

**ROLE OF VARIOUS SEEDS IN THE TREATMENT OF POLYCYSTIC OVARIAN SYNDROME (PCOS)**

Jobanpreet Kaur\*, Himani Dhiman, Riya Thakur, Shubham Sharma and Sonia Kaur

G.H.G. Khalsa College of Pharmacy, Gurusar Sadhar (Ludhiana) 141104.

**\*Corresponding Author: Jobanpreet Kaur**

G.H.G. Khalsa College of Pharmacy, Gurusar Sadhar (Ludhiana) 141104.

DOI: <https://doi.org/10.17605/OSF.IO/URJG7>

Article Received on 12/06/2021

Article Revised on 02/07/2021

Article Accepted on 22/07/2021

**ABSTRACT**

The most common endocrine condition in women is polycystic ovarian syndrome (PCOS). The disruption of reproductive and metabolic processes ranges from moderate to serious in clinical manifestation. Some of the more common dermatological symptoms include hirsutism, acne, infertility, and acanthosis nigricans. Women who have these dermatological manifestations should be tested for PCOS. The pathogenesis of PCOS is explained as a rise in luteinizing hormone (LH) secretion due to a change in gonadotropin-releasing hormone secretion. Hyperinsulinemia and insulin tolerance are caused by changes in insulin secretion and behavior. A deficiency in androgen synthesis causes increased ovarian androgen activity. To combat weight gain, healthy lifestyle measures such as calorie restriction, avoidance of high carbohydrate diets, restricted fat consumption, high fibrous diet, and avoidance of junk food are critical. Women who have polycystic ovary syndrome (PCOS) are more likely to have metabolic syndrome, type 2 diabetes, obesity, cardiovascular disease, and endometrial cancer. Herbal medicines, such as various types of natural seeds, are also widely utilized to treat a variety of ailments such as polycystic ovary syndrome and its manifestations, as well as its related signs and symptoms.

**KEYWORDS:** Infertility, Hyperinsulinemia, Endometrial, Hirsutism.**INTRODUCTION**

Anovulation, menstrual difficulties, amenorrhea, hirsutism, and miscarriage are all symptoms of a polycystic ovarian syndrome (PCOS). PCOS is the most frequent ailment among premenopausal and reproductive-age women. PCOS influences androgen synthesis, estrogen production, and androgen formation in women.<sup>[1]</sup> Infertility, also known as Stein Leventhal syndrome, affects approximately 48.5 million women aged 20–44 years<sup>[2]</sup>, with PCOS accounting for 6-15 percent of these cases<sup>[3]</sup>, although up to 70% of women with PCOS may go undiagnosed.<sup>[4]</sup> Despite the lack of definitive proof, scientists believe that a high level of androgens and endogenous hormones might be to blame for PCOS.<sup>[5]</sup> PCOS patients have about double the amount of testosterone as most women, and they are often insulin-resistant.<sup>[6]</sup> According to research, metabolic problems linked with PCOS include insulin resistance, dyslipidemia, obesity, Type 2 diabetes, cardiovascular disease, oxidative stress, and hereditary issues.<sup>[7-9]</sup> Hyperandrogenism and increased luteinizing hormone levels hinder ovarian development, resulting in premature granulosa cell luteinization and meiosis. As a consequence, the growth of antral follicles is halted, and oocyte formation suffers.<sup>[10,11]</sup> Mild PCOS is associated with regular ovulation and hyperandrogenism. When progesterone biosynthesis is disrupted and follicular estrogen is produced, this can lead to full-blown

PCOS.<sup>[12]</sup> Women with PCOS are currently treated using a range of methods, including nutritional modifications and pharmacological treatments. A change in lifestyle is linked to diet, weight loss, and exercise. Pharmacological therapies include antiandrogens (spironolactone, flutamide), hypoglycemic medicines (metformin and thiazolidinediones), and estrogen-progestin combos (oral contraceptives). Though successful, such therapy is costly and can have several side effects, including increased insulin tolerance, extended menstruation, gastrointestinal problems, and weight gain.<sup>[13,14]</sup> As a result, successful treatments based on natural products with fewer side effects are required.<sup>[15]</sup>

**PATHOGENESIS**

PCOS is characterized by high levels of luteinizing hormone (LH) and an LH: FSH ratio greater than two. Androgen activity increases in response to high LH levels (in theca cells of the ovary). Increased frequency of hypothalamic gonadotrophin-releasing hormone (GnRH) pulses is believed to be the cause of this rise in LH secretion.

