



## Systematic Review

## Nutraceutical Intervention of Seeds in the Treatment of Poly Cystic Ovarian Syndrome

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## ABSTRACT

1. Poly Cystic Ovarian Syndrome (PCOS) is characterized by multiple cysts formation in female ovaries. It is highly prevalent in developing countries like Pakistan and India. Its symptoms include irregular menstrual cycle, abnormal hair growth pattern, acne and mood swings. This disease is also associated with imbalance in androgen levels (which include testosterone and estrogen) and high insulin levels also called hyperinsulinemia. It also contributes in the development of type 2 diabetes, heart disease and cancers. Seed cycling is a modern method used in alternate medicine of treating PCOS by using different seeds in the different stages of menstrual cycle. **Objective:** In this review article we will find out how seed cycling is effective in the treatment of PCOS. Flax, sesame, pumpkin and sunflower seed combinations are being used at different stages of female menstrual cycle. **Methods:** Literature was searched through online databases such as PubMed, Google Scholar, Sci-Hub and others. **Results:** Flaxseeds contain lignans, omega 3 fatty acids and fibre which help in relieving the symptoms of polycystic ovaries. Sesame and sunflower seeds contain high number of fatty acids and lignans which helps in balancing hormonal disturbances in female. Losing weight by having diet rich in fibre improve the level of cholesterol and it is also beneficial decreasing the level of insulin resistance, which if not treated can progress into type 2 diabetes mellitus and its complications. **Conclusions:** Herbal medicine in Ayurveda has shown promising effects in relieving pre-menstrual symptoms, hormonal fluctuations

## INTRODUCTION

Polycystic ovarian syndrome (PCOS) is most common in women of childbearing age [1]. 52% Pakistani women are suffering from PCOS that is comparatively higher than UK percentage of women i.e. 20-25%. Environmental, genetic factors and inter marriages are the underlying causes [2,3]. In women PCOS is a reproductive disorder associated with high androgen levels, hypersensitivity and chronic ovarian disease [1]. The herbal name of flaxseed seeds is *Linum usitatissimum* [4,5] and Family is Linaceae. It is beneficial in decreasing BMI, insulin levels, total serum testosterone level, [3,6] best herb for treating PCOS. These are additionally called linseeds, and are thought of the most useful thick seeds [6]. Because of the presence of antioxidants like lignans and omega-3 unsaturated fats, flaxseeds help in bringing down cholesterol levels in the body viably [5]. As a result, the danger of getting heat infections goes down to a least. Flaxseeds additionally end up lessening circulatory strain while additionally forestalling

the development of harmful tumors in the body [5,7]. Sesame seeds, also called *Sesamum indicum*, contain supplements valuable for PCOS patients. Its solid fats help to balance blood glucose levels [7]. It additionally contains minerals like calcium, magnesium, and zinc. They have numerous medical advantages, for example, forestalling diabetes, lessening danger of malignant growth, shielding DNA from radiation harm, lessening indications of maturing, encouraging digestion, boosting oral wellbeing, and bringing down the danger of cardiovascular illness [6]. Seed cycling is natural and newly trending way that aims to improve the production and levels of hormones like estrogen and progesterone by eating flax and pumpkin seeds into first half of the menstrual cycle and sunflower and sesame seeds in the second half [8].

The lignan present in flax seed [5] and pumpkin seed helps in detoxify the excess estrogen in follicular phase. And the zinc and selenium present in sesame seeds and sunflower seeds

help in increase the production of progesterone in luteal phase [9]. Follicular phase and luteal phase both are the phases [10] of menstruation. In follicular phase eat 1-2 tablespoons each of raw, fresh ground flaxseeds and pumpkin seeds till ovulation (Day 1-15) [11]. Now from ovulation till luteal phase (Days 15-28) eat 1-2 tablespoons each of raw, fresh ground sunflower and sesame seeds. On the off chance that you ovulate at an alternate time in your cycle, at that point switch the seeds in like manner. In the event that your period comes consistently at an alternate time (e.g., 26 days rather than 28) at that point switch the seeds in like manner [12].

The hormone estrogen is considered to be the causal factor of PCOS [13]. Flaxseed extract in the amount of 500mg per day increase the level of serum estradiol in immature female rats [14]. In breast cancer lignans of flaxseed showed ant estrogenic effect. In breast cancer, the hormones are fluctuated as in the condition of oligo menorrhoea [15]. Secoisolariciresinoldi glycoside (SDG) is the main lignan in flaxseed which will be converted into weaker form of estrogen by the action of gut bacteria and have ant estrogenic effect [16]. Pharmacological interventions include anti-androgens (spironolactone, flutamide), hypoglycemic agents (metformin and thiazolidinedione) and estrogen-progesterone conversion (oral contraceptives). The effects of the most useful parts of these ingredients differ from the irregular menstrual system and are associated with various gastrointestinal symptoms, but weight gain increases insulin resistance [17]. Women studies have shown that overweight women with PCOS are obese especially in the lower abdomen. 100 women with infertile PCOS who received a combination of 100,000 IU of vitamins and 1,500 mg of metformin per day for 6 months significantly reduced their body mass index (BMI) [18].

