopausal transition. *Panminerva Medica*, 53(3 Suppl. 1), 65–70.

Fooladi, E., Bell, R. J., & Davis, S. R. (2012). Management strategies in SSRI-associated sexual dysfunction in women at midlife. *Climacteric*, 15, 306–316.

Gama, C. R. B., Lasmar, R., Gama, G. F., Abreu, C. S., Nunes, C. P., Geller, M., Oliveira, L., & Santos, A. (2014). Clinical assessment of *Tribulus terrestris* extract in the treatment of female sexual dysfunction. *Clinical Medicine Insights: Women's Health*, 7, 45–50.

Ghazanfarpour, M., Sadeghi, R., Roudsari, R.L., Khorsand, I., Khadivzadeh, T., & Muoio, B. (2016). Red clover for treatment of hot flashes and menopausal symptoms: a systematic review and meta-analysis. *Journal of Obstetric Gynaecology*, 36(3), 301–11.

Genazzani, A. R., Pluchino, N., Bernardi, F., Centofanti, M., & Luisi, M. (2006). Beneficial effect of tibolone on mood, cognition, well-being, and sexuality in menopausal women. *Neuropsychiatric Disease Treatment*, 2(3), 299–307.

Goldstein, I., Lines, C., Pyke, R., & Scheld, J. S. (2009). National differences in patient–clinician communication regarding hypoactive sexual desire disorder. *Journal of Sexual Medicine*, 6, 1349–1357.

Gotmar, A., Hammar, M., Samsioe, G., Nerbrand, C., Lidfeldt, J., & Spetz, C. (2008). Symptoms in peri- and post-menopausal women in relation to testosterone concentrations: data from the women's health in the Lund area (WHILA) Study. *Climacteric*, 11, 304–314.

Green, J., Denhamb, A., Ingram, J., Hawkey, S., & Greenwood, R. (2007). Treatment of menopausal symptoms by qualified herbal practitioners: a prospective, randomized controlled trial. *Family Practice*, 24(5), 468-474.

Guidozzi, F., Alperstein, A., Bagratee, J. S., Dalmeyer, P., Davey, M., De Villiers, T. J., Hirschowitz, S., Kopenhager, T., Moodley, S. P., Roos, P., Shaw, A., Shimange, O., Smith, T., Thomas, C., Titus, J., van der Spuy, Z., & van Waart, J. (2014). South African Menopause Society revised consensus position statement on menopausal hormone therapy. *South African Medical Journal*, 104(8), 537–543.

Hamilton, L. D., & Meston, C. M. (2013). Chronic stress and sexual function in women. *Journal of Sexual Medicine*, 10(10), 2443–2454.

Harlow, S., Gass, M., Hall, J. E., Lobo, R., Maki, P., Rebar, R. W., Sherman, S., Sluss, P. M., & De Villiers, T. J. (2012). Executive summary of the stages of reproductive aging workshop + 10: addressing the unfinished agenda of staging reproductive aging. *Menopause: The Journal of the North American Menopause Society*, 19(4), 1–9.

Heiman, J. R., Rupp, H., Janssen, E., Newhouse, S. K., Brauer, M., & Laan, E. (2011). Sexual desire, sexual arousal and hormonal differences in premenopausal US and Dutch women with and without low sexual desire. *Hormones and Behaviour*, 59(5), 772–779.

Hendrickx, L., Gijs, L., & Enzlin, P. (2014). Prevalence rates of sexual difficulties and associated distress in heterosexual men and women: results from an internet survey in Flanders. *Journal of Sex Research*, 51(1), 1–12.

Hendrix, L. (2011). Gynecology and obstetrics: menopause. In R. S. Porter, & J. L. Kaplan (Eds), *The Merck Manual*, 19th edition (pp. 2518–2520). New Jersey: Merck Sharp & Dohme Corp.

Hori, H., & Kunugi, H. (2013). Dopamine agonist-responsive depression. *Psychogeriatrics*, 13, 189–195.

