



Review Article

## A CRITICAL ANALYSIS OF DHATU AND DHATWAGNI DUSHTI IN THE PATHOGENESIS OF POLYCYSTIC OVARIAN SYNDROME

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### ABSTRACT

Menstrual health is integral to women’s reproductive status and well-being. Regular menstrual cycles and normal uterine bleeding are hallmarks of a healthy reproductive system, whereas irregular cycle and abnormal flow often indicate underlying pathology and are considered as disorders of *Artavavaha Srotas*. *Artava* constitutes an essential component of the female reproductive system and is considered the *Upadhatu* of *Rasa Dhatu* which is the first dhatu formed in the process of metabolism. The human body sustains vital endocrinal and metabolic functions through the structural and functional integrity of the *Dhatu*s and their respective *Dhatwagnis* that are influenced by the status of *Jatharagni*. The initial vitiation of *Rasa* and *Rasagni* causes *Artavavaha Srotas dushti* that is mostly seen in cases of females suffering from menstrual disorders. This pathological cascade further contributes to *Uttarottara dhatu dushti*, ultimately manifesting as a wide spectrum of disorders like polycystic ovarian syndrome (PCOS). According to WHO, PCOS affects an estimated 8 to 13% of reproductive-aged women. According to the Rotterdam criteria, PCOS is indicated by the presence of hyperandrogenism, oligo- or anovulation (manifesting as oligomenorrhea or amenorrhea), and/or ultrasound findings showing polycystic ovarian morphology.

### INTRODUCTION

*Rasa dhatu* is the first *dhatu* formed from *Ahara rasa* by the action of *Jatharagni* and is the precursor to subsequent *Dhatu*s. *Jatharagni* performs primary transformation and has significant role in controlling the function of *Dhatu*s and respective *Dhatwagnis* through various process of metabolism. *Rasa dhatwagni* transforms *Rasa dhatu* to *Upadhatu Artava* and *Uttarotara dhatu Rakta*. Any *Dushti* at the level of *Rasavaha srotas* leads to disturbance in the function of *Artava* and *Artavavaha srotas* in turn leading to *Yathochita kala artava adarshana* and *Alpa artava* particularly in *Kshaya awastha*.<sup>[1]</sup> Subsequent *Dushti* of the next dhatu *Rakta* causes acne and skin manifestations; *Medo dushti* causes conditions like *Sthoulya* and *Prameha*; and *Asthi dushti* causes changes

in the pattern of *Kesha* and *Loma* and so on involving the dhatu till the level of *Shukra*. These varied symptoms are present in condition PCOS which is having prevalence varying from 5% to 15%. Diagnosis of PCOS typically requires the presence of at least two of the following three criteria based on Rotterdam consensus: chronic oligo- anovulation, hyperandrogenism (either clinical or biochemical), and the presence of polycystic ovaries ( $\geq 12$  follicles measuring 2-9 mm in diameter and/or an ovarian volume  $> 10$  mL in at least one ovary). The condition PCOS is associated with comorbidities like anovulation and infertility, obesity, impaired glucose tolerance and type 2 diabetes mellitus.

In the management of complex conditions such as polycystic ovary syndrome (PCOS), a multi-disciplinary approach is essential. Many patients opt for Ayurvedic management due to its perceived safety and efficacy. Hence, we need to delve into the physiological aspects of the menstrual cycle and the pathological development of diseases like PCOS.

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Ayurveda holds that the majority of ailments have *Amashaya* as their primary point of origin resulting from imbalances in *Jatharagni* and *Rasa dhatu*. *Dhatu*s and *Dhatwagnis* are the prime components that contribute in the pathophysiology of PCOS that can be explored based on the principles of Ayurveda.

### AIMS AND OBJECTIVES

The objectives of the study are to identify the pathophysiology of the disorder PCOS that arises from *agni dushti* followed by *rasa dhatu dushti* and involving *uttarotar dhatu*s and *dhatwagnis* and to examine the symptoms and indicators of PCOS based on these factors.

### MATERIALS AND METHODS

**Methodology:** A conceptual study of PCOS and an analysis of its pathogenesis based on the information gathered from the literature on Ayurveda, as well as commentary, pertinent material from papers, journals, and reviews of contemporary gynaecological texts.

### Role of Agni and Rasa Dhatu in the Formation of Artava

*Agni* is the most basic requirement which is necessary for the survival of any human being hence *Acharya Charaka* says that it is the essential factor in maintenance of life<sup>[2]</sup>. *Jatharagni* and other types of *Agnis* like *Dhatwagni*, *Doshagni*, and *Bhootagni* are considered as the energy that causes changes or metabolism in the tissues and is responsible for major transformation of *Ahara rasa* to *Rasa dhatu*.

