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RELIABILITY OF SIDDHA SYSTEMS OF MEDICINE ON POLYCYSTIC OVARY SYNDROME WITH SCIENTIFIC JUSTIFICATION - A REVIEW

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ABSTRACT
Polycystic Ovary Syndrome (PCOS) is an ovary syndrome of women and it is mostly affected the younger generations. Every year the rate of affected women's count has been increased. It has been create difficulties on pregnancy and also shows troubles on menstruation, still the exact reasons for PCOS was not clearly known. Although, the allopathic medicines gives a treatment along with lots of side effects but it doesn't shows any notable effectiveness against PCOS. Even though the Indian system of medicines particularly siddha medicines, yoga practices and proper diet control makes remarkable cure against PCOS. This review is mainly focused on combined pathophysiology of PCOS, reliability of Siddha medicines and its scientifical justification of 9 herbal-drugs.

Key words: PCOS, Siddha drugs, Pathophysiology, Medicinal plants

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INTRODUCTION

Polycystic Ovary Syndrome is the common endocrine disorder mostly affecting reproductive age group women (Bassemtalaat, *et al*., 2018). The PCOS was found out during the year of 1935 by stein leventhal (Susanarentz, *et al.*, 2014, Bassemtalaat, *et al*., 2018). It creates physical and mental related problems with women, this disease developed by collective factors

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such as hyperinsulinemia, dyslipidemia, obesity, anovulation, insulin resistance and cystic follicles in ovary (Mohammed Azemuddin, *et al., 2019*, Susanarentz, *et al.*, 2014).

In worldwide 30-40% of women affected by PCOS related with impaired glucose tolerance in later period this condition may leads to type II diabetes mellitus, it affects 6-21% of reproductive age women and 40% of infertile women (Mohammed Azemuddin, *et al., 2019*, Behnaznavid, *et al., 2018).*

A younger women's life is very badly affected by PCOS. The patient with PCOS may experience that hirsutism, acne, obesity, menstrual disturbance, anovulation and infertility (Behnaznavid, *et al., 2018).*

Now-a-days clomiphene citrate is for the primary treatment of hyperestrogen related PCOS problem. It induces the ovulation by its anti-

estrogenic effect. It will act on endometrium and cervical mucus. Although clomiphene citrate produces a lot of side effects, mainly hot flush, breast discomfort, abdominal distention, nervousness, hair loss, headache, disturbed vision (Susanarentz, *et al.,* 2014, Cha-young kwon, *et al., 2020*, Bassemtalaat, *et al*., 2018 , Michael Khirysaleh, *et al.*, 2018, Zahra Abasian, *et al., 2018)*. Metformin has investigated as insulin sensitizing agent. It can develop the risk of multiple follicles along with a risk of multiple pregnancies ect. (Michael Khirysaleh, *et al.*, 2018, Zahra Abasian, *et al., 2018)*. Since, PCOS is defined as a multifaceted metabolic- endocrine disorder. Herbal medicines contain a more number of phytoconstituents those constituents are pharmacologically active. Which produces the pharmacological effects on female endocrine system and it beneficially reduces the incidence of malignancies, osteoporosis and cardiac obstacles. So far recent studies have been focused on herbal medicines mainly Indian system of medicines, it gives impact-able treatment strategies on PCOS (Susanarentz, *et al.*, 2014, Cha-young kwon, *et al., 2020*, Behnaznavid, *et al., 2018)*.

Siddha medicine is one of the oldest medicinal systems of India. It is a mother medicine of Tamil people; the researchers are proving with the available data, the siddha system of medicine is 12000 years old. Thousands of siddha literatures are available in the form of palm leaf manuscript and most of the siddha scriptures are not translating still now but the translated literature gives more knowledge about diagnosis, treatment of various diseases. Most of the people underestimate the Siddha medicine. It cures communicable, non-communicable as well as chronic diseases (Shukla SS, *et al., 2011)*.