**Hyperinsulinemia and Insulin Resistance:** Obese and non-obese PCOS women have greater rates of insulin resistance and hyperinsulinemia than age-matched monitors, and obese PCOS women have significantly lower insulin sensitivity than non-obese PCOS women.

According to studies, 30% to 40% of women with PCOS have reduced glucose tolerance, and a similar number experience type 2 diabetes by the age of 40.<sup>[16,17]</sup> Insulin has been shown to increase ovarian androgen production in both healthy and PCOS individuals. Insulin stimulates androgen synthesis specifically by binding to the insulin-like growth factor -I (IGF1) receptor on the ovary. IGF-I and IGF-II all improve hirsute reaction, alopecia, and acne, and IGF1 stimulated 5alpha reductase activity leads to the increased hirsute response, alopecia, and acne. IGF-II stimulates the synthesis of androgen by theca cells in response to LH.<sup>[18]</sup>

**Excess of Androgen:** The rise in LH, along with hyperinsulinemia, causes the ovary's theca cells to produce more androgen. The increased ovarian enzymatic activity involved in the synthesis of testosterone precursors is the key factor behind the rise in testosterone in PCOS.<sup>[19]</sup>

## SIGN & SYMPTOMS

**Dermatological Features:** Androgen levels above a certain threshold are linked to a variety of dermatological symptoms.<sup>[20,21]</sup> These signs and symptoms, such as oligo-ovulation, hyperandrogenism (hirsutism, male trait balding, acne, Acanthosis nigricans), obesity, hypertension, and dyslipidemia, may aid in the identification of PCOS.

**Menstrual Disorders:** Menstrual conditions can range from no menstruation (amenorrhea) to menstruation postponed for 35 days or longer (oligomenorrhea) to severe bleeding (menorrhagia). 91% of women with irregular menstrual periods have PCOS.<sup>[22]</sup>

**Acne:** Acne is one of the cutaneous forms of PCOS, so it's necessary to distinguish it from acne vulgaris, which affects almost 80% of teenagers and usually goes away by the third decade of life.<sup>[23]</sup> Acne manifests itself clinically by four pathological events: follicular canal hyperkeratosis, sebaceous hypersecretion, bacterial proliferation, and inflammation. Chronic hyperandrogenism increases sebum secretion, resulting in a fat accumulation and overlapping bacterial infection. Acne affects about one-third of PCOS patients<sup>[24]</sup>, and PCOS affects the majority of women with serious acne.<sup>[25]</sup> It's defined as females' excessive development of terminal hairs in androgen-dependent regions, with a distribution comparable to males.

It is a symptom of hyperandrogenism. According to various surveys, the prevalence of hirsutism in PCOS ranged from 50% to 89 percent.<sup>[26-28]</sup> For clinical assessment, the Ferriman-Gallwey score is often used, and a score of more than 8 is considered diagnostic.<sup>[29]</sup> Furthermore, hyperinsulinism leads to an increase in adrenal androgen secretion in PCOS patients by increasing the exposure to the hormone ACTH.<sup>[30]</sup>

**Acanthosis nigricans:** Acanthosis nigricans may

indicate a more severe health issue, such as pre-diabetes or PCOS.<sup>[31]</sup> It's a mucocutaneous lesion with hyperpigmentation and a dark brown hue, as well as thickening of the skin. It is distinguished by brown velvety oily, verrucous hyperpigmentation of the skin, which is most often found on the back of the neck and intertriginous areas such as armpits and groynes, under the breasts, and in thighs. Just 5% of women with PCOS have been confirmed to have it.<sup>[32]</sup>

**Infertility:** In women with PCOS, chronic anovulation is the most common cause of infertility. However, patients with normo-ovulatory yet subfertile<sup>[33]</sup> and frequent pregnancy failure were shown to have a higher frequency of polycystic ovary presentation on ultrasound.<sup>[34]</sup> Subfertility can be linked to a rise in LH plasma levels during the follicular process of the cycle, which allows the oocyte's second meiotic division to resume and the oocyte to be released prematurely.<sup>[35]</sup>

## DISEASES LINKED WITH PCOS

The metabolic syndrome is more common in women with PCOS. A metabolic syndrome is a collection of illnesses that often occur together and increase the risk of type 2 diabetes and cardiovascular disease.