Kalmbach, D. A., Kingsberg, S. A., & Ciesla, J. A. (2014). How changes in depression and anxiety symptoms correspond to variations in female sexual response in a nonclinical sample of young women: a daily diary study. *Journal of Sexual Medicine*, 11(12), 2915–2927.

Kang, B. J., Lee, S. J., Kim, M. D., & Cho, M. J. (2002). A placebo-controlled, double-blind trial of *Ginkgo biloba* for antidepressant-induced sexual dysfunction. *Human Psychopharmacology*, 17(6), 279–84.

Katz, M., De Rogatis, L. R., Ackerman, R., Hedges, P., Lesko, L., Garcia, M., & Sand, M. (2013). Efficacy of Flibanserin in women with hypoactive sexual desire disorder: results from the Begonia trial. *Journal of Sexual Medicine*, 10, 1807–1815.

Katz-Bearnot, S. (2010). Menopause, depression, and loss of sexual desire: a psychodynamic contribution. *Journal of the American Academy of Psychoanalysis and Dynamic Psychiatry*, 38(1), 99–116.

Kim, M., Lim, H., Yang, H. J., Lee, M. S., Shin, B., & Ernst, E. (2013). Ginseng for managing menopause symptoms: a systematic review of randomized clinical trials. *Journal of Ginseng Research*, 37(1):30–36.

Kingsberg, S. (2010). Hypoactive sexual desire disorder: when is low sexual desire a sexual dysfunction? Patient highlights. *Journal of Sexual Medicine*, 7(8), 2907–2908.

Kingsberg, S. A., & Rezaee, R., L. (2013). Hypoactive sexual desire in women. *Menopause*, 20(12), 1284–300.

Kotta, S., Ansari, S. H., & Ali, J. (2013). Exploring scientifically proven herbal aphrodisiacs. *Pharmacognosy Review*, 7(13), 1–10.

Kunle, O. F., Egharevba, H. O., & Ahmadu, P. O. (2012). Standardization of herbal medicines – a review. *International Journal of Biodiversity and Conservation*, 4(3), 101–112

Leach, M. J., & Moore, V. (2012). Black cohosh (*Cimicifuga spp*.) for menopausal symptoms. *Cochrane Database Systematic Review*, (9), CD007244.

Lethaby, A., Marjoribanks, J., Kronenberg, F., Roberts, H., Eden, J., & Brown, J. (2013). Phytoestrogens for menopausal vasomotor symptoms. *The Cochrane Library*, 12, 1–32.

Lipovac, M., Chedraui, P., Gruenhut, C., Gocan, A., Kurz, C., Neuber, B., & Imhof, M. (2011). Effect of red clover isoflavones over skin, appendages, and mucosal status in postmenopausal women. *Obstetrics and Gynecology International*, 2011, 949302.

Lutter, S., Schmalbach, K., Esch, H. L., & Lehmann, L. (2014). The isoflavone irilone contributes to the estrogenic potential of dietary supplements containing red clover. *Archives of Toxicology*, 88(2), 309–21.

Mazaro-Costa, R., Andersen, M. L., Hachul, H., & Tufik, S. (2010). Medicinal plants as alternative treatments for female sexual dysfunction: utopian vision or possible treatment in climacteric women? *Journal of Sex Medicine*, 7(11), 3695–714.

Meston, C. M., Rellini, A. H. & Telch, M. J. (2008). Short- and long-term effects of *Ginkgo biloba* extract on sexual dysfunction in women. *Archives of Sexual Behaviour*, 37(4), 530–547.

Mohammad-Alizadeh-Charandabi, S., Shahnazi, M., Nahaee, J., & Bayatipayan, S. (2013). Efficacy of Black cohosh (*Cimicifuga racemosa L*.) in treating early symptoms of menopause: a randomized clinical trial. *Chinese Medicine*, 8, 20.

Montgomery, K. A. (2008). Sexual desire disorders. *Psychiatry*, 5(6), 50–55.