METHODS:

All electronic databases were collected up to 2021. This study is mainly focused to elucidate the pharmacological potential of Siddha System of Medicine for the treatment of PCOS by scientific validation. So the official documents were collected through Siddha Books and it was justified with scientific studies.

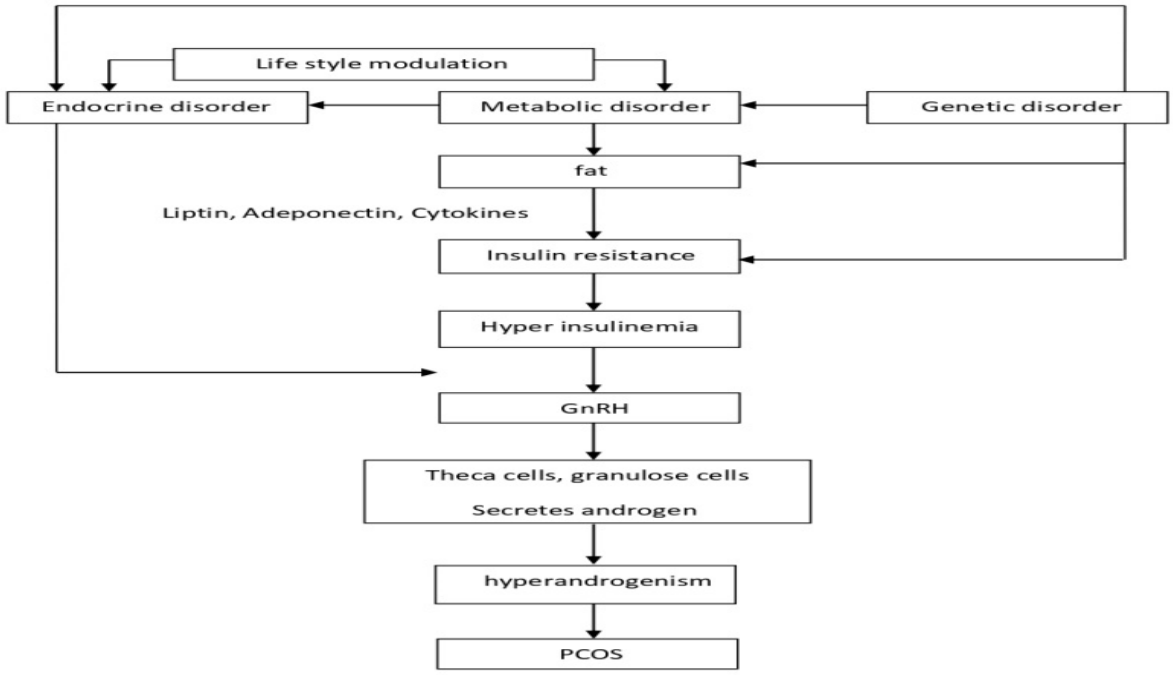
Pathophysiology of PCOS:

The complete pathophysiological mechanism was not clearly known due to complex nature of the disease (Mohammed Azemuddin, *et al., 2019)*. But it is characterized by endocrine, metabolic and genetic disorder (Zahra Abasian, *et al., 2018)*. There is numerous pathophysiological mechanism and theories have been submitted to describe the pathogenesis of PCOS (Mohammed Azemuddin, *et al., 2019)*. The PCOS mainly develops due to changes in endocrine hormones that are increased level of androgen and decreased level of estrogen.

Insulin resistance is considered the main pathological factor in the incidence of metabolic disturbances in women with PCOS. Insulin resistance can occur mainly due to the metabolic disorder of adipose tissue(fat), it produces the synthesis of liptin, adiponectin and cytokines which are mainly impede with insulin signalling pathway, in this case the functions of insulin is lack on body cells due to insensitivity of insulin receptors. So mistakenly the signals again pass to the pancreas to increase the insulin secretion to compensate for its shortage resulting in hyperinsulinemia (Zahra Abasian, *et al., 2018)*.

