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Advantages of seed cycling diet in menstrual dysfunctions: A review based explanation

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Abstract
The seed cycling/seed rotation diet is a new trend that claims to be effective for female menstrual dysfunctions such as irregular menstruation, menstrual cramps, infertility, menopausal symptoms (hot flashes, fatigue, etc.), and PCOS. The higher prevalence of hormonal imbalance in women is a contributing factor to all of these menstrual dysfunctions. The major hormones that control menstruation in females include progesterone, estrogen, luteinizing hormone (LH), and follicular stimulating hormone (FSH), and a simple imbalance in their concentration is the root cause of a variety of menstrual problems. The practice of eating specific seeds during the two main phases of the menstrual cycle (follicular and luteal) to promote a healthy balance of estrogen and progesterone levels in women is known as the seed rotation diet. During the follicular stage consumption of pumpkin seed and flax seed is advised and in the luteal stage consumption of sunflower seed and sesame seed is advised in this diet. Recent studies have shown that pumpkin seeds are rich in phytoestrogen which is a polyphenol compound that exerts a mammalian estrogenic-like effect in body. Similarly, flax seed in the first phase helps to bind the excess estrogen produced to maintain the hormonal homeostasis. Sesame seeds, which are high in zinc and lignans, are thought to help with progesterone balance during the luteal phase, while sunflower seeds, which are high in vitamin E and selenium aids in, increasing progesterone production and liver detoxification of excess estrogen. However, despite plenty of anecdotal accounts of its usefulness, scientific evidence to back its claims is still weak or lacking.

Keywords: Menstrual dysfunctions, seed cycling diet, hormonal imbalance

Introduction
Menstrual dysfunctions are a group of acute difficulties that women suffer around the world during their reproductive years and for a few years beyond menopause, and they have a significant impact on women's daily lives. Premenstrual syndrome (PMS), dysmenorrhea, amenorrhea, hypomenorrhea, menorrhagia, polymenorrhea, and oligomenorrhea are examples of prevalent menstrual dysfunctions [1] (Table. 1). Menstrual disorders are among the most common gynecological symptoms, particularly among adolescents, with PCOS and infertility being the most pressing issues nowadays. During the menstrual cycle, body undergoes many physiological and hormonal changes. The process begins with the brain triggering certain hormones to stimulate egg growth followed by the traveling of a mature egg from the ovary to the uterus through the fallopian tube and finally disposal through the vagina with blood in absence of fertilization. As a result, a simple disruption in the hormonal management of the menstrual cycle might result in a variety of menstruation issues. Treatment for these conditions varies depending on the origin, nature, and stage of life (before pregnancy, and old age). Anovulatory menstrual dysfunctions (missing periods, irregularities, and infrequent periods) are commonly treated with oral contraceptives, cyclic progestin, and non-medical treatments (nutritional therapy, dietary changes, and workouts, for example) [2, 3]. Treatments such as hormone-releasing intrauterine devices, hormone-containing drugs, and non-steroidal pharmaceuticals, among others, are currently in use for ovulatory menstrual dysfunctions (heavy or extended menstrual bleeding) with specific limits and sideeffects [4, 5, 6, 7].
Seed cycling/seed rotation is a developing diet trend that has been claimed to improve hormonal balance, fertility, and menstrual health dysfunctions in women of reproductive age and those approaching menopause. It mostly entails the ingestion of seeds such as flax, pumpkin, sesame, and sunflower seeds at various points throughout the month to regulate hormones that regulate female menstruation health (Fig. 1.). Pumpkin, seed, and flaxseed are

recommended to be ingested during the follicular period since they can aid in increasing estrogen levels while preventing excess estrogen production. Pumpkin seed contains phytoestrogens that mimic estrogenic activities [8], whereas flax seeds the second major seed prescribed in the diet contain lignans which bind to excess estrogen and maintain the hormonal balance. During the second phase of the menstrual cycle / the luteal phase, sesame seeds and sunflower seeds are believed to boost progesterone production in this diet. Sesame seeds are also rich sources of zinc which bestows similar effects to progesterone production and also contain lignans that help to block excess estrogen while progesterone rises. Sunflower seeds are a rich source of two vital micronutrients such are vitamin E and selenium. Vitamin E can elevate progesterone production, while selenium helps in the detoxification of excess estrogen from the liver. However, sesame seeds are beneficial for postmenopausal women by improving blood lipids, antioxidants, and sex hormones (Fig. 1).

