

## Efficacy Studies of Fenugreek Seeds Against Polycystic Ovarian Syndrome

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### Abstract

*Polycystic Ovarian Syndrome also called Stein-Leventhal Syndrome or chronic oligoanovulation is a condition related to hormonal imbalance that can cause menstrual disorders like oligomenorrhea or amenorrhea, infertility, hirsutism, obesity, suffering from prompt increase in weight or having trouble in losing weight and other symptoms in type two diabetes, oily skin, and acne. Most of the cases of PCOS are reported in 20s and 30s with complain of difficulty in becoming pregnant. According to the study, frequency of PCOS in the infertility clinics in Pakistan was 17.6%. In this study Fenugreek (Trigonellafoenum-graecum) was investigated to treat PCOD. The plant was also subjected to different physico-chemical and nutraceutical estimations. The present study is single blind randomized controlled trial in 90 premenopausal women diagnosed with PCOS using fenugreek seed powder, over a period of 90 consecutive days. During the course of study, the subjects were counseled about diet and exercise and were regularly monitored for any associated side effects related to the administration of fenugreek seed powder. Vital clinical estimations in the human subjects were carried out at the start of study and by the end of trail i.e. at day 90. Clinical estimations involved evaluation of BMI, FSH, LH, ovarian size, menstrual regularity and FBG. Overall results revealed that the prolong administration of raw fenugreek seeds in women having PCOS was particularly found effective. Intake of fenugreek seeds for three months had positive effect on regularity of menstrual cycle, maturation of eggs, reducing ovarian volume and infertility.*

**Keywords:** Polycystic Ovaries, Fenugreek, Infertility, Ovarian Size, Menstrual irregularities.

### Introduction

Polycystic Ovarian Syndrome also called Stein-Leventhal Syndrome or chronic oligoanovulation is a condition related to hormonal imbalance that can cause infertility. Normally ovarian follicles release a developed egg but in case of PCOS instead of releasing a developed egg, the underdeveloped egg gets trapped that leads to cyst formation inside the swelling follicle (Legge and Ambassador, 2017). Many studies have been done to determine the prevalence of PCOS throughout world. Even using same diagnostic criteria, great variation has been seen in results because of differences in population under study, limitation within sampling, protocols applied and lack of standardized definitions for the phenotype. Most of the cases of PCOS are reported in 20s and 30s with the complain of difficulty in becoming pregnant. According to study, frequency of PCOS in the infertility clinics in Pakistan was 17.6% (Hussein and Alalaf, 2013). The symptoms of PCOS include menstrual disorders like oligomenorrhea or amenorrhea, hirsutism, obesity, suffering from prompt increase in weight or having trouble in losing weight and other symptoms in type two diabetes, oily skin, acne, difficulty becoming pregnant. Psychosocial problems can also result from having PCOS.

Historically fenugreek has been used in Chinese and Ayurvedic medicine. The application involved several medical conditions like indigestion, labor induction, immune booster (Mullaicharam *et al.*, 2013). Preliminary animal and human trials propose possible hypoglycemic, antiplasmodiac, anticarcinogenic, anti-hyperlipidemic, prevent hair loss, antinociceptive, helps losing weight (Moradikor and Moradi, 2013)

and gastro protective properties of fenugreek seeds. Because of fenugreek's estrogen content and its ability to stimulate the uterus, it should be avoided during pregnancy.

## **Material and methods**

### **Experiment no 1**

Fresh fenugreek seeds were obtained from the commercial source from the local market of Rawalpindi and shifted to the Institute of Food and Nutritional Sciences PMAS Arid Agriculture University Rawalpindi. Following investigations were carried out in the central laboratory of institute.

#### **Moisture content**

According to Method No. 925.45, moisture content of fenugreek seed powder was measured as described in (AOAC, 2000).

#### **Ash content**

Method No. 940.26, as described in (AOAC, 2000) was used to calculate ash content in fenugreek seed powder.

#### **Total fiber content**

By following the Method 920.86, as described in (AOAC, 2000) fenugreek seed powder samples were tested after fat extraction for crude fiber content.

#### **Total protein content**

Kjeldhal apparatus was used to determine the nitrogen percentage in fenugreek seeds by using method of (AOAC, 2000).

#### **Total fat content**

For crude fat determination was done as explained in (AOAC, 2000).

#### **Mineral estimation**

The mineral contents in fenugreek were determined as described by AOAC (1999) method no. 923-07. The mineral contents will be estimated by using an Atomic Absorption Spectrophotometer (GBC-932 Australia).

#### **Total phenolic content**

Total phenolic contents (TPC) in terms of gallic acid (mg) will be determined by Folin-Ciocalteu (FC) assay as described by Beretta *et al.*, 2005.