Morali, G., Polatti, F., Metelitsa, E. N., Mascarucci, P., Magnani, P., & Brunenghi Marrè, G. (2006). Open, non-controlled clinical studies to assess the efficacy and safety of a medical device in form of gel topically and intravaginally used in postmenopausal women with genital atrophy. *Arzneimittel Forschung—Drug Research*, 56, 230–238.

Mosby's Medical Dictionary: herbal medicine. (n.d.). Mosby's Medical Dictionary, 8th edition (2009). http://medical-dictionary.thefreedictionary.com/herbal+medicine. Accessed 26.07.2016.

Murray, M. T. (2015). Menopause and anxiety. *Better Nutrition*, 77(4), 34–35.

Nijland, E. A., Weijmar Schultz, W. C., Nathorst-Boös, J., Helmond, F. A., Van Lunsen, R. H., Palacios, S., Norman, R. J., Mulder, R. J., & Davis, S. R. (2008). Tibolone and transdermal E2/NETA for the treatment of female sexual dysfunction in naturally menopausal women: results of a randomized active-controlled trial. *The Journal of Sexual Medicine*, 5(3), 646–56.

Oh, K. J., Chae, M. J., Lee, H. S., Hong, H. D., & Park, K. (2010). Effects of Korean red ginseng on sexual arousal in menopausal women: placebo-controlled, double-blind crossover clinical study. *Journal of Sex Medicine*, 7(4 Pt 1), 1469–77.

Oliff, H. (n.d.). Scientific and Botanical Monograph for Pycnogenol. American Botanical Society. http://abc.herbalgram.org/site/DocServer/Pycnog_FullMono120809_LOW.pdf?docID=1741. Accessed 10.08.2016.

Pebdani, M. A., Taavoni, S., Seyedfatemi, N., & Haghani, H. (2014). Triple-blind, placebo-controlled trial of *Ginkgo biloba* extract on sexual desire in postmenopausal women in Tehran. *Iranian Journal of Nursing and Midwifery Research*, 19(3), 262–265.

Perry, M. (2012). Lesser known symptoms of the menopause. *Practice Nursing*, 23(12), 613–616.

Pfaus, J. G. (2009). Pathways of sexual desire. *Journal of Sexual Medicine*, 6(6), 1506–1533.

Posadzki, P., Lee, M. S., Moon, T. W., Choi, T. Y., Park, T. Y., & Ernst, E. (2013). Prevalence of complementary and alternative medicine (CAM) use by menopausal women: a systematic review of surveys. *Maturitas*, 75(1), 34–43.

Postigo, S., Lima, S. M. R. R., Yamada, S. S., dos Reis, B. F., da Silva, G. M. D., & Aoki, T. (2016). Assessment of the effects of *Tribulus terrestris* on sexual function of menopausal women. *Revista Brasileira de Ginecologia e Obstetricia*, 38(3), 140–146.

Reed, S. D., Newton, K. M., LaCroix, A. Z., Grothaus, L. C., & Ehrlich, K. (2007). Night sweats, sleep disturbance, and depression associated with diminished libido in late menopausal

transition and early postmenopause: baseline data from the Herbal Alternatives for Menopause Trial (HALT). *American Journal of Obstetric Gynecology*, 196(6), 593.e1–593.e7.

Reiter, E., Gerster, P., & Jungbauer, A. (2011). Red clover and soy isoflavones – an in vitro safety assessment. *Gynecological Endocrinology*, 27(12), 1037–42.

Rosen, R. C., Brown, C., Heiman, J., Leiblum, S., Meston, C., Shabsigh, R., Ferguson, D., & D'Agostino, R., Jr. (2000). The Female Sexual Function Index (FSFI): a multidimensional self-report instrument for the assessment of female sexual function. *Journal of Sex and Marital Therapy*, 26, 191–208.

Seidlova-Wuttke, D., Jarry, H., & Wuttke, W. (2013). Plant derived alternatives for hormone replacement therapy (HRT). *Hormone Molecular Biology & Clinical Investigation*, 16(1), 35–45.

Shakeri, F., Taavoni, S., Goushegir, A., & Haghani, H. (2015). Effectiveness of red clover in alleviating menopausal symptoms: a 12-week randomized, controlled trial. *Climacteric: The Journal of the International Menopause Society*, 18(4), 568–573.