Even though this diet has gained popularity, scientific research on its effectiveness is limited. As a result, this article attempts to incorporate scientific studies that have demonstrated the therapeutic effects of these seeds on female menstruation health, as well as to explore the mode of action of these seeds in various menstrual dysfunctions.

Methodology:

A detailed literature search for this review article was conducted in two phages in electronic databases like Google scholar, Pubmed, Mendeley library, and Medline for the collection of research papers. The first phage literature search was conducted with the objective to find out the prevalence of menstrual problems in women of different ages. The keywords or combination of words like "prevalence of menstrual dysfunction" OR “prevalence of menstrual problems” were used and adapted for each database search. Each study included in this phage was selected based on the year of publication (2010-2022) and the number of menstrual problems reported (>3 types). Advanced search criteria like ‘words present in title only’, and ‘English language only’ were applied while searching publications on the cited databases.

The second phage search was undertaken with the objective to justify the effect of the seed cycling diet on menstrual health through scientific studies signifying the effect of individual components of this diet. The following keywords or combination of words were used and adapted for each database for the second phage search: (“flax seed and menstrual health”) AND (“sunflower seed and menstrual health”) AND (“pumpkin seed and menstrual health”) AND (“sesame seed and menstrual health”) AND (“phytoestrogen and menstrual health”) AND (“lignan and menstrual health”) AND (“vitamins and menstrual health”) AND (“minerals and menstrual health”). No time frame was specified for the literature search in this phase. Advanced search criteria like ‘words present anywhere in the article’, and ‘English language only’ were applied while searching publications on the cited databases.

For both phages thesis, dissertations, and unpublished studies were excluded from this review article. All the included studies were selected by screening the titles first, followed by abstract analysis. Selected studies were downloaded in a full-text article form and critically screened according to the inclusion and exclusion criteria of both phages.

Discussion

Menstrual dysfunctions and their prevalence:

Menstruation can be characterized as the periodic shedding of endometrial tissue along with some amount of blood through the vagina in absence of any pregnancy. The first menstruation of a female (menarche) is considered as an important developmental milestone of puberty and an indicator of maturity in females [9]. From the third year after menarche, clinical evidence suggests that the time between menstrual cycles is generally 21-34 days, and a flow lasting from 3 to 7 days with 35 ml (range 5-80 ml) of mean menstrual blood loss [10]. Variability in this menstruation trend will lead to menstrual dysfunctions (Table. 1.) [11, 12, 13]. However, the most discussed cause of this variability in menstrual trends is hormonal imbalance.

Table 1: Characteristics of common menstrual dysfunctions:

Sl. No	Menstrual Dysfunctions	Characteristics
1.	Dysmenorrhea	Mild to severe pain before or at onset of menstrual flow.
2.	Amenorrhea	No menstruation for ≥3 months
3.	Hypomenorrhea	Scanty blood flow/ shorter duration (<2 days)/ both
4.	Menorrhagia/Hypermenorrhea	Bleeding for >8 days/ >4 fully soaked pads per day
5.	Irregularity	Menstrual cycle <22 days / >35 days
6.	Premenstrual syndrome	Mood swings, headache, bloating, stress, anxiety, and backache
7.	Metrorrhagia	Inter-menstrual bleeding
8.	Menometrorrhagia	Prolonged and excessive bleeding, irregularity and frequent menstruations
9.	Polymenorrhea	Menstrual cycle <21 days
10.	Oligomenorrhea	Menstrual cycle ≥35 days,
11.	Mastalgia	Tenderness / soreness of breast just before or during menstruation

From the table, we can conclude that the most prevalent menstrual problem recorded with the highest percentages are dysmenorrhea (range: 15-96%), followed by PMS (33-96%), irregularity of period (10-62%), oligo-menorrhea (6-22%), menorrhagia (1-37%), and polymenorrhea (2-21%).

Menstrual dysfunctions and hormonal imbalance

A female experiences an average of 450 menses throughout her life which makes it a topic very engrossing for researchers and clinicians. Moreover, a complete knowledge of the interplay of hormones in the physiology of menstruation is