It includes high blood pressure, abdominal obesity, and high blood cholesterol.<sup>[36]</sup> Women with PCOS have between four and seven times an increased risk of developing prediabetes and type 2 diabetes than women without PCOS. PCOS women are more likely to acquire diabetes during pregnancy (gestational diabetes). This risk increases if you are overweight when pregnant.<sup>[37]</sup>

Women with PCOS are believed to have a greater chance of heart failure or stroke in the future. Although being overweight can increase these risks, they tend to be increased in PCOS even though obesity is not a factor.<sup>[38]</sup> Chronic anovulation (a lack of eggs produced daily) results in a lack of menstruation or uterine lining shedding (endometrium). If this occurs, the endometrium will thicken, increasing the likelihood of irregular cells developing into cancerous cells as a woman ages.<sup>[39]</sup>

## NATURAL REMEDIES FOR THE TREATMENT OF PCOS

**Flax Seeds:** *Linum usitatissimum*, the botanical name for flax, has long been used as a medicine to treat a variety of ailments. Flax seeds are claimed to contain the largest dietary lignan content, with secoisolariciresinol diglucoside (SDG) being the most prevalent lignin.<sup>[40]</sup> Excess testosterone, which is considered to have a role in PCOS pathophysiology, appears to be suppressed by lignans.<sup>[41,42]</sup> Flaxseed supplementation (30 g/day) affected hormonal levels in a 31-year-old woman with PCOS, according to a report. The patient ingested 83 percent of the flaxseed dosage over the course of four months. After four months of follow-up, BMI, cholesterol, gross serum testosterone, and free serum testosterone levels all fell considerably according to

measurements of height and weight and fasting blood tests obtained at baseline and four months later. At the end of the study, the patient also registered a drop in hirsutism. This case study identified a clinically meaningful drop in androgen levels with a concomitant decline in hirsutism.<sup>[43]</sup>

**Pumpkin Seeds:** Pumpkin seeds are rich in omega-3 fatty acids, which can help balance high cholesterol and insulin levels associated with PCOS. They also include  $\beta$ -sitosterol, which can help to suppress excess androgens and relieve PCOS symptoms including hirsutism, acne, and weight gain.<sup>[44]</sup> Androgenic alopecia (hair loss) is due to zinc deficiency.<sup>[45]</sup> It can also aid in the treatment of androgenic alopecia by blocking testosterone from being converted to dihydrotestosterone, or DHT.<sup>[46]</sup>

**Sesame Seeds:** Sesame seeds have a high content of the plant sterols sesamin and sesamol, which tend to lower cholesterol in PCOS.<sup>[47]</sup> Sesame seeds are high in nutrients that are useful to PCOS sufferers. Its balanced fats aid in blood glucose regulation. Calcium, magnesium, and zinc are among the minerals contained in them.<sup>[48]</sup> Lignans, phytosterol, vitamin B1, B6, calcium, and magnesium are all beneficial to hormonal equilibrium. Sesame seeds, with their high zinc content, serve as hormone regulators and enhancers, assisting ovulation in women and alleviating menstrual symptoms. Besides, sesamin has been shown to shield the liver from oxidative stress.<sup>[49]</sup>

**Chia Seeds:** Chia seeds have been shown to lower blood pressure and heart disease, can help regulate blood sugar levels in type 2 diabetes<sup>[50]</sup>, and are an anti-inflammatory that protects against autoimmune diseases and cancer according to reports.<sup>[51]</sup> Chia seeds have also been shown in rats to inhibit or normalize insulin resistance, which is a problem for women with PCOS.<sup>[52]</sup> It has a high protein content of over 20% and a high omega-3 fatty acid content of 60%. Chia seeds increase testosterone levels and help to boost the consistency of eggs produced by the ovary, resulting in increased fertility. Take 1 teaspoon of chia seeds into your morning cereal.

**Sunflower seeds:** These are high in magnesium and selenium and contain a lot of vitamin E, which helps to promote progesterone development. Sunflower seeds have a high content of cholesterol-lowering plant sterols, making them good for your heart. Sunflower seeds aid in the energization of the body as well as the regulation of hormonal equilibrium.<sup>[53]</sup>

**Fenugreek Seeds:** Swarop et al., used fenugreek seed in an open-label, one-arm, non-randomized post-marketing surveillance analysis. *Trigonella foenum-graecum* is the botanical name for fenugreek. It was investigated for its effectiveness in the treatment of PCOS. The sample included 50 premenopausal women with PCOS who were between the ages of 18-45 and had a BMI of less

than 42. The analysis aimed to see whether *Trigonella foenum-graecum* seed extract could reduce ovarian volume and ovarian cysts.