Shin, B. C., Lee, M. S., Yang, E. J., Lim, H. S., & Ernst, E. (2010). Maca (*L. meyenii*) for improving sexual function: a systematic review. *BMC Complementary and Alternative Medicine*, 10, 44.

Sims, K. E., & Meana, M. (2010). Why did passion wane? A qualitative study of married women's attributions for declines in sexual desire. *Journal of Sex & Marital Therapy*, 36, 360–380.

Sparavigna, A., Tenconi, B., De Ponti, I., Bulgheroni, A., & Scarci, F. A controlled, randomized, open label study in postmenopausal women to assess the safety and the efficacy of a vaginal moisturizer: An instrumental approach. *Open Journal of Obstetrics and Gynecology*, 3, 395–399

Staccini, L. (2015). Psychological treatment of female sexual dysfunction: a critical review of the literature. *Rivista de Psichiatria*, 50(6), 265–73.

Sungur, M. Z., & Gündüz, A. (2014). A comparison of DSM-IV-TR and DSM-5 definitions for sexual dysfunctions: critiques and challenges. *Journal of Sexual Medicine*, 11(2), 364–373.

Toffol, E., Kalleinen, N., Urrila, A. S., Himanen, S., Porkka-Heiskanen, T., Partonen, T., & Polo-Kantola, P. (2014). The relationship between mood and sleep in different female reproductive states. *BMC Psychiatry*, 14, 177.

Traish, A. M., Botchevar, E., & Kim, N. N. (2010). Biochemical factors modulating female genital sexual arousal physiology. *Journal of Sexual Medicine*, 7(9). 2925–2946.

Van Die, M. D. (2011). Phytoestrogens in menopause. *Australian Journal of Medical Herbalism*, 23(1), 11–17.

Wang, S., Dunlap, T. L., Howell, C. E., Mbachu, O. C., Rue, E. A., Phansalkar, R., Chen, S. N., Pauli, G. F., Dietz, B. M., & Bolton, J. L. (2016). Hop (*Humulus lupulus L.*) extract and 6-prenylnaringenin induce P450 1A1 catalyzed estrogen 2-hydroxylation. *Chemical Research Toxicology*, 29(7), 1142–1150.

Weaver, A. D. & Byers, E. S. (2013). Eye of the beholder? Sociocultural factors in the body image and sexual well-being of heterosexual women. *International Journal of Sexual Health*, 25, 128-147.

Woods, N. F., Mitchell, E. S., & Smith-DiJulio, K. (2010). Sexual desire during the menopausal transition and early postmenopause: observations from the Seattle midlife women's health study. *Journal of Women's Health*, 19(2), 209–217.

World Health Organization (WHO). (2016). Traditional medicine: definitions. http://www.who.int/medicines/areas/traditional/definitions/en/. Accessed 26.07.2016.

Wylie, K., & Mimoun, S. (2009). Sexual response models in women. *Maturitas* 63(2), 112–115.

Yang, H. M., Liao, M. F., Zhu, S. Y., Liao, M. N., & Rohdewald, P. (2007). A randomised, double-blind, placebo-controlled trial on the effect of Pycnogenol® on the climacteric syndrome in peri-menopausal women. *Acta Obstetricia et Gynecologica*, 86, 978–985.

Yih, J. M., Killinger, K. A., Boura, J. A., & Peters, K. M. (2013). Changes in sexual functioning in women after neuromodulation for voiding dysfunction. *Journal of Sexual Medicine*, 10, 2477–2483.

Zanoli, P., Zavatti, M., Rivasi, M., Benelli, A., Avallone, R., & Baraldi, M. (2009). Experimental evidence of the anaphrodisiac activity of *Humulus lupulus L.* in naïve male rats. *Journal of Ethnopharmacology*, 125(1), 36–40.

Zwickl, S., & Merriman, G. (2011). The association between childhood sexual abuse and adult female sexual difficulties. *Sexual and Relationship Therapy*, 26(1), 16–32.