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REVEALING THERAPEUTIC POTENTIAL OF SIDDHA FORMULATION SOOTHAGA CHOORANAM IN POLYCYSTIC OVARIAN SYNDROME MODEL IN WISTAR RATS

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ABSTRACT

Polycystic ovary syndrome (PCOS) is a complicated metabolic–endocrine condition that affects between 4% and 18% of reproductive-age women. There is uncertainty about the genetic propensity to PCOS, and no genetic screening test has been validated. Anovulation, menstrual irregularity, amenorrhea, hirsutism, and infertility are all symptoms of PCOS. At the moment, the most often used treatment method is the administration of drugs such as clomiphenecitrate, metformin, and tamoxifen. Despite of the clinical efficacy aforementioned class of drugs reveals potential side effects, hence women's use of herbal treatments has grown in recent years, and it has been proven to be connected with a decrease in infertility concerns. Herbal medicine research can give much-needed knowledge regarding efficacy and safety, which can then be communicated to the clinical setting and utilised to educate patients. Such study should seek to bridge gaps in existing understanding. The main objective of the present investigation is to evaluate the efficacy of the siddha formulation Soothaga Chooranam (SC) in the management of dehydroepiandrosterone (DHEA) induced PCOS model in rats Dehydroepiandrosterone (DHEA) induced PCOS model in rodents is a well explored screening technique for ascertaining efficacy of the test drug in rodents. It was evident from result analysis of the present investigation that the weight of ovary sample belongs to group II rats shown progressive increase when compare to group I. Treatment with SC at both the dose level shown marginal decrease in the weight of the ovaries. From the immunoassay analysis it was predicted that FSH level of group II rats shown pronounced decrease when compare to control group I. Treatment with SC to group III and IV at the dose of 250 and 500 mg/kg shown viable increase in the level of FSH hormone. LH level haven’t shown wide variation between the control and treatment group rats. It was concluded from the data’s of the present study that the formulation SC alleviates the DHEA induced hormonal stress and also improves the FSH level, hence may be considered for clinical management of PCOS in hospital setup.

KEY WORDS: ***PCOS, Siddha, Soothaga Chooranam, DHEA, FSH, Metformin***

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1. Introduction

Polycystic ovary syndrome (PCOS), the most common hormonal illness in women of reproductive age, is a complex endocrine and metabolic disorder that manifests as irregular menstrual periods, dyslipidemia, excessive body weight, oxidative stress, hyperandrogenism, and infertility [1, 2]. PCOS affects between 5% and 10% of reproductive-age women and 40% of those afflicted experience infertility, making it the most common cause of anovulatory infertility [3]. Normal ovarian function is disrupted in women with PCOS primarily by hyperandrogenism and high levels of luteinizing hormone (LH) [4], resulting in numerous cysts [5]. PCOS increased the frequency of gonadotropin-releasing hormone (GnRH) pulses, favoring LH synthesis over follicle stimulating hormone (FSH) production [6]. This increase in LH stimulates androgen synthesis in the theca cells, but a relative FSH shortage affects the granulosa cells' capacity to convert androgen to estrogen, impairing follicle development and ovulation [7].

Chemical and hormonal PCOS therapy are linked with a variety of adverse effects, including hyperplasia, uterine bleeding, and unknown hazards [8], as well as a high cost [9]. Nonetheless, these medicines may be ineffective in some circumstances. As a result, some research are examining complementary herbal therapy as a possible treatment for PCOS [10].

Herbal supplements containing bioactive phytochemicals may be discovered to provide anti-inflammatory, antioxidant, and fertility-stimulating activities [11]. It increases sex potential and pregnancy rate in sheep by directly stimulating progesterone production. It has been shown to treat hormonal imbalances, the primary cause of anovulation and uterine growth problems [12,13].

Siddha treatments make use of a wide range of ingredients, including herbs, minerals, metals, animal products, and even seaweed. The siddha guidelines govern the cleansing, detoxification, processing, and quality means of manufacturing siddha medications. Each formulation contains hundreds of possible phytotherapeutics that may exhibit positive pharmacological action in the biological system. Soothaga Chooranam (SC) is one such potential siddha formulation comprises of unique blend of herbal ingredients that are indicated for the management of metabolic and hormonal. The main objective of the present investigation is to evaluate the efficacy of the siddha formulation SC in the management of dehydroepiandrosterone (DHEA) induced PCOS mode in rats.

