

## Research Article

# Therapeutic Potential of *Nigella Sativa* for Female Sexual Disorder in Middle Aged and Elderly Women: A Pilot Study

Khola Noreen<sup>1</sup>, Farah Ayyaz<sup>2</sup>, Sadia Khan<sup>2</sup>, Lubna Meraj<sup>3</sup> and Mohammad Akram Randhawa<sup>4\*</sup>

<sup>1</sup>Department of Community Medicine, Rawalpindi Medical University, Pakistan

<sup>2</sup>Department of Gynecology, Benazir Bhutto Hospital, Pakistan

<sup>3</sup>Department of Medicine, Rawalpindi Medical University, Pakistan

<sup>4</sup>Department of Pharmacology, Rawalpindi Medical University, Pakistan

**\*Corresponding author**

Mohammad Akram Randhawa, Department of Pharmacology, Rawalpindi Medical University, New Teaching Block, Holy Family Hospital, Rawalpindi, Pakistan

**Submitted:** 26 April, 2025

**Accepted:** 19 May, 2025

**Published:** 22 May, 2025

**ISSN:** 2379-0547

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**OPEN ACCESS****Keywords**

- Nigella Sativa Seed
- Honey
- Black Seed Oil
- Female Sex Disorders
- Middle-Aged/Elderly Women

**Abstract**

**Introduction:** Female Sexual Disorders (FSD) hinder race-propagation and deteriorate life-quality. Middle-aged/elderly women are more likely to suffer because of low serum estrogen; causing vaginal smooth muscle shrivel, mucosal thinning and decreased secretions; resulting into dyspareunia, distress and disturbed family relations. Topical estrogen improves symptoms, but its systemic absorption produces side-effects. Oral Nigella sativa seed (Black-Seed, BS) has been shown to control menopausal symptoms because of estrogen like effects. Present study aimed to evaluate efficacy of BS powder and oil in middle-aged/elderly women with FSD.

**Methods:** Forty women, aged 45-65 years, visiting Gynecology Department of Teaching Hospital of Rawalpindi Medical University, with FSD symptoms were recruited. Participants were randomly divided into four groups (10 each), A, B, C & D, receiving BS-powder (oral) & BS-oil (topical), BS-oil (topical), BS-powder (oral) & Olive-oil (topical), and Olive-oil (topical), respectively. Patients consumed grounded BS, mixed with equal amount of honey, one teaspoon twice daily and applied BS-/Olive-oil on external genitalia and outer-1/3 of vagina every night for one month; and allowed to mate with spouses twice weekly during this period. Female Sex Function Index (FSFI), pre- and post-intervention was assessed with FSFI-questionnaire and results compared statistically. Results: Study revealed highly significant improvement in FSD symptoms (Desire, arousal, lubrication, orgasm, satisfaction and pain) in group A (BS oral & BS-oil topical) as compared to B, C & D.

**Conclusion:** Oral BS with topical BS-oil effectively improved FSD symptoms in middle-aged/elderly women, because of systemic and topical estrogenic, anti-inflammatory and analgesic potential, besides lubrication.

**ABBREVIATIONS**

FSD: Female Sex Disorders; MSD: Male Sex Disorders, FSFI: Female Sex Function Index, BS: Black Seed, TQ: Thymoquinone

**INTRODUCTION**

Human sexual function is important for propagation of race and quality of life. Sexual dysfunction can cause a reduction in the growth of human population as well as impairment in the family relations. Male Sexual Dysfunction (MSD), especially erectile dysfunction, has been extensively studied and effective remedies have been investigated for its treatment. However, Female Sexual Dysfunction (FSD) is relatively less understood, perhaps because of social and ethical reasons [1,2]. In our community women,

particularly elderly ladies, are usually reluctant to discuss about sex issues.