So the hyperinsulinemia cause the layer event on GnRH frequency which stimulate LH secretion than FSH (Zahra Abasian, *et al., 2018)*. These hormonal changes at surface of the theca cells and granulosa cells leads to increased the secretion of androgen and decrease the secretion of estradiol directly or indirectly that stops the maturation of follicles and disturbs ovulation.Finally, the increased level of androgen production on female reproductive system leads to PCOS possibilities. Genetic factor also can interfere with PCOS (Mohammed Azemuddin, *et al., 2019*). The flow chart given in the figure:1

Figure 1: Pathophysiology flow chart



Clinical Symptoms of PCOS:

PCOS produce many tinny fluid filled cysts in the ovaries, high level of male sex hormones in blood, irregular (or) skipped periods and infertility these are the common symptoms of women with PCOS. Also it creates the other problems that are hirsutism, Acne, alopecia, darkening of skin particularly neck region and headache these are the notable clinical symptoms of PCOS.

Plants used in the Siddha medicine for the treatment of PCOS:

***Gymnema sylvestre* - (Tamil Name: Chirukurinchan**)

G. sylvestre is herb belongs to the family of Apocynaceae, which is widely distributed India, Malaysia, Srilanka and it is commonly used in the treatment of type-I and type-II diabetes mellitus, and also used for reduce blood cholesterol level; reduce body weight, metabolic syndrome, amenorrhea (Ramasubramania Raja R, *et al., 2017)*.

The great Siddhar Agathiyar has written in their literature (Agathiyar gunapadam) explained about one of the uses of *Gymnema sylvestre*.

That is, "Maru uthiram illa matharku" which refers amenorrhea or irregular menstrual cycle. That was scientifically proven by animal studies *G. sylvestre* shows significant reduction in blood glucose level and acts as an insulin sensitivity enhancing agent and also reduces serum androgen level by improving insulin sensitivity. Those activity produced by may be due to the presence of secondary metabolites mainly gymnemic acid, gymnemagenin, gymnestrogenin, stigmasterols (Ramasubramania Raja R, et al., 2017). The plant placed in Figure: 2

***Fumaria parviflora* – (Tamil Name: Thara)**

F. parviflora is annular herb belongs to the family of Fumariaceae, it is widely distributed in Middle East Asia. It has pharmacologically anti-diabetic property, hepatoprotective and anti-microbial activity against several strains particularly for fungal infection candida albicans,it is common infection of women with PCOS (Fateme Kooshki, *et al., 2020)*.

The Siddhar Agathiyar has written in their literature (Agathiyar Gunapadam), describes the uses of *Fumaria parviflora.*

That is "Patruthira chikkalvidum" which refers amenorrhea or irregular menstrual cycle. It was scientifically proven, the protopine alkaloid isolated from ethanolic extract of *F. parviflora* which stimulate rat uterus muscle on *In-vitro* studies. The In-vivo studies shows remarkable estrogen like effect it was confirmed by vaginal smear and uterine weight test finally, it fails to produce progesterone or testosterone like activities (Ali Esmail Al-Snafi, *et al., 2018)*. The plant placed in figure: 3

***Anethum gravieolens* - (Tamil Name: Chathakuppai)**

A.gravieolens is annular herb belongs to the family of umbelliferaceae, it grows in south Asia and

Europe. Commonly it has anti-hyperlipidaemic activity, anti-microbial activity, anti-inflammatory and analgesic activity (Ali esmail al-snafi, *et al., 2014)*.

The Siddhar says about uses of this plant that is "Suthaga kattu neengum" which refers amenorrhea or irregular menstrual cycle.