*Rasa* is the initial progenitor *Dhatu* which forms the fundamental basis of other tissues in the process of transformation with the help of *Rasagni*. *Artava* that is considered as the byproduct of *Rasa dhatu* maintains the function of *Artavavaha srotas*. The role of *Rasa dhatu* in the female reproductive tract is through its *Preerana* action responsible for follicular growth and development. The *Jeevana* function of *Rasa dhatu* ensures maturation of *Beeja/ovum* which is essential before *Beeja nishkramana* or *Cyavana* (ovulation process) as a healthy live matured ovum ensures an optimum conception. *Beeja cyavana* is an important function of *Shukra dhatu* and its role in specific functions related to female reproductive system is important.

### Role of Shukra and Ojus in Maintaining Function of Artavavaha Srotas

According to *Acharya Charaka*, *Shukra* is considered to be one the component included in *Pitrija bhava*, a part of *Shadbhavas*, that contributes in the growth and development of embryo. This shows that *Shukra* contributes to various metabolism and function in both sexes right from embryological state. In

females, *Artava* along with *Shukra* contributes in the maintenance of *Artavavaha srotas* function<sup>[3]</sup>.

*Acharya Bhavamishra* consider *Artava* as the 7<sup>th</sup> *Dhatu* after *Majja* and *Shukra* as the 8<sup>th</sup> *Dhatu* in the chronology of *Dhatu* formation<sup>[4]</sup>. The process of steroidogenesis in both sexes follows a complex network that controls different organs and systems including reproductive system. Pregnenolone and progesterone occupy a unique and central position in steroidogenesis and endocrine function. Pregnenolone, derived from cholesterol through the action of cytochrome P450 side-chain cleavage enzyme (CYP11A1), serves as the foundational substrate for the synthesis of glucocorticoids, mineralocorticoids, estrogens, and androgens<sup>[5]</sup>. Estrogen can be considered as the *Artava tatva* especially *Artavagni* and androgen as the *Shukra tatva* especially *Shukragni* which perform specific metabolism and regulate the *Artavavaha srotas*. Thus, the *Dhatugata* interconversion of *Artava* and *Shukra* in the order of chronology can be explained.

*Acharya Sushruta* explains presence of *Shukra* all over the body of all humans.

सप्तमी शुक्रधरा, या सर्वप्राणिनां सर्वशरीरव्यापिनी ॥२०॥

यथा पयसि सर्पिस्तु गूढश्चेक्षौ रसो यथा ।

शरीरेषु तथा शुक्रं नृणां विद्याद्विषग्वरः ॥Su sha 4/२१॥

The role of *Shukra* in females is just not limited to reproductive system but it pervades all over the body in *Sukshma* form. This explains the presence of androgens, estrogen and progesterone all over the body and their influence is not limited to reproductive system and this is how they are responsible for *Bala*, *Varna* and *Pushti* of humans during the reproductive phase of life. Androgens have similar function as per contemporary science. Androgens in women, as well as in men, are intrinsic to maintenance of (i) reproductive competency, (ii) cardiac health, (iii) appropriate bone remodeling and mass retention, (iii) muscle tone and mass, and (iv) brain function, in part, through their mitigation of neurodegenerative disease effects<sup>[6]</sup>.

*Acharya Bhavamishra* have mentioned that the *Sthoola amsha* of *Rasa dhatu* is transformed into *Shukra* and *Artava* in women<sup>[7]</sup>. This explains the role of *Rasagni* in transformation process from *Rasa* to *Shukra* and *Artava* and *Rasagni* controls the action of *Shukragni* and *Artavagni*. *Shukra dhatwagni* corresponds to the function of Luteinizing Hormone (LH) that initiates the production of androgens in the theca cells of the maturing follicles in the ovaries. The selected follicles in the ovaries undergo the growth and development every month. *Preerana* and *Jeevana* are the basic functions of *Rasagni* that corresponds to the function of FSH which is responsible for follicular growth and maturation of ovum. The biochemical

transformation namely aromatization of androgen precursor to oestrogen is indirectly guided by FSH that upregulate the FSH receptors and aromatase enzyme (CYP19) in the granulosa cells<sup>[8]</sup>.