FSD may be defined as a disorder of sexual desire, arousal, orgasm, satisfaction and pain that results in significant personal distress; and is a multifactorial, age-related, progressive problem [3,4]. The incidence of FSD varies between different populations, geographical location and age groups, and is generally more prevalent than MSD. A survey conducted in Europe to find the prevalence of sexual dysfunctions among people aged 40-80 years reported that overall 23% of men and 32% of women had some form of sex disorder and the problem was more prevalent in the elderly persons [5]. In the United States of America, the prevalence of FSD has been reported as 43% [6]. An Iranian study reported a prevalence of FSD as

31.5%, which increased with age and was 26% in women aged 20-39 years, while 39% in those > 50 years [7]. The prevalence is also said to be higher in patients having chronic illness like hypertension and diabetes, e.g., a recent study conducted in Pakistan reported the prevalence rate of FSD as 64% in diabetic type-2 patients [8].

Prevalence of FSD is greater in middle-aged and post-menopausal women because of decrease in estrogen levels, which causes vaginal smooth muscle atrophy, thinning of mucosa and decrease in secretions, leading to dyspareunia, pain and discomfort. These changes cause psychological distress and significantly impair overall wellbeing and quality of life [9]. Previously, FSD was mainly considered as a psychological problem and treated by psychoactive medicaments. Perhaps that is why there are only two drugs approved by FDA for the management of FSD, Flibanserin and Bremelanotide, which act via central nervous mechanisms and are approved for the management of desire and arousal disorders in the premenopausal women [10,11].

Currently, particularly in middle-aged/elderly women, FSD is being described as an age-related hormonal deficiency associated with organic changes in the cavernous tissue of external genitalia, particularly vagina [12]. Because of similarities in the cavernous tissue in both genders, drug effective in improving MSD are being investigated for the management of FSD, such as Sildenafil (5-Phosphodiesterase Inhibitor) and Alprostadil (Prostaglandin-E analog) [13], but not yet approved by FDA. Topical estrogen is used as a substitution therapy, improves FSD symptoms, but there is a risk of systemic absorption and adverse effects which makes it a less preferable mode of treatment. Alternative therapies should be considered, which might provide safer and effective remedies [14].

Amongst herbal medicines, one such alternative option is *Nigella sativa* (Black Seed, BS). BS belongs to plant Family of Ranunculaceae and is evolving as a wonder herb with a religious and historical background. BS possesses a broad range of pharmacological properties and therapeutic potential and has promising benefits in improving various health conditions [15]. Abu Ali Ibn Sina (Named as Avicenna in Western Medical literature) refers to BS in his famous book, "The Canon of Medicine", as seed that boosts up energy and helps to reduce stress and anxiety [16]. BS has earned the title in Arabic as 'Habbatul Barakah', meaning the seed of blessing [17].

A novel herbal remedy, containing Black seed as one of its components, was shown to treat menopausal symptoms including hot flashes, irregular periods, sleep problems,

weight gain, vaginal dryness, and mood changes in elderly women [18]. Studies conducted to investigate the effects of BS, given as oral pellets, its extracts and active component (Thymoquinone and linoleic acid) administered via intra-gastric gavage in ovariectomized rats showed significant improvement in menopausal parameters, such as increased estrogen levels and estrogen like effects on vagina and uterus [19]. Hence, there is enough evidence to support the positive effects of BS, its extracts and active constituents in FSD. Authors could not find a direct study evaluating the efficacy of oral and topical Black seed combination therapy for treating FSD in middle-aged/elderly women. It is anticipated that topical BS seed oil, besides its lubricant and estrogen like activity will also contribute via its well-known anti-oxidant, anti-inflammatory and analgesic properties in treating FSD. Therefore, the present research aimed to conduct a pilot study to evaluate the efficacy of combination of BS oil (Topical) and seed powder (Oral) mixed with equal amount of honey, for ease of ingestion and boost compliance, in middle-aged/elderly women having symptoms of FSD.