#### **Radical scavenging activity**

Radical scavenging activity of methanolic extracts was determined spectrophotometrically at 517 nm against 2,2-diphenyl-1-picrylhydrazyl (DPPH) radical as described by Beretta *et al.*, 2005.

### **Experiment no 2**

#### **Study population**

Patients having PCOS (n=130) were screened according to selected inclusion exclusion criteria for the clinical trial. Among them 104 patients fulfilled required criterion and 90 subjects properly followed the treatment plan. The study protocol was approved by the ethical committee of Military Hospital Rawalpindi. Every patient provided properly signed consent forms with enough information to make an informed decision about their participation in this research. Diagnosis of PCOS was made on the basis of

Rotterdam criteria and selected inclusion exclusion criterion. Inclusion criteria will be premenopausal women between 18-45 years of age,  $BMI \leq 35$ , average renal functions, and patients agreeable to give conversant consent. Exclusion criteria will be women having menopause, patients with hysterectomy, women having congenital adrenal hyperplasia, women having Cushing's syndrome, women having diagnosed androgen secreting tumors, patients having thyroid dysfunction, patients with hypogonadotropic and hypo-gonadism, pregnant women. All of the subjects involved in clinical trial were confirmed about the absence of kidney, liver or heart disease along with the absence of pregnancy.

### **Preparation of fenugreek powder**

Fresh and dried fenugreek seeds (15kg) were obtained from the commercial source and shifted to the Institute of Food and Nutritional Sciences. Fenugreek seeds were thoroughly washed, dried and then grounded to fine powder. This fine powder was packed in bottles. Each bottle weighed 150 gm.

### **Study design**

This randomized control blind study was based upon human beings for 90 days. Levels of treatment were randomized, and with an active-control trial in 3 parallel groups having PCOS. Along with the oral administration of fenugreek powder patients were counselled regarding modifications in their diet and lifestyle. Selection of subjects was done on the basis of inclusion exclusion criteria and Rotterdam criteria. Patients meeting the eligibility criteria were placed in three groups by lottery method. Three groups were made i.e. control group ( $T_1$ ) who received medication (diane-35/primollet-N, metformin/Glucophage), experimental group 2 who received fenugreek powder (5gm) and experimental group 2 to whom 10gm of fenugreek powder was administered. There were thirty patients in each group.

### **Assessment of efficacy**

Laboratory investigations including serum FSH and serum LH were done at baseline, at the end of 1 month, at the end of 2 month and by the end of 3 month. Whereas BMI (Basal Metabolic Index), ultrasonographic scan and FBG (Fasting Blood Glucose levels) were done at baseline and by the end of study. Improvement in menstrual cycle disorders i.e. oligo/amenorrhea was defined as change in cycle frequency or decrease in cycle length or occurrence of pregnancy.

### **Statistical analysis**

Data collected in the first experiment was analysed through one-way anova. Data obtained in the second experiment was subjected to Completely Randomized Design (CRD) in two factor factorials. Means were compared by LSD using statistical software Statistix 8.1 as described by Steel *et al.*, (1997).

## **Results**

### **Experiment no 1**

**Moisture Content:** The moisture content of fenugreek seeds (mean  $\pm$  SD) is  $5.56 \pm 0.41\%$  in the present study.

**Ash Content:** In present study, ash content determined in 100g of raw fenugreek is  $4.32 \pm 0.23\%$ .

**Total fiber Content:** In this study, mean values for crude fiber in 100g of raw fenugreek seed is  $5.76 \pm 0.30\%$ .

**Total protein Content:** According to present study, crude protein in 100g of raw fenugreek seeds is  $30.5 \pm 0.18\%$ .

**Total fat Content:** The average fat content of 100g of raw fenugreek seeds in this study is  $4.26 \pm 0.47\%$ .

**Mineral Estimation:** In current research study, minerals like phosphorus, calcium and iron were identified.  $70.5 \pm 0.68$  mg/g of calcium,  $544.5 \pm 1.26$  mg/g of phosphorus and  $11.6 \pm 0.59$  mg/g of iron was found in seed powder.

**Total Phenolic Content:** Total Phenolic Contents (TPC) of raw fenugreek sample was estimated in the range of  $45.4 \pm 0.02$  (GAE/100 g ( $p < 0.05$ )).

