Impact of Milled Flaxseeds in Elevating the SHBG (Sex Hormone Binding Globulin) Levels among young Women Diagnosed with Polycystic Ovarian Syndrome (PCOS)

Jeyamani Divya Christodoss1, Vasantha Esther Rani2, Parvathi Krishnan3
1Assistant Professor, Loyola College, Chennai, India
2Professor, Fatima College, Madurai, India
3Ph.D Scholar, Loyola College, Chennai, India

Abstract: Upsurge in the labour industry has increased the working population among men and women and this paradigm shift of globalization has posed a challenge for employed parents especially women in almost all modern societies in balancing their lifestyle. Thus research is necessitated in different cultural contexts for enhancing the productivity of women by improving their physical, emotional and social wellbeing. Women at their reproductive age are more prone to hormonal disorders and the most common endocrine disorder among women in their reproductive age is polycystic ovarian syndrome (PCOS) characterized by obesity, hyperinsulinemia, hirsutism and increased levels of androgen. The aforementioned factors can be attributed to lifestyle ailments such as obesity, depression, diabetes and hypertension especially for women in the age group of 21-52 years. In women of Indian subcontinent, prevalence rates of PCOS are as high as 50% and are responsible for 18% of infertility and metabolic syndrome was diagnosed in 46% of women with PCOS. Healthy lifestyle must be adopted to combat these diseases with a proper balanced diet, physical activity and by giving due respect to the biological clock. Flaxseed containing health-promoting phytochemicals, fibre components such as lignan and omega-3 fatty acids is one of the new super foods recently discovered as an ideal botanical agent to manage PCOS symptoms along with reducing cholesterol, cardiovascular diseases, obesity, diabetics and high blood pressure. In this project, the investigator analyses the efficacy of delivering the goodness of flaxseed rich in lignan and essential fatty acid Alpha Linolenic Acid (ALA) in a suitable food matrix desirable for efficient absorption in the blood stream in order to elevate the serum levels of Sex Hormone Binding Globulin (SHBG) which in turn facilitates to lower the free circulating testosterone levels and thus normalising the clinical symptoms associated with PCOS conditions.

Keywords: Flaxseed, Polycystic Ovarian Syndrome, Metabolic syndrome, SHBG, Androgens, Intervention Studies

INTRODUCTION

Increased globalization has made women to play a pivotal role in the society and their health status determines their productivity at home and at work and the nation at large. Polycystic ovarian syndrome (PCOS) is a hormonal imbalance disorder that affects around one out of 10 women and is characterized by obesity, hyperinsulinemia, hirsutism, increased levels of androgen. The most important contributing factor to PCOS can be attributed to lifestyle ailments such as obesity, depression, diabetes and hypertension of women in the age bracket of 21-52 years. Healthy dietary habits and lifestyle modifications must be adopted to combat these disorders with a balanced diet in addition to nutraceutical formulations and increased physical activity giving due respect to biological clock.

PCOS was first described by Stein and Leventhal in 1935 with significant clinical implications like menstrual irregularities, hirsutism, infertility, with suboptimal obstetrical outcome and long term complications like impaired glucose tolerance, diabetes mellitus type 2, dyslipidaemia, coronary artery disease and endometrial hyperplasia [1]. It is the most frequent cause of hyperandrogenism and oligo ovulation which have substantial psychological, social and economic consequences.

Medical management emphasizes and advocates a strong multidisciplinary approach as pharmaceutical treatments appear to be moderately or minimally effective in treating individual symptoms. At the same time conventional pharmaceutical management is limited by the prevalence of contraindications in
women with PCOS due to the non-effectiveness in some circumstances, side effects and preferences of women with PCOS for alternatives to pharmaceutical management. A potential alternative treatment such as natural functional foods and herbal medicine remedies explains the reproductive endocrinological effects in PCOS and associated oligo/amenorrhoea and hyperandrogenism.