## MATERIALS AND METHODS

This interventional study was conducted on middle-aged and elderly ladies reporting to the Gynecology & Medicine Departments of a teaching hospital of Rawalpindi Medical University (RMU), Rawalpindi. Data was collected from 30 June, 2023 to 30 June, 2024 after taking ethical approval from Institutional Research and Ethics Forum of RMU (Ref. No. 220/IREF/RMU/2022, dated 20-8-2022). Non-probability convenient sampling was used to recruit women between 40 to 65 years. As a pilot study, 10 participants were recruited for each group after taking informed consent. Females having stable family relationship, suffering from FSD symptoms as estimated from pre-intervention "Female Sex Function Index" (FSFI) score were included in the study. FSFI is a validated tool for the measurement of six domains of FSD, i.e., desire, arousal, lubrication, orgasm, satisfaction and pain (Relief) [18]. Reliability of FSFI tool was established by taking the data from 15 ladies and Cronbach's alpha calculated was found to be 0.8, which suggests a good reliability score.

Ladies suffering from chronic diseases like cancer, diabetes, cardiovascular diseases, psychological disorders, gynecological problems like infection and those using hormone replacement were excluded.

Patients were randomly divided into four groups (10 each), as under:

Group A: receiving BS-powder (oral) and BS oil (topical)

Group B: BS oil (topical) only

Group C: BS-powder (oral) & Olive oil (topical)

Group D: Olive oil (topical) only.

Freshly grounded BS was immediately mixed with equal amount of honey and given as one teaspoon (containing 2.5-3 gram of BS) orally twice daily for one month. While, BS/Olive oil (7 drops) was prescribed for application on external genitalia and outer-1/3 of vagina, every night for one month. The participants were advised to mate with spouses twice a week during this period and apply 7 drops of black seed oil/or olive oil in outer 1/3 of vagina around 15 minutes before coitus as well. Data was collected individually from every enrolled participant during an interview-based session. The questionnaire used consisted of two parts, the first was regarding sociodemographic profile of the participants and the second included 19 questions for the estimation of FSFI score. Data regarding FSD was recorded once before intervention, then women were given specific intervention according to group allotted. Each enrolled lady was called for interview at three points, once at baseline, for collection of pre-treatment data, then after 15 days of taking intervention, to ensure compliance, and finally after one month to take post-treatment data.

Female FSFI score was determined, pre-and post-treatment, in all groups and the results compared statistically. Mean and standard deviations were calculated for quantitative variables and frequency and percentages for qualitative variables. Student 't' Test was used to compare mean scores across different domains. Data was analyzed using SPSS Version 26. P-value <0.05 was taken as statistically significant.

## RESULTS AND DISCUSSION

A total of 40 middle aged women with mean age of  $51 \pm 2.17$  participated in the study. The sociodemographic characteristics of study participants and their results are shown in (Table 1). While results of FSFI score for various FSD symptoms, pre- and post-intervention, are given in (Table 2). The following paragraphs provide a detailed comparison of the effects of various treatments on parameters of Female Sexual Function Index (FSFI) across four groups (A, B, C, and D) of patients.

### Group A (BS Powder + BS Seed Oil)

Group A showed the most consistent and significant improvements across nearly all parameters, indicating that combination of oral and topical BS had both systemic and local benefits in alleviating FSD symptoms. The

**Table 1:** Sociodemographic variables and their results.

Variables	Categories	Frequency(n)	Percentage (%)
Age (years)	40-45	8	20
	46-50	14	35
	51-55	10	25
	56-60	4	10
	> 60	4	10
Weight	underweight	16	40
	Normal weight	10	25
	Overweight	14	35
Marital status	5-15	8	20
	16-25	14	35
	More than 25	18	45
Number of children	1-3	18	45
	4-6	18	45
	> 6	4	10
Occupation of husband	Employed	26	65
	Unemployed	4	10
	Personal business	10	25
Monthly income	20,000-40,000	10	25
	41,000-60,000	4	10
	61,000-80,000	10	25
	> 80,000	16	40

arousal improved from 3.09 to 3.6 ( $P = 0.008$ ), orgasm from 3.31 to 3.86 ( $P = 0.008$ ), lubrication from 3.3. to 4.3 ( $p < 0.001$ ), satisfaction from 3.27 to 4.04 ( $p = 0.007$ ) and pain (relief) from 3.37 to 4.5 ( $p = 0.001$ ). However, there was a moderate clinical improvement in desire (3.05 to 3.6), but statistically not significant ( $p = 0.091$ ).