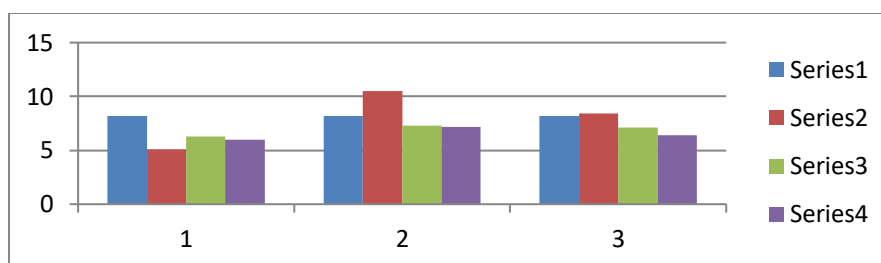
**Radical Scavenging Activity:** The Radical Scavenging Activity (RSA) by using DPPH radical in the raw fenugreek seeds samples was estimated as  $20.1 \pm 0.70$  ( $p < 0.05$ )

## Experiment no 2

### Effect on follicle stimulating hormone

Following graphical representation shows change in FSH levels. No significant difference was observed in control and experimental groups on completion of treatment as compared to baseline.

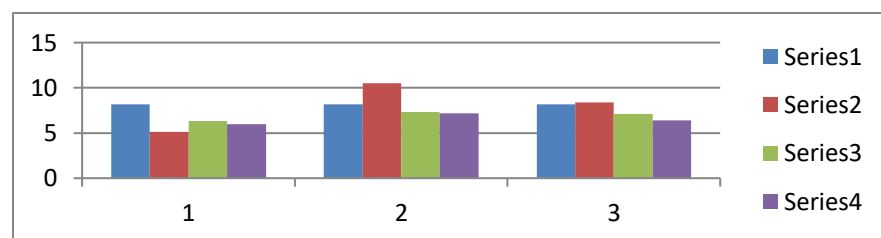
Figure 1:



### Effect on luteinizing hormone

Following graphical representation shows change in LH levels. LH levels were decreased in controlled as well as experimental groups. However, decrease in controlled group was more than the experimental groups i.e. T<sub>2</sub> and T<sub>3</sub>. After control group desired effect was noticed in the mean value of experimental group 3.

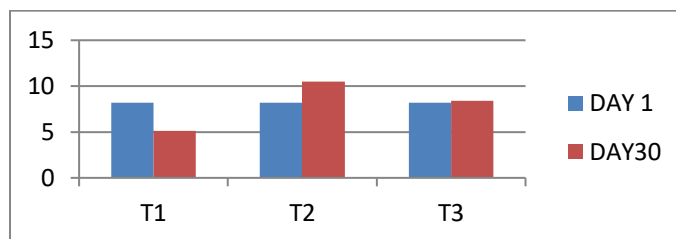
Figure: 2



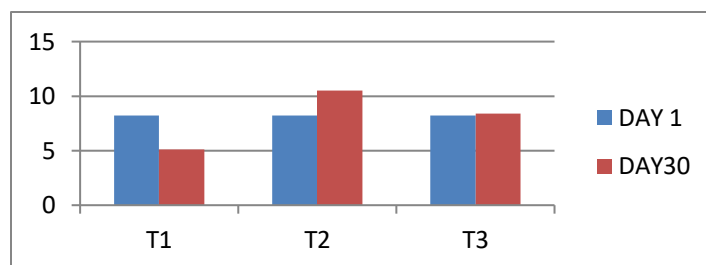
### Changes in ovarian volume

Following graphical representation shows change in ovarian volume (fig 3: left ovary and fig 4: right ovary). By the end of study significant reduction in ovarian volume was noticed in all the three groups. In relation to left ovary, highest effect was noticed in control group and regarding right ovary great effect was noticed in the ovarian volume of subjects in experimental group 3.

**Figure: 3**



**Figure: 4**



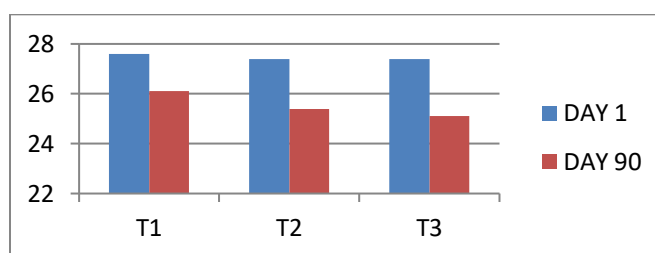
### **Effect on menstrual regularity**

By the end of study 80% patients of controlled group secured normal cycle. In experimental group2, 60%patients had normal whereas in experimental group3 93.3% patients secured the normal menstrual cycle.

### **Effect on BMI**

Following graphical representation shows change in BMI levels. Slight difference in the mean values was observed in all groups by the end of 90 days treatment plan.