## METHODS

For this systematic review, articles were being collected from Nov 2020, to March 2021. In this rigorous process we made library of 140 articles out of which we selected 111. Various keywords were used to make browsing efficient and wholesome like poly cystic ovary syndrome, flaxseed, sesame seed, sunflower seed, pumpkin seed and oligo menorrhoea etc. The researches from the last decade i.e., from the year 2010 to 2020 were included (Table 1, Figure 1). Included keywords were (flaxseeds, sunflower seeds, PCOS, Seed Cycling, phases of Menstrual cycle, Follicular phase and Luteal Phase) for the researches. The focus was minimum on review articles and maximum on clinical trials in inclusion criteria. Valid research engines for the collection of data were used. The researches before 2010 were not included. Irrelevant researches were excluded.

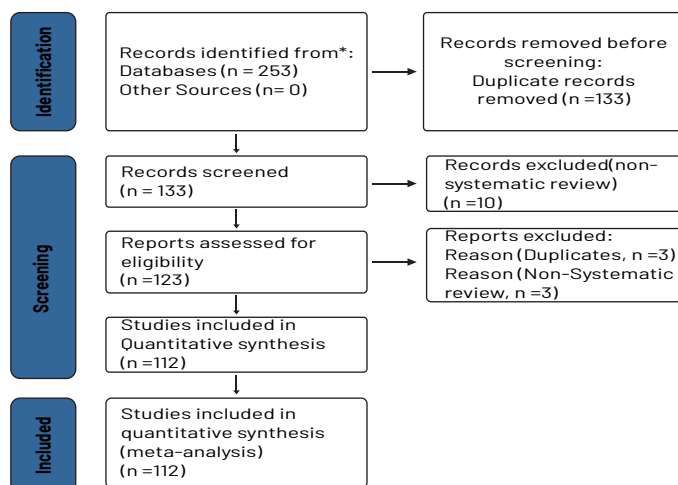


Figure 1: Consort Diagram

## Nutraceutical Intervention of Seeds:

### Flax Seeds:

Flax plants are ancient plants of the world. Flaxseed is a delicious food [13]. It is mainly grown in west of Mediterranean to India [19]. Seeds and oils were used in herbal medicine for treating inflammation, cold, respiratory diseases, muscle pain, abdominal pain by masses. 7 They are also used as supplement in hormone replacement therapy. Hence flax seeds, oils and fibers are very beneficial for the humans [20]. Flax seeds are rich in fiber [13]. This is especially true if the soil is rich in nutrients especially nitrogenous matter. The seeds are also rich source of phytoestrogens called lignano [7]. A diet rich in fiber and lignins is also recommended for patients [21]. Addition of flaxseed in the diet will help to get rid of toxins present in the body [22]. A new clinical study from Duke University showed that daily flaxseed supplementation (30g powder per day) could lower testosterone levels by up to 80% of PCOS patients [23].

And flaxseed help is to tenderness in breasts (premenstrual syndrome is a symptom) that can occur after ovulation. Flaxseed lignan affects the activity of enzymes responsible for estrogen production (such as aromatase), allowing the heart to be controlled by circulating sex hormones and metabolites [24]. Phytoestrogens bind to their receptors especially 17- $\beta$  estradiol receptors and then shows there main anti-diabetic and hypoglycemic effects [19]. Linolenic acid works by effecting protein kinase A and cyclic monophosphate adenosine functions which in turn maintain beta pancreatic cells and insulin secretion [25]. Nowadays main cause of infertility is PCOS. Flax seeds help in reducing weight by delaying gastric emptying, creating feeling of fullness [26]. ALA works by suppressing appetite and promoting apoptosis of adipocyte. It mainly helps in reducing BMI and weight [27]. On the other hand, lignans are suggested to have chemo preventive properties in cancer

[21]. SDG is emerging as a potential ant carcinogenic agent. SDG is thought to be possibly effective in reducing breast tumor [28].

#### Pumpkin Seeds:

Pumpkin (*Cucurbita*) belongs to the family *Cucurbitaceae* generally grown in the different regions of the globe as a fruit vegetable [29]. Pumpkin is the one of the most famous plant which is used as the cure of many disorders due to the presence of many components and phytochemicals [30].