### Group B (BS Oil, Topical Only)

Black Seed oil applied topically alone showed moderate and statistically significant benefits, especially for lubrication and pain relief, which improved from 3.33 to 3.89 ( $P = 0.012$ ) and 3.42 to 4.1 ( $P = 0.005$ ), respectively. While there was little improvement in desire, arousal, orgasm and satisfaction; changed from 3.12 to 3.36 ( $P = 0.104$ ), 3.12 to 3.3 ( $P = 0.226$ ), 3.28 to 3.29 ( $P = 0.201$ ), and 3.1 to 3.43 ( $P = 0.088$ ), respectively.

### Group C (BS Powder and Olive Oil)

Oral Black Seed and olive oil demonstrated systemic benefits, with significant improvement in all parameters, including desire, arousal, orgasm, lubrication, satisfaction and pain relief, i.e., increased from 2.94 to 3.48 ( $p < 0.041$ ), 2.91 to 3.27 ( $p = 0.011$ ), 3.21 to 4.05 ( $p = 0.019$ ), 3.14 to 3.8 ( $p = 0.008$ ), 3.08 to 3.92 ( $p < 0.018$ ), and 3.98 to 4.64 ( $p = 0.014$ ), respectively. However, the effects were less marked than Group A (BS oral plus black seed oil topical).

### Group D (Olive Oil, Topical - Control)

Olive oil alone showed some improvement, particularly in lubrication and orgasm, which increased from 3.6 to 4.2

**Table 2:** Results of Female Sex Function Index (FSFI) for various parameters of female sex activity in elderly women, pre- and post-intervention and comparison of mean scores across different domains using independent sample student t-test.

Group	A*		B*		C*		D*	
	Pre Mean±SD	Post Mean±SD	Pre Mean±SD	Post Mean±SD	Pre Mean±SD	Post Mean±SD	Pre Mean±SD	Post Mean±SD
Desire	3.05 ± 0.6	3.6 ± 0.8	3.12 ± 0.5	3.36 ± 0.5	2.94 ± 0.5	3.48 ± 0.3	3.46 ± 0.5	3.6 ± 0.3
	$p = 0.091$		$p = 0.104$		$p < 0.041$		$p = 0.512$	
Arousal	3.09 ± 0.7	3.6 ± 0.8	3.12 ± 0.7	3.33 ± 0.7	2.91 ± 0.5	3.27 ± 0.6	3.53 ± 0.5	3.76 ± 0.5
	$p = 0.008$		$p = 0.226$		$p = 0.011$		$p = 0.325$	
Lubrication	3.3 ± 0.5	4.3 ± 0.5	3.33 ± 0.5	3.89 ± 0.7	3.21 ± 0.4	4.05 ± 0.6	3.6 ± 0.5	4.2 ± 0.3
	$p = 0.001$		$p = 0.012$		$p = 0.019$		$p = 0.017$	
Orgasm	3.31 ± 0.4	3.86 ± 0.8	3.28 ± 0.5	3.29 ± 0.6	3.14 ± 0.4	3.8 ± 0.6	3.24 ± 0.3	3.8 ± 0.5
	$p = 0.008$		$p = 0.201$		$p = 0.008$		$p = 0.009$	
Satisfaction	3.27 ± 0.4	4.04 ± 0.8	3.1 ± 0.4	3.43 ± 0.6	3.08 ± 0.8	3.92 ± 0.9	3.54 ± 0.5	3.76 ± 0.6
	$p = 0.007$		$p = 0.088$		$p < 0.018$		$p = 0.484$	
Pain	3.37 ± 0.7	4.5 ± 0.5	3.42 ± 0.6	4.1 ± 0.6	3.98 ± 0.8	4.64 ± 0.6	3.8 ± 0.1	4.45 ± 0.4
	$p = 0.001$		$p = 0.005$		$p = 0.014$		$p = 0.108$	