very essential for perceiving menstrual dysfunctions more precisely and concluding a treatment for the same. The very first menstruation (menarche) starts when the gonadotrophin-releasing hormone (GnRH) starts secreting from the hypothalamus in a pulsatile and periodic manner towards the age of menarche. GnRH then stimulates the anterior pituitary to release FSH and LH which acts on ovaries. Ovaries under the influence of FSH release estrogen from their granulose cells and a little amount of progesterone from theca cells under LH influence. This stage is named the proliferative stage or the follicular stage that lasts from the 1st to14th day of a menstrual cycle. During this stage estrogen levels increase to promote follicular growth (from primordial to graafian follicle), endometrial growths, and to facilitate the establishment of sperm channels [14]. Towards the end of this stage, the excess estrogen gives negative feedback to the hypothalamus to reduce the production of FSH as the graafian follicle needs to be ruptured for ovulation to happen. This period is just before ovulation when FSH is reducing in concentration as LH is increasing is denoted as LH surge. The second phase or the luteal phase lasts from day 14th-day 28th. It is characterized by the increased production of progesterone and slowly reduced estrogen levels. At beginning of the second phase, the egg from the mature follicle is released and the corpus luteum is created under the effect of progesterone and LH surge. Again towards the end of the luteal stage, excess progesterone gives negative feedback to the anterior pituitary to decrease the production of FSH and LH. During this decline of hormones corpus luteum works as a secretory vessel of progesterone and estrogen to maintain the levels. Progesterone secreted from the corpus luteum towards the end of the phase slows down the endometrial proliferation, decreases lining thickness creates more complex glands, etc. and estrogen on the other hand secreted at a comparatively lower concentration (only from the corpus luteum) aids in endometrial proliferation. At around the 28th day and just before that the corpus luteum starts to degenerate in absence of implantation of a fertilized ovum. Therefore the estrogen and progesterone levels decrease rapidly causing the uterine endometrial wall to shed which is called menses and it lasts grossly from 0-5th day of the next menstrual cycle (Fig. 1) [15, 16, 17, 18].

Studies have suggested that mild elevation of female androgens (hyperandrogenism) is the most common endocrinopathy in women which affects about 10-20% of them[19]. It is the causative factor for disruptive gonadal functions and menstrual irregularities. Moreover, it has a direct link to the degree of menstrual irregularities in women because of its direct correlation with testosterone levels and the length of the follicular phase, and its indirect correlation with the length of the luteal phase[20]. Therefore imbalance of the essential gonadal hormones is crucial among the few factors for the menstrual changes and dysfunctions recorded across age, ethnicity, and body weights [21, 22].

Pumpkin seed and its role in menstrual dysfunctions

The oil of pumpkin seeds has proved to contain a high percentage of phytoestrogens, minerals (Zn, Mg, Cu, Mn, Fe, P) and sterols (secoisolariciresinol, lariciresinol) [23, 24]. Phytoestrogens as the name suggest mimic the function of estrogen due to their ability to bind with the estrogen receptors8. These are polyphenols present in plant extracts and are present in pumpkin seeds at a concentration of 265 mg/100g of seeds [25]. Rodent model studies have proven the estrogenic activities of pumpkin seeds such as regulating lipid metabolism, bone remodeling, and mammary gland and uterus epithelial cell development [26, 27, 28]. Due to these effects, phytoestrogens and phytoestrogen-containing diet are suggested to be useful for the prevention and treatment of vasomotor menopausal symptoms especially hot splashes and night sweats. Unfortunately, demonstrable evidence for such effects is weak at present, with most clinical trials showing no or minimal results which require more scientific in-depth studies [29, 30, 31, 32].

Moreover, the zinc in pumpkin seeds supports progesterone production towards the progesterone rise in the second phase of the menstrual cycle. The mineral zinc promotes the formation of the corpus luteum, which is responsible for producing progesterone and stimulates the uterus to thicken in preparation for potential implantation [33]. Zinc has been proven associated with progesterone levels in the body by few researchers. The study by Kechrid *et al.*, in 2006 suggested that zinc supplementation can improve the progesterone level significantly in the non-pregnant mice group [34]. A similar type of result was also reported by Nishi, in 1996 where hypogonadism led by Zn deficient diet was recorded [35]. Om and Chung (1996) showed that zinc deficiency led to inhibition in LH and estrogen levels [36]. Nonetheless, a remarkable finding supporting the relation between zinc and estrogen was that zinc was a significant stimulator in estradiol synthesis [37]. Another theory that strongly supports the relationship between estrogen and zinc is the oxidants and luteal formation and progesterone theory. An increased intracellular oxidant level impairs luteal formation and also progesterone production which can be reduced by antioxidants like Zn/Cu-superoxide dismutase. These Zn-superoxide dismutases require Zn to function [38].