The researchers discovered that fenugreek seed extract reduced ovarian volume and the number of ovarian cysts. Fenugreek saponins and flavonoids enhance insulin-mediated glucose metabolism, insulin sensitivity, and hormone regulation, as well as lowering cholesterol. Menstrual intervals became more frequent as a result of that. It also boosted the levels of luteinizing hormone and follicle-stimulating hormone. A Fenugreek seed extract has been shown to help women suffering from PCOS symptoms.<sup>[54]</sup>

### ROLE OF DIET IN PCOS

Recent research has shown that the new health supplement myoinositol can help improve fertility by enhancing insulin sensitivity. Its natural sources are citrus fruits, beans nuts, legumes, sprouts, and grains like oats and bran.<sup>[55]</sup> Spinach and other green leafy vegetables are high in nutrients and low in calories. They're still a good source of vitamin B. Furthermore, greater than 60% of PCOS patients are Vitamin B deficient. This vitamin deficiency has been attributed to PCOS symptoms including irregular hours, rapid hair growth, and obesity. Fresh leafy vegetables such as spinach, cabbage greens, kale, broccoli, and other green leafy vegetables are recommended.<sup>[56]</sup>

Vitamin D alters anti-müllerian hormone (AMH) signaling, follicle-stimulating hormone sensitivity, and progesterone synthesis in human granulosa cells, and thereby plays a physiologic function in reproduction, including ovarian follicular growth and luteinization. PCOS is associated with nutritional deficiencies. Menstrual irregularity and insulin resistance have been linked to vitamin D supplementation.<sup>[57]</sup> Consume whole grains, low-GI foods, and low-calorie foods such as barley, barnyard millet, Job's tear, and Kodo millet. These awned grains have fewer carbohydrates and more dietary fibers, which aid in weight management. More advanced low carbohydrate ketogenic diets have been documented to dramatically reduce weight, LH/FSH ratio, testosterone, fasting insulin, and insulin tolerance, according to research performed by C.L. Harrison et al.<sup>[58,59]</sup> Avoid fast food because its metabolism disrupts carbohydrate metabolism, causing Advanced Glycation End Products (AGE) to develop, which are cytotoxic and kill ovarian cells, altering their functional aspects.<sup>[60]</sup>

### CONCLUSION

An ovarian cyst is a disease that is becoming more frequent these days. Infertility, menstrual irregularities, obesity, puberty, and hirsutism are all symptoms of PCOS. Nature has provided us with a plethora of herbal therapies for ovarian cysts that can be used in conjunction with other treatments in both benign and malignant cases. Overall, further study into this complicated disorder is needed. Scientists are working to

learn more about this condition, which is characterized by an imbalance of male hormones, ovulation, and cyst formation.