\*Group A: Black seed powder (Oral) plus black seed oil (Topical)

\*Group B: Black seed oil (Topical)

\*Group C: Black seed powder (Oral) and olive oil (Topical)

\*Group D: Olive oil (Topical)

( $p = 0.017$ ) and 3.24 to 3.8 ( $p = 0.009$ ), respectively; likely due to the emollient effects of olive oil, but less pronounced as compared to oral BS consuming groups. However, olive oil alone had weak and statistically very insignificant effect on desire, arousal, pain and satisfaction; which changed from 3.46 to 3.6 ( $p = 0.512$ ), 3.53 to 3.76 ( $p = 0.325$ ), 3.54 to 3.76 ( $p = 0.484$ ) and 3.8 to 4.45 ( $p = 0.108$ ), respectively.

Results of the study demonstrated most pronounced improvement in Group A, BS powder mixed with honey (oral) and BS oil (topical), which showed improvement in all six domains of female sexual dysfunction. The most promising effect was on lubrication and pain relief ( $p = 0.001$ ), followed by satisfaction, arousal and orgasm ( $P = 0.007$ ,  $0.008$  &  $0.008$ ), while there was a moderate clinical improvement in desire but statistically not significant ( $P = 0.091$ ). The beneficial effect of Black seed in reducing pain and improving lubrication relates to its anti-inflammatory and analgesic properties. Previous evidences support the beneficial role of BS extracts and its active constituents in reducing inflammation and oxidative stress and the underlying mechanisms involve the prevention of biosynthesis of important mediators of inflammation, such as 5-LO, COX, PGD2 and LTs, as well as inhibition of proinflammatory cytokines including interleukins (ILs) and TNF- $\alpha$  [21,22].

Evidence supports that estrogenic effect of BS improves vaginal mucosal health. This effect is linked to presence of utero-trophic properties of BS due to flavonoid and phenolic compounds which have proven estrogenic properties [23]. In addition, there is evidence that BS has role in systemic hormonal modulation thus contributing towards the underlying hormonal imbalance

in menopausal women, highlighted in the study conducted by Khadhim et al, which showed elevated levels of thyroid hormone along with estrogen and luteinizing hormone in rats treated with BS [24]. Moreover, the most abundant component of BS-oil, Thymoquinone, have been shown to possess anti-oxidant, anti-inflammatory and anticancer activity [25]. Thus, the synergistic action of BS in oral and topical forms in Group A highlights the importance of both the local and systemic aspects of FSD and are adequately managed by the combination of BS powder and oil.

Group B (BS oil topical) showed good improvement in pain relief ( $p = 0.005$ ) and lubrication ( $p = 0.012$ ). This localized effect can be attributed to anti-inflammatory, analgesic and lubricant effects thus reducing pain and discomfort during intercourse. However, this group showed no significant improvement in arousal and desire because of limited systemic effects, which support the importance of the addition of topical application of BS-oil in treating localized symptoms of FSD. Results of Group C (Oral BS powder honey mix and topical olive oil) supports systemic benefits of BS and topical benefits of olive oil by showing improvement in almost all domains. However, these effects are a bit less conspicuous than Group-A. Because topical BS-oil have additional estrogenic and anti-inflammatory effects, besides lubrication, as compared to olive oil.

Group D (Control group), receiving only topical olive oil, showed moderate improvement in lubrication ( $p = 0.017$ ) and orgasm ( $p = 0.009$ ) and relatively mild and statistically insignificant effects on desire, arousal, satisfaction and pain relief. These findings further validate the systemic benefits of oral BS, beyond lubrication by olive oil.