2. Materials and Methods

2.1. Animals

Healthy female adult Wistar albino rats of weighing between 200-220 g were used for the study. The animals were housed in poly propylene cages and were kept in well ventilated with 100% fresh air by air handling unit. A 12 light / dark cycle were maintained. Room temperature was maintained between 22 ¬+ 2o C and relative humidity 50–65%. They were provided with food (Sai feeds, Bangalore, India) and water ad libitum. All the animals were acclimatized to the laboratory for 7 days prior to the start of the study. The experimental protocol was approved by The Institutional Animal Ethics Committee of Sathyabama Institute of science and technology, Chennai, Tamil Nadu, India. SU/CLATR/IAEC/XVII/177/2021

2.2. Experimental Methodology [14-17]

Animals were checked two weeks for regular cycles by smear test. Adult wistar female rats were randomly divided into four groups of six animals each: Control (group I), PCOS (group II), and experimental groups (group III & IV). The control group rats received sesame (s.c, 0.2 ml) as a solvent. PCOS in rat induced by subcutaneous injection of dehydroepiandrosterone (DHEA) at the dose of 6 mg/100 g body weight, dissolved in 0.2 mL of sesame oil for up to 20 days. After induction, rats displayed several salient features of PCOS including menstrual dysfunction and polycystic ovaries. Induction of PCOS will be ascertained by consistent estrus cycle in rats. PCOS induced experimental rats of groups III and IV received 250 and 500 mg/kg doses of test drug SC for the period of four weeks. Efficacy of test drug which reverse the cycle back to the normal will be taken as an endpoint.

2.3. Sample Collection [18]

At the end of the study, before sacrifice, the animals were fasted for overnight with free access to water. Animals were sacrificed with excess anesthesia. Blood samples were collected from retro orbital and cardiac puncture and then hormone estimation were carried out by using Cobas e411 immuno assay analyzer.

2.4. Histopathology [19]

Ovaries from the experimental rats were dissected out and fixed in 10% buffered neutral formal saline and processed. After fixation, tissues were embedded in paraffin. Fixed tissues were cut at 10 µm and stained with hematoxylin and eosin. The sections were examined under light microscope for histological changes.

3. Results

3.1. Effect of Effect of SC on serum hormone level(s)

From the result analysis of the present investigation it was clear that the weight of ovary sample belongs to group II rats shown progressive increase when compare to group I. Treatment with SC at both the dose level shown marginal decrease in the weight of the ovaries. From the immunoassay analysis it was predicted that FSH level of group II rats shown pronounced decrease when compare to control group I. Treatment with SC to group III and IV at the dose of 250 and 500 mg/kg shown viable increase in the level of FSH hormone. LH level haven't shown wide variation between the control and treatment group rats. As shown in Table 1.

Table 1: Effect of Effect of SC on serum hormone level(s)

Group	FSH (mIU/ml)	LH (mIU/ml)	Ovary Weight (mgs)
Control	8.35 ± 0.27	6.58 ± 0.33	119.2 ± 3.72
PCOS	2.083 ± 0.07**	6.183 ± 0.19	188.8 ± 1.79**
PCOS + 250 mg/kg SC	2.717 ± 0.10*	6.383 ± 0.19*	163.7 ± 3.49
PCOS + 500 mg/kg SC	3.517 ± 0.22	6.283 ± 0.22*	138 ± 4.98**

Values represent mean ± SEM of 6 experimental animals. * P< 0.05; ** P< 0.01; *** P < 0.001.

3.2. Effect of SC on histopathology of rat ovary

Histopathological analysis of ovary sample belongs to group I showing normal Corpora lutea (CL), atretic follicles (AF) and interstitial tissue (IT) appears normal. Significant increase the number of follicles at varying stages and corpus luteum with numerous signs of proliferation were observed in sample belongs to group II. Treatment with SC at the dose of 250 mg/kg (group III) and 500 mg/kg (group IV) has significantly reduced the follicle number further restored the histology of corpus luteum almost similar to that of the normal control rats. As shown in Figure 1.