Scientifically it has proved the benefits of *A.gravieolens*. It improves the condition of type-II diabetic mellitus and metabolic syndrome. Payahoo et al., found that serum insulin level decreasing effect of *A. gravieolens* and significantly reduce blood lipid level and increasing body metabolism. The main factors of PCOS are lack of fat metabolism and insulin resistance that pathological factors can be overcome by the activity of A. gravieolens (Fatemeh Haidari, *et al* ., 2020). The plant placed in figure: 4

***Crocus sativa* - (Tamil Name: Kungumappoo)**

C. sativa is a small herbaceous perennial plant, it belongs to the Iridaceae family, it is widely distributed in Eastern Mediterranean, Asia, and Persia well grown in cool place with higher altitude. Still now 150 phytoconstituent were isolated (Ali Esmail Al-Snafi, *et al., 2016)*, it has three main pharmacologically active principles that are crocin, picrocrocin and safranal. A carotenoid crocin is a rare phytoconstituent in nature, which is responsible for its yellow-orange colour, picrocrocin gives a slight bitter taste, safranal is a volatile compound which gives specific aroma of the plant (Ibtissam Mzabri, *et al., 2019)*.

The great Siddhar Agathiyar has predicted the uses of saffron against PCOS. So, Siddhar Agathiyar wrote in their literature Agathiyar gunapadam.

That is, "maathar karuppai uthirathodangalatrum" and "suthagakattu" which means it will induce the menstruation for women and for the treatment of amenorrhea, irregular menses and dysmenorrhoea. The words of Agathiyar were confirmed by scientific validation. The crocin is an active principle of *crocus sativa* which significantly reduced free testosterone level in serum, FSH, LH and increased serum estrogen level in blood, this study was performed by using Letrazole induced polycystic syndrome on rat model (Yasmin M, *et al.,2019)*. The plant placed in figure: 5

***Citrullus colocynthis* - (Tamil Name: Aartru thumatti)**

C.colocynthis is a trailing perennial herb and it is belongs to the cucurbitaceae family, mostly it is grown in dried region of the world and it is spread all over North Africa, South Europe and whole of Asia. The plant has numerous potential phytoconstituents like cucurbitacines - A, B, C, D, E & L, Cucurbitacin glycosides, colocynthin and colocynthetin these are peculiar chemical constituents of this plant (Mohammad Hossein Barzegar, et al., 2017, Manish Kapoor, *et al., 2020)*.

The great siddhar Therayar says about one of the uses of this plant that is "Suthakathin undaiudaichalonge yothu suthagakattu neengum" in Therayar gunavakadam, which refers amenorrhea and irregular menses.

Here the Siddhar Therayar statement was scientifically proved by *in-vivo* studies. The anti PCOS activity was confirmed by hydroalcoholic extract of citrullus colocynthis using estradiol valerate induced rat model, the final conclusion of this studies were given significant hormonal and follicle development in PCOS and also it decreased the serum concentration of LH, FSH, testosterone, and insulin (Mohammad Hossein Barzegar, *et al*., 2017). The plant placed in figure: 6

***Erythrina variegtata* - (Tamil Name: Kaliyana murukku)**

E.variegata is a tree and it is fast-growing plant and nearly reaches 50-60 feet height, it belongs to the Fabaceae family, it is indigenous to spread all over the world. The plant has wide range of phytoconstituent with potential pharmacological activity. Erythrabyssin-II, dihydrifolinin, octocosylferulate these are unique chemical constituent of this plant (Shalini Karunanithi, *et al*., 2017, Kumar, *et al., 2018)*.

According to Siddha medicine the siddhar describe one of the uses of *E.varegata* on female reproductive system.

That is, "Suthakavali, Paruthauddailaika, Malattunoi neenga" which refers mainly to treat dysmenorrhea, obesity and infertility. The above mentioned clinical symptoms mainly involve in pathogenesis of PCOS.

The above Siddhar statement was confirmed with scientific validation of *E.variegata* for PCOS. It gives combined pharmacological activity against PCOS. the experiment was performed by using Letrozole induced PCOS, the ethanolic extract of *E.variegata* decrease the body weight, total cholesterol, reproductive organ weight and increased HDL level, increased estrogen level, potential anti-oxidant effect and hypoglycemic activity which could be more useful in management of PCOS condition. The plant placed in figure: 7

***Sesamum indicum* - (Tamil Name: Yellu)**

S.indicum is a annular herb belongs to the Pedaliaceae family, generally it is available in white

seed or black seed, it is geographically distributed in India and Africa, it has potential phytoconstituent like omega-6, omega-3, PUFA, linoleic acid and α-linolenic acid which plays an important role in human health (Shantha T.R, *et al,. 2014* , Vijay.R, *et al., 2015)*.