Pumpkin seeds oil accommodates rich vitamin E such as  $\alpha$ -tocopherol and  $\gamma$ -tocopherol that shows the positive health effects [31]. Its oil has demonstrated to suppress high percentage of the phytoestrogens and sterols such as secoisolariciresinol and lariciresinol [32]. Pumpkin seeds contain the healthy omega-3 fatty acids that can help out to manage the high cholesterol and high insulin levels seen in PCOS treatment. They also contain beta-sitosterol that can remove unwanted androgens and treat the hirsutism, acne and weight gain symptoms of PCOS [33]. They help your body to waste the extra estrogen that can be out of the balance during follicular phase of your cycle. The lignans in these seeds, bind to excess estrogen in your body and help to eliminate it [34]. Additionally, high levels of zinc in the pumpkin seeds prevent the excess of estrogen from converting to the harmful forms of testosterone, as well as prime your body for progesterone production in the luteal phase of your cycle [35]. Some women may feel symptomatic relief and notice hormone levels balancing within the first month, while others may take 3 to 4 months before they observe any improvements. The therapy is based on slow and steady strategy [36].

#### Sesame Seeds:

Sesame seeds are wealthy in dietary fiber, protein, nutrient B, copper, manganese, calcium, and magnesium [6]. They have numerous medical advantages, for example, forestalling diabetes, shielding DNA from radiation harm, diminishing indications of maturing, encouraging processing, boosting oral wellbeing, and bringing down the danger of cardiovascular infection [37]. Nutrients A, D, E, C, B6 and minerals like zinc, selenium are the supplement profiles which are vital for creating insusceptibility in human body [6]. Dark sesame has been shown to play a role in the inhibition of myocardial remodeling and prevent the occurrence and development of atherosclerosis, total cholesterol (TC), low density lipoprotein (LDL) levels, and blood lipids [26]. It also helps in lowering the antioxidant stress that damage healthy cells and cause inflammation [38]. Lipid imbalance, CVDs and bone resorption are some of the late complications of PCOS that can potentially benefited from sesame [39]. Sesame seeds are low in

carbohydrates. Therefore, these seeds are very easy to manage insulin levels and hormonal disorders [40]. Sesame seed also help in relieves constipation. Sesame seeds improve the clearing time every week [41]. Likewise, sesame seeds may incorporate a lot of filaments and the fiber may be encouraging the quantity of stool [37]. In a 2020 study, fifty-four albino rats were fed on 10 percent flaxseed oil and 10 percent sesame oil in their diet collectively. The results concluded marked improvements in decreasing rats' weight, improving lipid profile and decreasing subcutaneous fat [42]. Sesame seeds are stacked with lignans that encourage cell reinforcement action in our body and help in better ingestion of lipolysis. Sesame seeds help in curing PCOS [43]. The herbal extract of sesame helped in regulating the blood glucose level and also help in weight loss [7].

| Seed Name                                       | Research Finding   |
|---|--|
| Flax seed [44-46]                               | Decreases menopausal symptoms, Increased quality of life   |
| Flaxseed oil [47,48]                            | Increase in the level of estrogen, progesterone and calcium. May alter the level of these endogenous sex hormones.                 |
| Flaxseed Oil [49,50]                            | 60 mg per day of 7-hydroxymatarezinol balance the level of estrogen. Improves levels of sex hormones, insulin, dylipidimia and BMI |
| Flaxseed and spearmint combination extract [51] | Improved levels of dehydroepiandrosterone, estrogen, progesterone and testosterone   |
| Sesame seed [52-54]                             | Effective alternative to initiate menses and control heavy bleeding cycles, dysmonnorhea, lowers BMI                               |
| Sesame seed oil [55]                            | Inhibition of testosterone and restoration of follicular development in ovarian tissue. Decreases hirsutism                        |
| Pumpkin and flaxseed mixture [56]               | Boost in MUFA and PUFA, anti-atherosclerotic activity  |
| Pumpkin seed [57-59]                            | Reduce hot flashes, joint pain and headaches, improve HDL cholesterol levels, anti-oxidative                                       |
| Pumpkin seed oil [60]                           | Hypoglycemic effect  |
| Sunflower and sesame seeds [61]                 | Balance the progesterone and estrogen in the body  |
| Mixture of pumpkin, sunflower and chia [42]     | Decreased levels of testosterone, LDL, triglycerides, insulin and body mass  |

**Table 1:** Literature Review of Included Studies.

## CONCLUSIONS

The studies reinforce that the dietary intervention of seeds at different stages of menstrual cycle can play a pivotal role in diminishing the symptoms of polycystic ovary syndrome. The nutraceutical elements present in the seeds can greatly balance the levels of hormones and reduce weight. Further researches on it will help to strengthen the current knowledge.

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