## REFERENCES

- Patelanuradha Jitendra, Thakor Akanksha Pravin. Prospective use of Tephrosia Purpurea in Remedial Treatment of PCOS: Study in Wistar Rat. ISCA J. Biological Sci., 2012; 1(3): 1-6.
- M. N. Mascarenhas, S. R. Flaxman, T. Boerma, S. Vanderpoel, and G. A. Stevens, "National, regional, and global trends in infertility prevalence since 1990: a systematic analysis of 277 health surveys," PLoS Medicine, 2012; 9: 12, Article ID e1001356.
- B.C.J.M. Fauser, B.C.Tarlatzis, R.W.Rebaretal., "Consensus on women's health aspects of polycystic ovary syndrome (PCOS): the Amsterdam ESHRE/ASRM- sponsored 3rd PCOS consensus workshop group," Fertility and Sterility, 2012; 97(1): 28.e25–38.e25.
- J. Boyle and H. J. Teede, "Polycystic ovary syndrome—an update," Australian Family Physician, 2012; 41(10): 752–756.
- Rosenfield RL, Ehrmann DA. The pathogenesis of polycystic ovary syndrome (PCOS): the hypothesis of PCOS as functional ovarian hyperandrogenism revisited. Endocr Rev., 2016; 37(5): 467-520.
- Kamel HH. Role of phyto-oestrogens in ovulation induction in women with polycystic ovarian syndrome. Europ J Obstet, 2009; 168: 60-63.
- Faghfoori Z, Fazelian S, Shadnoush M, Goodarzi R. Nutritional management in women with polycystic ovary syndrome: a review study. Diabetes Metab, 2017; 11(1): S429-S432.
- Apter D. Endocrine and metabolic abnormalities in adolescents with a PCOS-like condition: consequences for adult reproduction. Trends Endocrinol Metabol, 1998; 9(2): 58-61.
- Chatterjee B, Suri J, Suri JC, Mittal P, Adhikari T. Impact of sleep-disordered breathing on metabolic dysfunctions in patients with polycystic ovary syndrome. Sleep Med, 2014; 15(12): 1547-1553.
- Ajmal N, Khan SZ, Shaikh R. Polycystic ovary syndrome (PCOS) and genetic predisposition: a review article. Eur J Obstet Gynecol Reprod Biol, 2019; 3: 100060.
- Minanni SL, Marcondes JAM, Wajchenberg BL, Ana MC, Fortes MAHZ, Rego MA, Vezozzo DP, Robard D, Giannella- Neto D. Analysis of gonadotropin pulsatility in hirsute women with normal menstrual cycles and in women with polycystic ovary syndrome. Fertil Steril, 1999; 71(4): 675-683.
- Leo VD, Musacchio MC, Cappelli V, Massaro MG, Morgante G, Petraglia F. Genetic hormonal and metabolic aspects of PCOS: an update. Reprod Biol Endocrinol, 2016; 14(38): 27423183.
- Jang M, Lee MJ, Lee JM, Bae CS, Kim SH, Ryu JH. Oriental Medicine Kyung-Ok- Ko Prevents and Alleviates Dehydroepiandrosterone-Induced Polycystic Ovarian Syndrome in Rats. Plos one, 2014; 9: 2-13.
- Bates GW, Legro RS. Longterm management of polycystic ovarian syndrome (PCOS). Mol Cell Endocrinol, 2013; 373: 91-97.
- Ramachandran S, Sanjay AS, Dhanaraju MD. Antiamnesic effect of Piracetam potentiated with Emblica officinalis and Curcuma longa in aluminium induced neurotoxicity of Alzheimer disease. Int J Adv Res., 2013; 1: 185-196.
- Ehrmann DA. Medical progress: Polycystic ovary syndrome. J Engl J Med, 2005; 352: 1223-36.
- Tsilchorozidon T, Overton C, Conway GS: The Pathophysiology of polycystic ovary syndrome. Clin Endocrinol (Oxf), 2004; 60: 1-17.
- Third report of the national cholesterol education program expert panel on detection, evaluation and treatment of high blood cholesterol in adults (Adult Treatment panel III) final report. Circulation, 2002; 106: 3143-421.
- Hill KM; Update the pathogenesis and treatment of PCOS. Nurse Pract, 2003; 28: 8-25.
- Keen, Mohammad Abid; Shah, Iffat Hassan; Sheikh, Gousia. Cutaneous Manifestations of Polycystic Ovary Syndrome: A Cross-Sectional Clinical Study, 2017; 8(2): 104-110.
- Zhao, Xiaomiao; Ni, Renmin; Li, Lin ; Mo, Yaqin ; Huang, Jia; Azziz, Ricardo; Yang, Dongzi. Defining hirsutism in Chinese women: a cross-sectional study, 2011 Sep; 96(3): 792-6.
- Joham, Anju E; Teede, Helena J; Ranasinha, Sanjeeva; Zoungas, Sophia; Boyle, Jacqueline. Prevalence of infertility and use of fertility treatment in women with polycystic ovary syndrome: data from a large community-based cohort study, 2015 Apr; 24(4): 299-307.
- Simpson NB, Cunliffe WJ. Disorders of the sebaceous glands. In: Burns T, Breathnach S, Cox N, Griffiths C, editors. Rook's Text Book of Dermatology. 7th ed. Oxford: Blackwell Science, 2004; 1-75.
- Balen A, Conway G, et al. Polycystic ovary syndrome: the spectrum of the disorder in 1741 patients. Hum Repr., 1995; 10: 2107-2111.
- Eden JA. The polycystic ovarian syndrome presenting as resistant acne successfully treated with cyproterone acetate. Med J Australia, 1991; 155: 677-680.
- Chang WY, Knochenhauer ES, Bartolucci AA, Azziz R. Phenotypic spectrum of polycystic ovary syndrome: Clinical and biochemical characterization of the three major clinical subgroups. Fertil Steril, 2005; 83: 1717-23.
- Azziz R, Woods KS, Reyna R, Key TJ, Knochenhauer ES, Yildiz BO. The prevalence and features of the polycystic ovary syndrome in an unselected population. J Clin Endocrinol Metab, 2004; 89: 2745-9.
- Saxena P, Prakash A, Nigam A, Mishra A.