The great Siddhar Agathiyar said that in Agathiyar gunavakadam, about one of the use of *S.indicum* plant. He described that "Uthirathai thallum" [34] which refer immenogogue action of the drug.

The above Siddhar statement was confirmed with scientifical studies; the sesame significantly increases the serum estrogen level and maintains the regular menstruation patient with irregular menses (Maryam Yavari, *et al., 2016*, Farah Jawad Al-Masoudi, *et al., 2019)*. The plant placed in figure: 8

***Ficus religiosa* – (Tamil Name: Arasa maram)**

F.religiosa is a perennial tree, it belongs to Moraceae family, normally, it planted in near road and temple areas; it is widely distributed in south Asia, India, Srilanka and Malaysia. It has numerous phytoconstituent like phytosterols, triterpene alcohol, long chain hydrocarbons and aliphatic alcohols which shows various pharmacological activities (Enit Beena Devanesan, *et al., 2018*, Ali Esmail Al-Snafi, I, et al., 2017).

The siddhar says one of the uses of F.religiosa that is,"Sulagathil undakum kolarugalai pokum" which refers solve the problem with uterus and ovary.

The words of siddhar was justified by scientifical validation, it has potential anti-oxidant capacity. The β-sitosterol – D – glycoside shoes significant anti-hypoglyceamic activity, anti lipideamic activity and it has potential fertility action on female reproductive system (Ali Esmail Al-Snafi, I, et al., 2017). The plant placed in figure:9

***Saraca asoca* – (Tamil Name: Asogamaram)**

S. asoka is a medium size (9 M) evergreen tree and it is belongs to Caesalpiniaceae family, it is distributed in india particularly Himalayas, kashi and lushai hils (Anupam Bisht, *et al.,* 2017), it has wide range of phytoconstituents, the bark contain mainly epicatechin, procyanidine B2, leucocyanidin and epiafzelechin. The leaves contain Quercetin, β sitosterol, gallic acid and ellagic acid. The flowers contain oleic acid, linoleic acid, Palmitic acid and stearic acid (Furkanahmad, *et al.,* 2016).

The siddhar says that "Karuppai kutram neeki balappadum" which refers, cures the diseases related with female reproductive system.

The statement of siddhar was proved with current scientifical investigation; the ethanolic extract of *S.asoca* shows significant action on reducing blood glucose level, lipid level and exhibits estrogen like action on female rats

(Priyanka Kantivan Goswami , *et al.,* 2012, Prerana Shetty, *et al.,* 2020, EllappanThilagam, *et al.,* 2021). The plant placed in figure: 10

Figure 2: Twigs of Gymnema sylvestre.	Figure 3: Fumaria parviflora plant with flowers.
	
Figure 4: Fruits of Anethum graveolens	**Figure 5: Flowers of crocus sativa**

Figure 6:plant and fruit of Citrullus colocynthis

Figure 7: Leaves of Erythrina variegtata

Figure 8: white and black seeds of Sesamum indicum

Figure 9: Leaves of Ficus religiosa

Figure 10: Entire plant of Saraca asoca

CONCLUSION:

In this review mainly discussed about combined Pathophysiology, clinical symptoms of PCOS and scientifically evaluated the reliability of siddha medicine on treatment of PCOS, here totally 09 Siddha drugs were used for scientific justification and that was proved. Finally we concluded that the ancient siddha medicine and siddha scriptures gives a miraculous knowledge about the treatment strategies on PCOS, there are lots of literature still awaiting for translations and scientific validation so researchers should focus on this area.

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Conflicts of interest

There are no conflicts of interest.

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