Prevalence of PCOS among adult women
PCOS being a complex and a common cause of reproductive and endocrine disorder impacts almost 20% of women in the reproductive age. Polycystic ovary syndrome (PCOS) is a heterogeneous endocrine disorder that affects about 6%-8% women worldwide. In women of Indian subcontinent, prevalence rates of PCOS are as high as 50% have been detected. It is responsible for 18% of infertility and 40% of hirsutism cases in a study conducted at Srinagar. Women diagnosed as having PCOS before pregnancy have an increased risk of developing gestational diabetes [1]. The exact prevalence of PCOS is not known as the syndrome is not defined precisely. The estimated prevalence in women of reproductive age is 5-10%. Under the new criteria Rotterdam-2003, the prevalence among the general female population will raise up to 10%. [2].

Prevalence of PCOS among adolescent girls
Adolescence is an important phase in the life cycle of women with a transition from childhood to adulthood necessitating a lot of physical, intellectual and emotional upheaval, rapid body growth causes them anxiety and cultural pressures of today’s world add further stress to their uncertainty. PCOS diagnosed among adolescent girls have been found to manifest dermatological effects having deleterious effect on an adolescent’s self-image and peer interaction also other metabolic abnormalities leading to weight gain and menstrual uncertainties affect body image causing further stress including the family members of the affected individual [3].

Treatment modality for PCOS
The study of diet in the treatment of PCOS has focused on weight reduction since roughly half of women with PCOS are obese, and weight loss is helpful in normalizing hormonal levels and clinical symptoms[4][5][6]. While other components of the diet have been suggested as potentially beneficial in ameliorating the hormonal disequilibrium associated with PCOS, beyond weight management the current dietary recommendations provided for this disease parallel those established for the general population, i.e., a low fat, moderate protein diet with increased amounts of fruits, vegetables, and whole grains [7]. However, over the past few decades, high fiber diets have been shown to influence the hormonal milieu [8], and may hold promise in the treatment of PCOS. Previous research suggests that consumption of high lignan foods may cause binding of testosterone in the enterohepatic circulation and subsequent excretion [9].

Flaxseed
Flax (Linum usitatissimum) belonging to family Linaceae, is a blue flowering annual herb producing small flat seeds which vary in their colour from golden yellow to reddish brown color and it also possesses crispy texture and nutty taste. Flaxseed is considered as functional food owing to the presence of three main bioactive components- alpha-linolenic acid, lignans and dietary fiber [10].

Flaxseed lignan and its role in PCOS
Lignan a dietary fibre has been found to increase levels of sex hormone binding globulin and thus reduce the amount of free circulating testosterone [9, 11], though such a reduction has not been observed in all studies [12]. Lignan also may hinder the production of 5 α-reductase, the enzyme responsible for converting testosterone into dihydrotestosterone; the more biologically active and potent form [13]. Also it was found that high lignan diets may be protective against prostate cancer, another disorder which is linked to high androgen levels [14]. Prior studies on the use of isolated lignan (flaxseed) suggest that it may decrease androgen levels and normalize lipid levels; however, most of this research has been conducted in male subjects [9, 15-17]. Currently, there is only one case study which has reported a clinically significant decrease in androgen levels with a concomitant decrease in hirsutism demonstrating a need for further research of flaxseed supplementation on hormonal levels and clinical symptoms thus helping to regulate androgen levels in women with PCOS in addition to other pertinent metabolic parameters [18].

Chemical nature of Lignans
Lignans, very complex classes of bioactive polyphenolic phyto-chemicals, formed by the coupling of two coniferyl alcohol residues are widely distributed in the plant kingdom. There are two general types of lignans: i) those found in plant seeds like secoisolariciresinol diglucoside (SDG), isolariciresinol, matairesinol, lariciresinol and ii) those found in animals and humans known as mammalian lignans[19]. Phenolic lignans are found in most fiber-rich plants and flaxseed is particularly the richest known source of lignans (9–30 mg per g), with lignan production at 75–800 times that of other oil seeds, cereals, legumes, and fruit and vegetables [20].