Table 2: Selected Studies citing prevalence of menstrual dysfunctions among women:

Study ID	Country, region	Study Design	Age group	Sample Size	Menstrual Problems					
					Dysmenorrhea	Irregular cycle	PMS	Menorrhagia	Polymenorrhea	Oligomenorrhea
Bahrami *et al.*, 2022 [83]	Iran (Mashhad and Sabzevar)	Descriptive survey	10-19 yr	897	68.80%	18.70%	47.60%	2.10%	3.10%	15.60%
Kanmani *et al.*, 2016 [84]	India (Tamil Nadu)	Descriptive survey	12-18 yr	166	28.30%	36.70%	-	-	8.40%	4.80%
Shiferaw *et al.*, 2014 [85]	Ethiopia	Cross-sectional	17-24 yr	470	85.10%	46.20%	72.80%	4.30%	3.80%	14.90%
Antherjanam *et al.*, 2016 [86]	India (Kerala)	Cross-sectional	13-18 yr	1722	71.50%	-	-	-	22.30%	18.10%
Omidvar *et al.*, 2011 [87]	India (Mysore)	Cross-sectional	18-27 yr	194	78.20%	11.90%	-	4.10%	2.20%	6.00%
Dambhare *et al.*, 2012 [88]	India (Maharashtra)	Cross-sectional	10-19 yr	1100	56.15%	57.90%	56.16%	1.25%	8.38%	22.10%
Karout N., 2015 [89]	Saudi Arabia (Al Khobar)	Cross-sectional	18-20 yr	342	96.30%	36.40%	95.60%	9.10%	21.30%	21.60%
Karki *et al.*, 2017 [90]	Nepal (Kathmandu)	Cross-sectional	18-23 yr	171	53.80%	35.70%	67.30%	2.90%	4.10%	9.90%
Ali *et al.*, 2020 [91]	Saudi Arabia (Al Neelain)	Cross-sectional	18-24 yr	149	94.00%	55.00%	-	2.63%	-	-
Tabassum *et al.*, 2020 [92]	Pakistan (Balochistan)	Cross-sectional	>18y r	100	15.00%	62.00%	>50%	13.00%	-	-
Gaddala *et al.*, 2021 [93]	India (Telengana, Karimnagar)	Cross-sectional	19-25 yr	100	86.00%	25.00%	83.00%	12.00%	6.00%	19.00%
Varghese *et al.*, 2019 [94]	India (kerala, Thiruvanantha puram)	Descriptive survey	13-18 yr	350	79.00%	24.00%	84.00%	4.00%	12.60%	-
Yaliwal *et al.*, 2020 [95]	India (Karnataka)	Cross-sectional	10-19 yr	1016	62.00%	33.36%	-	12.20%	11.60%	21.80%
Samreen *et al.*, 2016 [96]	India (Kashmir)	Cross-sectional	15-45 yr	810	51.00%	10.00%	48.00%	24.00%	1.85%	8.88%
Ekpenyong *et al.*, 2011 [1]	Nigeria (Uyo)	Cross-sectional	16-23 yr	393	-	-	33.10%	37.50%	-	19.90%
Nwankwo et ak., 2010 [97]	Nigeria (Enugu)	Cross-sectional	10-19 yr	495	25.00%	31.10%	-	4.60%	19.20%	12.10%