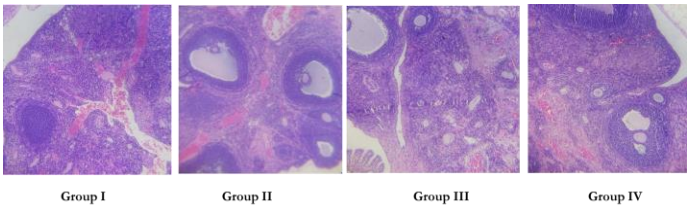

Figure 1: Effect of SC on histopathology of rat ovary

4. Discussion

PCOS is one of the most prevalent endocrine diseases in women [20]. PCOS is caused by dysfunctions in the hypothalamic-pituitary axis and insulin activity [21].The long-term effects of this condition include increased androgens and obesity, insulin resistance and type 2 diabetes, and oxidative stress [22,23]. Alteration of antioxidant systems may result in pathological effects such as PCOS and disruption of ovarian steroid production in women [24]. In these individuals, decreased gonadotropin production is coupled with increased luteinizing hormone (LH) secretion relative to follicle-stimulating hormone (FSH) [25]. Numerous medicinal therapies are available for PCOS, although the most of them are just transitory in nature. Given the adverse effects of these medications, it is critical to identify and provide substitute medications [26].

Although the specific etiology of PCOS is unknown, it appears that genetic and environmental variables play critical roles in its development [27]. In general, four risk factors have been identified for PCOS: (a) aberrant ovarian morphology [28], (b) ovarian androgen overproduction [29], (c) a functional malfunction in the hypothalamic-pituitary axis with increased LH/FSH secretion [30], and (d) insulin resistance and hyperinsulinemia [31]. Hyperandrogenism, insulin resistance, and hyperinsulinemia are all factors that contribute to metabolic alterations and clinical symptoms in individuals with PCOS [32]. Complementary and alternative medicine are frequently used to prevent, regulate, and lessen the consequences of PCOS [33].

DHEA induced PCOS model in rodents is a well explored screening technique for ascertaining efficacy of the test drug. DHEA increased the expression of proinflammatory factors (TNF-α, IL-1β, and IFN-γ) in the ovarian and uterine tissues. The pathology of DHEA in rodent typically resembles to that of the PCOS in women [34]. From the result analysis of the

present investigation it was clear that the weight of ovary sample belongs to group II rats shown progressive increase when compare to group I. Treatment with SC at both the dose level shown marginal decrease in the weight of the ovaries. From the immunoassay analysis it was predicted that FSH level of group II rats shown pronounced decrease when compare to control group I. Treatment with SC to group III and IV at the dose of 250 and 500 mg/kg shown viable increase in the level of FSH hormone. LH level haven't shown wide variation between the control and treatment group rats.

Women with PCOS are predisposed to a range of metabolic syndrome and endocrinological problems, including obesity, insulin resistance, infertility, and miscarriage [35]. Additionally, there is mounting evidence that PCOS is associated with an increased prevalence of thyroid diseases, such as nodular goiter and autoimmune thyroiditis [36].Histopathological analysis of ovary sample belongs to group I showing normal Corpora lutea (CL), atretic follicles (AF) and interstitial tissue (IT) appears normal. Significant increase the number of follicles at varying stages and corpus luteum with numerous signs of proliferation were observed in sample belongs to group II. Treatment with SC at the dose of 250 mg/kg (group III) and 500 mg/kg (group IV) has significantly reduced the follicle number further restored the histology of corpus luteum almost similar to that of the normal control rats.

5.Conclusion

PCOS is classified as a complex condition, and the specific mechanism of its pathophysiology is unknown. This feature of the siddha formulation SC may be a result of the phytocomponents present in the formulation. It was concluded from the data's of the present study that the formulation SC alleviates the DHEA induced hormonal stress and also improves the FSH level, hence may be considered for clinical management of PCOS in hospital setup

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