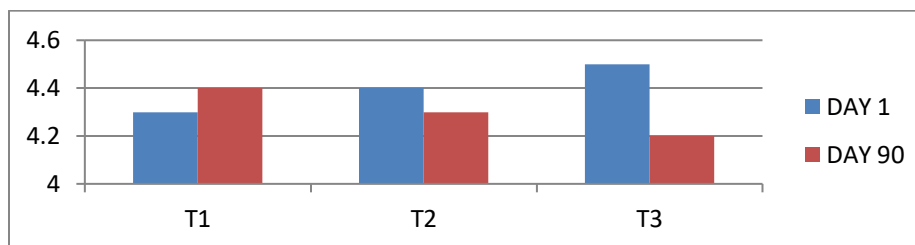
**Figure: 5**



### **Effect on fasting blood glucose**

Following graphical representation shows change in FBG levels. According to results there is no marked difference between the mean values of control group (4.3-4.4) experimental group 2 (4.4-4.4) and experimental group 3 (4.5-4.3) at day 1 and day 90.

Figure: 6



## Discussion

First experiment was based upon the investigation of compositional characteristics of fenugreek seeds. Compositional analysis revealed that fenugreek seeds contain considerable amount of protein and fiber. Mineral estimation of seeds was shown to be rich source of phosphorus and iron. Antioxidant activity was measured by total phenolic content in terms of Gallic acid and radical scavenging activity.

Second experiment was a randomized control blind study was based upon female subjects for 90 days. Levels of treatment were randomized, and with an active-control trial in 3 parallel groups having PCOS. Patients meeting the eligibility criteria were placed in three groups by lottery method. Total 130 patients having PCOS were screened according to selected inclusion exclusion criteria. Among them 103 patients met the required criterion. 2 patients using 10gm of fenugreek seed powder became pregnant during the course of study. Treatment amiability was good and most of the subjects did not record any adverse effects regarding fenugreek seed powder use.

Regarding BMI results for whole groups presented shows slight difference in all groups because diet remained same throughout the study period with slight modification, so not much difference in all group were seen. High BMI leads towards obesity which is the major cause of insulin resistance and patients having pcso are prone to have insulin resistance. Polycystic ovaries have more capacity of causing insulin resistance then obesity (Cresswell *et al.*, 2003).

There was no significant difference found in the levels of FSH among the experimental groups, however slight modification was observed in control group. Our results regarding FSH are in agreement with Bashtiana *et al* 2013. Swaroop *et al* demonstrates the effects of fenugreek seed extract on LH and FSH for the period of three months. After giving fenugreek extract for the duration of three months noticed remarkable increase in LH levels on completion of the Furocyst treatment in comparison to baseline and noteworthy increase in follicle stimulating hormone was also observed at the completion of study. Marked decrease in ovarian volume is also documented with zero toxic effects of fenugreek usage.

Concerning luteinizing hormone overall results showed decrease in LH in the entire group that is a good sign for the treatment of PCOS. Increment of the dosage of fenugreek from 10gm may show better results. LH levels are increased in PCOS. One possible clarification for this may be premature activation of LH-induced mitotic arrest, the process that occur at the mid cycle LH surge. Hypersecretion of LH and insulin are important features of PCOS.

In relation to ovarian volume, mean of ovarian volume is  $4.9 \pm 0.03 \text{ cm}^3$  in premenopausal females and  $2.5 \pm 0.01 \text{ cm}^3$  in postmenopausal females (Pavlik *et al.*, 2000). Extract obtained from fenugreek seeds in combination with metformin didn't had authentic effect on insulin resistance but extract of fenugreek seed along with metformin gave promising results in women with pcos by improving their sonographic results and menstrual cyclicity (Bashtiana *et al.*, 2013).

Improvement in menstrual cyclicity and ovulatory function was observed in all groups. Whereas, best results were observed in experimental group using 10mg of fenugreek powder in which 93.3% of patients secured regular menstrual cycle. Our results are in agreement with Bashtiana *et al* (2013). Van Hoff *et al* (2000) in his study declared that in adolescents PCOS is mostly present in association with irregular menstrual cycle, oligomenorrhea or increased levels of androgen and LHD.

PCOS is frequently linked with insulin resistance and defects in insulin secretion. In PCOS insulin resistance is not only the cause of adrenal and ovarian steroidogenesis, but also release of LH from pituitary gland. (Dunaif 1997). Undue levels of insulin cause ovaries to produce excessive amount of testosterone that in turn causes alopecia, hirsutism and acne. (Kandarakis & Dunaif 2012). Insulin resistance increases the release of LH while disrupting LH:FSH ratio. Reducing insulin resistance can also restore ovulatory menstrual cycles (Dunaif 2008). Generally, about 50% to 70% of patients having PCOS have variable amount of IR. In PCOS patients' risk of type 2 DM is 5- to 10-times higher than usual (Ovalle & Azziz 2002). Medicines, traditional therapies, dietary measures (low carb diet, avoid processed food), exercise and avoiding sedentary lifestyle can help lowering IR.

## Conclusion

Overall results revealed that the prolong administration of raw fenugreek seeds in women having pcos was particularly found effective.

Intake of fenugreek seeds for three months had positive effect on regularity of menstrual cycle, maturation of eggs, reducing ovarian volume and infertility.

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