- Polycystic ovarian syndrome: Is obesity a sine qua non? A clinical, hormonal and metabolic assessment in relation to body mass index. *Indian J Endocrinol Metab*, 2012; 16: 996-9.
29. Ferriman D, Gallwey JD. Clinical assessment of body hair growth in women. *JC Endoc Metab*, 1961; 21: 1440-1447.
  30. Lanzone A, Fulghesu, et al. Differential androgen response to adrenocorticotrophic hormone stimulation in polycystic ovarian syndrome: relationship with insulin secretion. *Fertil Steril*, 1992; 58: 296-301.
  31. Gruber DM, Berger UE, Sator MO, Horak F, Huber JC: Computerized assessment of facial hair growth. *Fertil Steril*, 1999; 72: 737-9.
  32. Araujo LM, Porto MV, Netto EM, Ursich MJ. Association of acanthosis nigricans with race and metabolic disturbances in obese women. *Braz J Med Biol Res.*, 2002; 35: 59-64.
  33. Eden JA. The polycystic ovary syndrome. *Aust NZJ Obstet Gynecol*, 1989; 29(4): 403-416.
  34. Sagle M, Bishop K, et al. Recurrent early miscarriage and polycystic ovaries. *BMJ.*, 1988; 297: 1027-1028.
  35. Homburg R, Armar NA, et al. Influence of serum luteinising hormone concentration on ovulation, conception, and early pregnancy loss in polycystic ovary syndrome. *BMJ*, 1988; 297: 1024-1026.
  36. Ehrmann D et al: Prevalence and predictors of the metabolic syndrome in women with polycystic ovary syndrome. *J Clin Endocrinol Metab*, 2006; 91(1): 48-53.
  37. Meyer C et al: Overweight women with polycystic ovary syndrome have evidence of subclinical cardiovascular disease. *J Clin Endocrinol Metab*, 2005; 90(10): 5711-6.
  38. McCartney CR, Marshall JC: Polycystic Ovary Syndrome. *N Engl J Med*, 2016; 375: 54-64.
  39. Chittenden BG, Fullerton G, Maheshwari A, Bhattacharya S: Polycystic ovary syndrome and the risk of gynaecological cancer: a systematic review, Published by 398-RBM Online, UK, 2009: 398-405.
  40. Thompson LU. Flaxseed, lignans and cancer. In: Cunnane SC, Thompson LU, editors. *Flaxseed in human nutrition*. Chicago, IL: AOCS Press, 1995; 219-236.
  41. Johnsson Pernilla, *Bioactive Phytochemicals in Flaxseed with Particular Emphasis on the Secoisolariciresinol Oligomer [Doctoral Thesis]* Swedish University of Agricultural Sciences, Uppsala, 2009.
  42. Nowak Debra A., Denise C, Snyder, Ann J. Brown and Wendy Demark-Wahnefried, The effect of flaxseed supplementation on hormonal levels associated with polycystic ovarian syndrome: a case study. *Curr Top Nutraceutical Res*. Author manuscript; available in PMC, 5(4), 2007.
  43. Tilburt JC, Kaptchuk TJ. *Bulletin of the World Health Organization*. 86<sup>th</sup> ed., 2008: 594-599.
  44. Reddy SP, Nazia B, Sumith M, Bakshi V. Beneficial effect of Curcumin in Letrozole induced polycystic ovary syndrome, *Asian Pac J Repr.*, 2016; 5(2): 116-122.
  45. Aiempanakit K, Jandee S, Chiratikarnwong K, Chuaprapaisilp T, Auepemkiate S. Low plasma zinc levels in androgenetic alopecia. *Indian J Dermatol Venereol Leprol*, 2017; 83(6): 741. doi:10.4103/ijdv.IJDVL\_680\_16
  46. Upadhyay K, Gupta NK, Dixit VK. Development and characterization of phyto-vesicles of  $\beta$ -sitosterol for the treatment of androgenetic alopecia. *Arch Dermatol Res.*, 2012; 304(7): 511-519. doi:10.1007/s00403-011-1199-8.