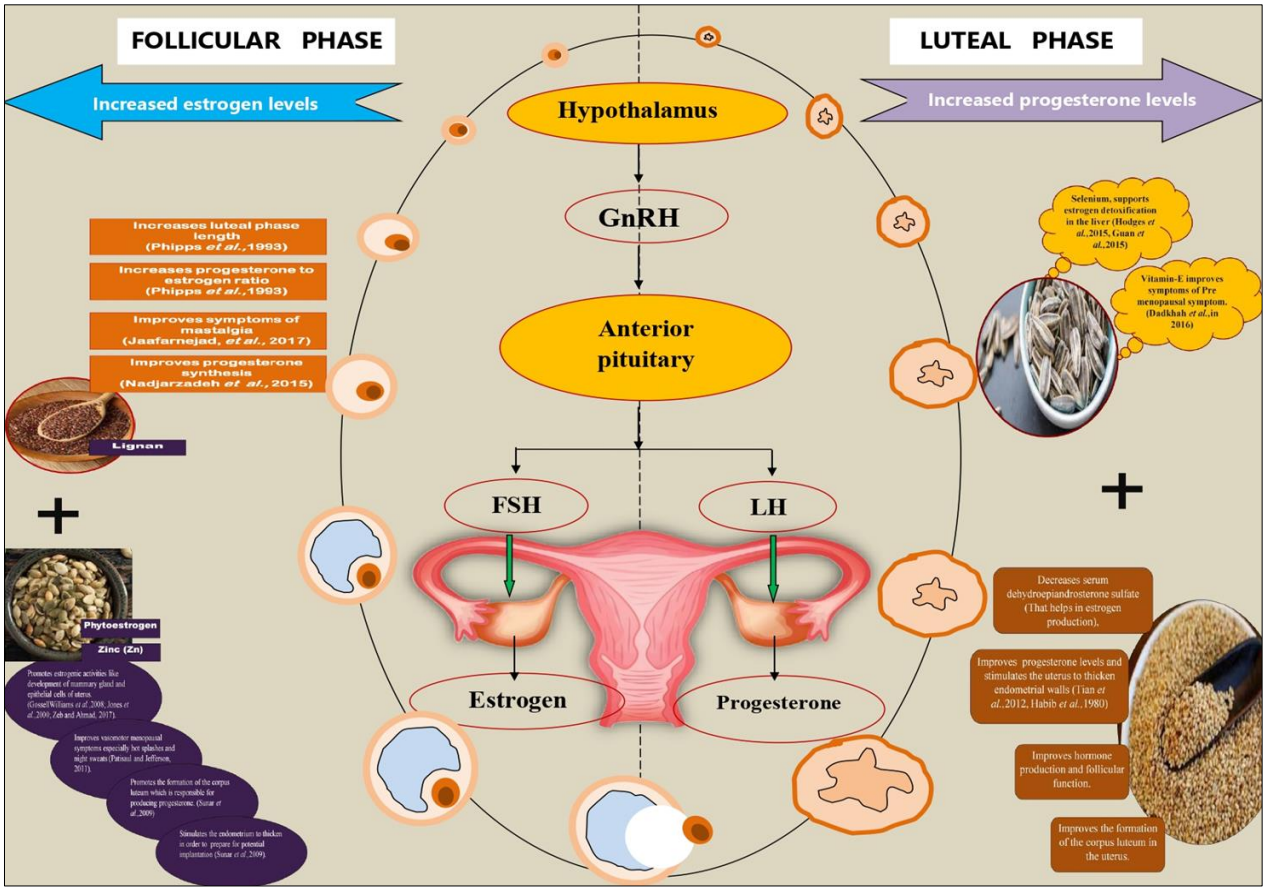

Fig 1: Role of Seed cycling diet in menstrual health

Flaxseed and its role in menstrual dysfunctions

Literature suggests that flaxseed helps in lengthening the luteal phase, improving ovulation, and reducing common PMS symptoms such as mastalgia (cyclic breast pain) and cramping. Several human trials have proved that flax seed consumption can cure menstrual irregularity due to the presence of a specific compound named lignin [39, 40, 41]. Lignans are a group of phytochemicals that have been shown to possess weak estrogenic and antiestrogenic properties depending upon duration, dose, and stage of development [42, 43, 44, 45, 46, 47, 48, 49]. A balanced randomized cross-over design study recorded an increased luteal phase length and higher progesterone to estrogen ratio in the flax seed ingested group than in control [50]. Again Vaziri *et al.*, in 2014 suggested that flaxseed was effective in reducing mastalgia which was later substantiated by the results of the study conducted by Jaafarnejad, *et al.*, in 2017 [51, 52]. Mastalgia condition generally started in the later luteal phage and before menstruation started due to the increased estrogen, decreased progesterone, and elevated prolactin concentrations [53]. This may explain the recommendation of flax seed from the 1st to 14th day of a menstrual cycle under the seed cycling diet. Again few research articles witnessed improved menstrual cycles/regularity and increased progesterone secretion due to the supplementation of omega-3, [54] which could be another reason for flax seed recommendation in this diet.

Similarly, negative effects or antiestrogenic effects of flax seed lignans were reported by several studies [55, 56, 57, 58, 59]. According to in-vitro and in-vivo studies, flax seed/ lignan (especially enterolactone) ingestion is associated with increased synthesis of sex hormone-binding globulin or sex steroid-binding globulin (SHBG) protein concentration [60, 61] which can be a possible explanation for the antiestrogenic effect of lignan on menstrual cycle [62].

Sunflower seed and its role in menstrual dysfunctions

Sunflower seeds are a rich source of vitamin E and minerals like calcium, iron, magnesium, phosphorus, potassium, sodium, zinc, copper, manganese, and selenium [63]. Out of these important constituents, the principal nutrients that are believed to be crucial for menstrual health in the seed cycling diet are Vitamin-E and selenium. The trace mineral selenium supports estrogen detoxification in the liver [64, 65] which helps bind excess estrogen during the luteal phase when estrogen declines and progesterone rises [66, 67].