The capsules are the usual dosage form of ground powder of BS used in most of the studies reported for the evaluation of its beneficial effects in various clinical conditions, such as hypertension, depression and anxiety. It is anticipated that during the process of capsule formation, the volatile oil active components (e.g., Thymoquinone) could evaporate. A possible explanation for the controversial results reported in these studies could be the use of sub-therapeutic doses &/or evaporation of the active components. In order to overcome this problem, in the present study, BS was grounded in manual grinder and powder immediately mixed in equal amount of honey. Thick mixture prepared in this way can be easily taken with a teaspoon, containing about 2.5-3 grams of BS, amounting to 5-6 grams daily dose.

Moreover, black seed and honey mixture can be easily prepared at home in low cost and gives better compliance because of improved taste with honey. Half-teaspoon of honey, with black seed and taken after meals is least likely to increase blood sugar levels. Rather, it has been documented that BS powder mixed in honey when supplemented with allopathic medicines further decreased blood sugar level in a diabetic patient, allowing reduction in their doses [26]. BS is reported to regulate blood glucose levels through mechanisms such as inhibition of glucose absorption, stimulation of insulin secretion and increase in insulin sensitivity [27]. Honey has also been documented to improve glycemic control via promoting glucose uptake by tissues and enhancing pancreatic beta-cell function [28].

So far only two drugs, Flibanserin and Bremelanotide, have been approved by FDA for the treatment of FSD, which are recommended for desire and arousal disorders in premenopausal women and act by alterations in the levels of central- neurotransmitters, such as norepinephrine, serotonin, and dopamine [10,11]. But presently, the pathophysiology of FSD is being explained as a bio-physio-psychological model, i.e., age related biological changes, mainly hormonal (Estrogen) deficiency, leading to biochemical and physiological alterations in the body including external genital organs. To mention particularly in relation to sexual function are vaginal smooth muscle atrophy, mucosal thinning, decreased secretions and dryness, causing dyspareunia (Painful intercourse), which result into lack of interest, fear and distress and can lead to disturbed family relations. Therefore, therapeutic approaches of FSD should include, besides care of psychosocial aspects, attention to the relief of dryness and dyspareunia, particularly in the middle-aged and elderly women [29].

Dyspareunia and fear linked to painful intercourse can lead to anxiety. BS is reported to possess anxiolytic properties in experimental model of anxiety. In stressed mice, thymoquinone reversed the decreased brain GABA content [30]. In an in vitro study, the methanolic extract of BS was shown to inhibited the release of excitatory transmitters such as glutamate and aspartate, whereas, inhibitory transmitters', gamma-aminobutyric acid and glycine, were increased in cultured rat cortical neurons [31]. The regular use of oral BS-powder mixed in honey and topical BS-oil would relieve dyspareunia and fear and associated anxiety and distress, thus improve quality of life and family relations.

## CONCLUSIONS

From the results of the present study, it is anticipated that combination of freshly prepared BS powder mixed with honey (oral) and BS oil (topical), because of central nervous effects, estrogen like activity, anti-inflammatory and analgesic properties would relieve anxiety and distress; improve desire, arousal and orgasm; alleviate pain of intercourse and fear; as well as improve overall satisfaction, quality of life and family relations of middle-aged/elderly ladies. Further studies with larger sample are needed to validate these observations and considering BS as therapeutic option for management of FSD.

## ACKNOWLEDGEMENTS

Authors gratefully acknowledge the cooperation of the faculty and staff of the Department of Medicine and Gynecology, Benazir Bhutto Hospital, Rawalpindi Medical University (RMU), Rawalpindi, Pakistan. Authors are also very thankful to the Institutional Research and Ethics Forum of RMU for granting approval of the study. Our special thanks are due to the patients who consented for participation in the study.

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