The principal dietary lignan present in flaxseed is SDG which occurs as a component of a linear ester-linked complex. Chemically, the C6-OH of the glucose of SDG is esterified to the carboxylic acid of

Available online at http://saspublisher.com/sajb/
hydroxymethylglutaric acid. Accumulation of SDG is coherent with LuPLR gene expression and synthesis of PLR enzyme during mature seed development [21]. The biological activity of SDG results from their conversion to the mammalian lignans enterolactone (EL) and enterodiol (ED) by the intestinal microflora in the upper part of the large bowel. The mammalian lignans differ from plant lignans in that mammalian lignans have the hydroxyl groups in the meta position while plant lignans have the oxygenated substituents primarily in the para positions [22]. Mammalian lignan production from intake of whole or milled flaxseed supplemented baked products is dependent on time and dose but not on processing. The processed flaxseed supplemented muffin or bread did not affect the quantity of lignan excretion in women which reflect stability and bioavailability of plant and mammalian lignans in human biological metabolism [23].

MATERIAL AND METHODS
This was a randomized single blinded controlled clinical trial conducted among young women in the age group age group of 21 – 35 years in the metro of Chennai. The objective of the study was to evaluate the efficacy of the lignan rich milled flaxseed in elevating the serum hormonal levels such as SHBG (Sex hormone binding globulin) which has been proven to reduce the amount of free circulating testosterone along with metabolic parameters such as serum glucose and serum cholesterol levels among the same population. Subjects who agreed to participate were not statistically different from non-participants with regard to age, weight, BMI and gender. The two groups assigned for the study were similar in all observed variables after randomization (computer generated). The study protocol was approved by the Independent Ethics Committee (IEC), Ethica Norma and all participants provided signed informed consents. Participants for the study with PCOS were diagnosed using Rotterdam criteria in the age group of 21 – 35 years in the metro of Chennai. According to the Rotterdam criteria any two of the following symptoms were used for inclusion of the subjects, that is, irregular periods 8 -9 cycles / year, signs of hyperandrogenism (hirsutism -FG score greater than 8, serum testosterone levels > 180 ng/dl) and polycystic ovaries in the ultrasound. The experimental group (12 participants) receiving milled flaxcrackers (30g) and control group (12 participants) receiving wheat crackers were assigned and the supplementation of 30g dosage was administered for duration of 4 months. Biochemical levels for serum SHBG, glucose and cholesterol were assessed before and after supplementation of the flax crackers. Descriptive statistics like frequency and percentage would be used to identify the sample characteristics and the mean pre-test and post-test score difference would be compared by applying ‘t’ test.

RESULTS AND DISCUSSION
The serum glucose, cholesterol and SHBG (Sex Hormone Binding Globulin) levels before and after supplementation of milled flaxseed crackers are represented in the graph and table below:

Fig-1: Pre and Post supplementation of flax crackers on the serum levels of glucose and cholesterol

Available online at http://saspublisher.com/sajb/
Diabetes is a metabolic syndrome and is characterized by increases in central adiposity, serum triglycerides, serum glucose, blood pressure, inflammation and decreases in HDL-cholesterol that elevates risk of insulin resistance [24]. The animal and human studies revealed that high fat diet containing 0.5 to 1.0 % SDG reduces liver triglycerides content, serum triglycerides, total cholesterol, and insulin and leptin concentrations that resulted in significantly reduced visceral fat gain as com-pared to group of mice receiving high fat diet without SDG [25]. Another study have shown that female rats receiving glucosuria induced diet with SDG have 80 % less chances of glucosuria as compared to rats have 100 % chances of glucosuria receiving diet without SDG [26] ( Prasad K, 2001). SDG reduces C-reactive protein concentrations which are associated with insulin resistance and diabetes mellitus in type 2 diabetics [27]. Daily consumption of low-fat muffin enriched with SDG (500 mg/day) for 6 week can reduce CRP concentrations [27]. The earlier studies indicate that flaxseed lignan supplements have beneficial associations with C-reactive protein and also suggest that lignans have possible lipid- and blood pressure-lowering associations [28].