Vitamin E the second focal nutrient of sunflower seeds proved to improve PMS in some human studies. Dadkhah *et al.*, in 2016 conducted a randomized double-blind, controlled trial with 86 women facing PMS. 100 mg vitamin E supplementations were provided to the women for 2 months. After the study, the mean score of the syndrome significantly decreased in the experimental group as compared to the placebo [68]. Another study conducted by Mandana *et al.*, in 2013 to compare the effect of vitamin E, vitamin B6, calcium, and omega-3 on the treatment of premenstrual syndrome showed statistically significant differences regarding the physical symptoms, and mental symptoms of the vitamin E group. This double-blind clinical randomized trial study was carried out on two hundred girls with moderate and severe forms of premenstrual syndrome divided into 4 groups. The vitamin-E supplementation group received 100 mg of Vit-E daily for three consecutive cycles [69]. Similar results were recorded in a single double-blind trial that evaluated the effects of vitamin E supplementation in PMS. In that trial, 41 women with PMS received 400 IU/day of vitamin E for three cycles. The results showed a significant improvement in some affective and physical symptoms in the vitamin E group [70].

Sesame seed and its role in menstrual dysfunctions

Sesame seed is a good source of omega-3, omega-6, and vitamin E which is self-explanatory for its recommendation in the seed cycling diet. Due to the presence of these nutrients sesame seed is also believed to improve hormone production and follicle function as sunflower seed and flax seed. Again as pumpkin seed, the higher concentration of Zn in it is predicted to improve the formation of the corpus luteum in the uterus, which is responsible for producing progesterone and stimulates the uterus to thicken in preparation for potential implantation [71, 72]. Sesame also contains lignans which help to block excess estrogen during the luteal phase as flax seeds and pumpkin seeds. In a randomized, placebo-controlled, crossover study supplementation of sesame seeds showed decreased serum dehydroepiandrosterone sulfate (helps in estrogen production), and increased serum sex hormone-binding globulin (binds excess sex hormones) and urinary 2-hydroxy estrone (estrogen metabolites) in postmenopausal women [73]. This study supported the lignan theory of sesame seeds.

PCOS and Seed cycling diet

Polycystic ovary syndrome is a complicated disease characterized by interconnected genetic, endocrine, environmental, and behavioral variables that result in different reproductive, metabolic, and psychological characteristics [74]. Irregularity and longer menstruation cycles are believed to be the hallmark of this syndrome. Studies revealed that PCOS is reported in 85-90% of women suffering from oligomenorrhea whereas 30-40% in women struggling with amenorrhea [75, 76]. Similarly, hyperandrogenism accounts for the presence of PCOS in grossly 80% of women [77]. Although the etiopathogenesis of PCOS is poorly understood yet, genetic factors, endocrine factors, and environmental factors are some of the broad areas that include all the identified causes for the onset of this syndrome [78, 79]. Other than genetic factors the other two factors are modifiable for which these are always been topics of interest for researchers. Endocrine factors for PCOS include FSH deficiency, hypersecretion of LH, and hyperandrogenemia. Shreds of evidence suggested that hyperandrogenemia condition arouse due to the overproduction of androgens from ovaries or reduced production of sex hormone-binding protein from hepatocytes in PCOS patients. In-vitro studies have suggested that high levels of androgen suppressed oocyte maturation rate and also contributed to the inhibition of its meiotic maturation resulting in faulty folliculogenesis [80, 81, 82]. Though a direct effect of seed cycling diet in improving PCOS is not yet scientifically explored, as discussed in this paper the individual seeds have proven their efficacies in correcting hormonal imbalances (hyperandrogenism, LH: FSH ratio) and improving menstrual problems which can be served as a base for anticipating a positive effect of seed cycling diet on PCOS management and prevention. Hence extensive clinical studies are needed for this diet and its therapeutic benefits.

Conclusion

According to the literature cited in this paper it can be

concluded that menstrual dysfunctions and menstrual morbidities are prevalent in younger women than older which are affecting their physical as well as psychological well-beings resulting in disrupting their productivity. Though the existing treatments available are efficient to manage these dysfunctions, but they come with their repercussions. Hence seed cycling diet, as a diet based therapy can be studied further to establish its evidence based dose dependent effectiveness on female menstrual health.

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