  47. Michailidis D, Angelis A, Aligiannis N, Mitakou S, Skaltsounis L. Recovery of sesamin, sesamol, and minor lignans from sesame oil using solid support-free liquid-liquid extraction and chromatography techniques and evaluation of their enzymatic inhibition properties. *Front Pharmacol*, 2019; 10: 723. doi:10.3389/fphar.2019.00723.
  48. Khanage, Shantaram Gajanan; Subhash, Tarkasband Yogita; Bhaiyyasaheb, Inamdar Rahat. HERBAL DRUGS FOR THE TREATMENT OF POLYCYSTIC OVARY SYNDROME (PCOS) AND ITS COMPLICATIONS. 2019.
  49. Sirato-Yasumoto S, Katsuta M, Okuyama Y, Takahashi Y, Ide T. Effect of sesame seeds rich in sesamin and sesamol on fatty acid oxidation in rat liver. *J Agric Food Chem*, 2001; 49(5): 2647-2651.
  50. V. Vuksan et al. 2007. Supplementation of Conventional Therapy with the Novel Grain Salba (*Salvia hispanica* L.) Improves Major and Emerging Cardiovascular Risk Factors in Type 2 Diabetes: Results of a Randomized Controlled Trial. *Diabetes Care*, 30(11): 2804-10.
  51. N.Ali et al. 2012. The Promising Future of Chia, *Salvia hispanica* L. *Journal of Biomedicine and Biotechnology*. Article ID 171956.
  52. A.G. Chicco et al. 2008. Dietary Chia Seed (*Salvia hispanica* L.) Rich in Alpha-linolenic Acid Improves Adiposity and Normalises Hypertriaclyglycerolaemia and Insulin Resistance in Dyslipaemic Rats. *British Journal of Nutrition*, 101(1): 41-50.
  53. Minhas, Sonia; Srivastava, Rachana; Khanna, Poonam. Polycystic ovary syndrome (PCOS) is a commonly found hormonal ailment in Reproductive age women triggering irregular menstrual cycles, excessive body / facial hair, miscarriage, infertility, baldness, acne, high-level androgens (male hormone), pelvic pain, high anxiety and depression. Here are some seeds which have been found to help in relieving symptoms of PCOS. Nov 2017.
  54. Swaroop A, Jaipuria AS, Gupta SK, Bagchi M, Kumar P. Efficacy of a Novel Fenugreek Seed Extract (*Trigonella foenum-graecum*, Furocyst TM) in Polycystic Ovary Syndrome (PCOS). *International Journal of Medical Science*, 2015.
  55. Gerli S, Mignosa M, Di Renzo GC. Effects of inositol on ovarian functions and metabolic factors in women with PCOS: A randomized double-blind

- placebo- controlled trial. *Eur Rev Med Pharmacol Sci.*, 2003; 7(6): 151-15.
56. Kajal A, Gaikwad, Rutuja; Dewaikar, Vd. Surekha. **ROLE OF DIET IN PCOS (LIFE STYLE DISORDER)**, 2019; 145-151.
  57. Irani M, Merhi Z. Role of vitamin D in ovarian physiology and its implication in reproduction: a systematic review. *Fertil Steril*, 2014; 102: 460–8.e3.
  58. Charak, Charak Samhita, English translation Editor Prof. Priyvrat Sharma vol. 1 Chaukhamba Oriental, 2014. Sutrasthan Chapter 21/20, p. 146.
  59. J.C. Mavropoulous, W. S. Yancy, J.Hepburn, and E.C.Weshman. “The effects of a low carbohydrate, ketogenic diet on polycystic ovarian syndrome: A pilot study.” *Nutrition and Metabolism*, vol. 2, article 35, 2005.
  60. E. Diamanti-Kandarakis, C. Piperi, P. Karkolopoulour et. al. Accumulation of dietary glycotoxins in reproductive system of normal female rats. *Journal of Molecular Medicine*, 2007; 85(12): 1413-1420.