However a study conducted on individuals with well-controlled diabetes were consistent with the findings of the present study and showed that taking milled flaxseed and flaxseed oil supplement had no effect on glycemic control [29]. Another work conducted work on diabetic people and observed that omega-3 supplementation had no effect of omega-3 on glycemic control was observed [30]. It was also reported that flaxseed oil supplementation had no effect on glycemic control in diabetic patients [31]. However, despite lack of change in fasting blood glucose and insulin concentration after supplementation with flaxseed there has been an improvement in long-term glycemic control in diabetic patients [32].

From this current study it has been observed that on a diet with flaxcrackers made with milled flaxseeds for a period of four months among young women diagnosed with PCOS according to the Rotterdam criteria there is seen a 10.4% increase in the blood glucose levels and a 2.3% increase in the total blood cholesterol levels after the four months supplementation period .However there is has been an increase though not significant in the serum SHBG levels which is promising for a long term supplementation. However, it is observed that on a diet with flaxcrackers made with milled flaxseeds for a period of four months there is a considerable increase of 12.06% in the serum SHBG levels before and after supplementation though not significant at 5 % level of confidence. These results are promising for a long term supplementation of flaxcrackers with more stringent lifestyle modifications and dietary compliance coupled with moderate physical activity. The control group on
wheat crackers showed no significant changes in the serum levels of glucose, cholesterol and SHBG levels and also in comparison with the group on flaxcrackers.

CONCLUSION

Polycystic Ovary Syndrome (PCOS), a metabolic malady and the cause of all lifestyle disorders in women is a common endocrine abnormality in women of reproductive age and the prevalence is 4 – 8% among the vulnerable group as estimated. The incidence and prevalence of PCOS is on the increase globally and is galloping with the rising prevalence of metabolic disorders such as type 2 diabetes and obesity. According to various investigations and clinical trials in PCOS, to date, the study of diet in the treatment of PCOS has focused mainly on weight reduction since roughly half of women with PCOS are obese and weight loss is found to be helpful in normalizing hormonal levels and clinical symptoms related to this disorder. In addition to the omega 3 content (ALA) content, lignan as the dietary fiber present in flaxseed acts as an antioxidant to reduce the androgen levels and helps to normalize the lipid levels in the body. Young women in this generation are more dependent on fast food due to lack of time leading to imbalanced diet, inadequate physical exercise and sleeping quality leading to a sedentary life style coupled with stress and emotional strain to the individual. Improving the health status of women in order to increase their productivity at home and at work and creating awareness of an epidemic of dietary and lifestyle disorders leading to various health complications among working women professionals is the need of the hour. Polycystic ovarian syndrome (PCOS) is one of the most common endocrine disorders in adolescent and adult women, and importantly has both reproductive and metabolic consequences, additionally women with clinical features of PCOS have an increased risk of cardiovascular events and death. In women of Indian subcontinent, prevalence rates of PCOS are as high as 50% and are responsible for 18% of infertility and metabolic syndrome was diagnosed in 46% of women with PCOS. All the above mentioned factors thus open up new avenues to scientifically explore and improve the lifestyle and productivity of the women who make major contributions to the society and to complement these changes flaxseed is a promising functional food with its high lignan content that can have a significant impact on the metabolic and hormonal levels on consuming for a longer duration.

REFERENCES


30. Rastmanesh. Effects of Fish Oil on Cytokines, Glycemic Control, Blood Pressure, and Serum Lipids in Patients with Type 2 Diabetes Mellitus J Obes Weight Loss Ther. 2013, 3.