The microenvironment created by FSH eventually results in the process of ovulation. The *Pushti* of the *Beeja* (ovum) is under the influence of *Rasagni* that is followed by the formation of corpus luteum that produces progesterone. Progesterone maintains the vital of the ovum after its escape from the follicle. This specific function of progesterone corresponds to the *Ojagni*. *Ojus* is the essence of *Saptadhatu*<sup>[9]</sup> and along with *Ojagni* in *Artavavaha srotas* it maintains the vitality of ovum that aids in the process of fertilization. Acharya Charaka mentions *Ojus* as *Garbha rasa* which is essential for the nourishment of the *Garbha*<sup>[10]</sup>. The optimum level of progesterone maintains pregnancy as per contemporary science. The *Para ojus* remains at heart till death of the individual whereas the *Apara ojus* maintains body strength and resist against the disease which is *Sarva sharira vyapi*<sup>[11]</sup> including *Artavavaha srotas*. Imbalance in *Ojus* can lead to various disorders related to the menstrual cycle. It is essential to understand the Guna and relation of *Ojus* with *Artava*. According to Cakrapani, in the early phases of *Artava* formation, *Artava* demonstrates traits of *Sowmya guna* which is similar to the innate features of *Rasa dhatu* and *Ojus*. For any new growth and maintaining the stability of the tissues, the presence of *Somatmaka guna* of *Ojus* in the tissues is essential. *Ojagni* along with *Artavagni* plays an important role in the formation of new blood vessels and the glands of endometrium in the proliferative phase of the menstrual cycle. *Sowmya guna* maintains the stability and growth of endometrium so as to facilitate implantation of the live fertilized ovum. This justifies the statement of Acharya Sushruta related to the function of *Ojus* as *Balen sthir upachita mamsen*<sup>[12]</sup>.

During the *Rajasrava kala*, *Artava guna* changes to *Agneya guna* under the influence of *kala* (time). This shift is analogous to the transformation of solid matter into vapor due to the influence of fire, or the conversion of sugarcane juice, initially inducing a "*Kapha*" quality, later transforming into wine through fermentation, altering its properties as *Tridoshakara*.<sup>[13]</sup> The dynamic interplay between *Dhatu*s, *Dhatwagni*, and the influence of time and elemental forces in the formation and transformation of *Artava* illustrates the intricate mechanisms underlying menstrual physiology according to Ayurvedic principles. Menstruation is a physiological process that is controlled by the timed release of GnRH pulsation, which in turn triggers the release of LH and

FSH, consequently regulating the uterine endometrial stages, follicular development and ovulation.

### Role of *Agni*, *Ushma*, *Pitta* and *Vayu* in Maintaining the Respective *Srotas* and Influence on *Artavavaha Srotas*

*Pitta dosha* is essential for regulating the metabolism as it changes the state of one element to another. *Pachaka Pitta sthana* is between *Pakwashaya* and *Amashaya* near *Jatharagni*<sup>[13]</sup>. *Pachaka pitta* along with *Jatharagni* transforms *Ahara* to *Ahara rasa* subsequently resulting in *Rasa dhatu*<sup>[14]</sup>. This further nourishes the respective *Dhatu*s with the help of respective *Ushma*, *Vayu* and *Srotas* in their *Anupahata Avastha* (physiologic state). Maintaining the vital balance and proper function of these processes is crucial for overall health, including aspects like growth (*Upachaya*), strength (*Bala*), complexion (*Varna*), and lifespan (*Sukhayusha*). Additionally, the strength, energy, and normal function of the *Dhatu*s contribute to overall well-being. However, in condition of *Upahata* (pathological state) *Ushma*, *Vayu* and *Srotas* involving *Rasa vaha srotas* can impact the function of *Artava vaha srotas* affecting the reproductive health of the woman. *Vayu* regulates the bodily function and supports the process of metabolism at various tissue levels. *Prana vayu sthana* is *Shiras* and it is said to be the governing force that controls the function of the rest of the *Vayu*s in the body. GnRH function and its releasing site hypothalamus corresponds to the site of *Prana vayu*.



GnRH maintains the function of hormones released from pituitary, gonads and other parts of the body through various feedback mechanism.

*Samana vayu* being *Agni sameepastha* supports the process of formation, transformation, digestion and regulation of metabolism in *Amashaya* and *Koshta*. *Artavavaha srotas* is the part of the *Koshta* is influenced by the function of *Samana vayu*. Hence it can be interpreted that the metabolism and the transformation of hormones that takes place in the ovaries at the cellular level with the help of specific enzymes are regulated by the *Prana vayu* in

coordination of *Samana vayu* and *Dhatwagnis* like *Rasagni* (its function corresponds to FSH), *Artavagni* (its function corresponds to oestrogen), *Shukragni* (its function corresponds to LH) and *Ojagni* (its function corresponds to progesterone)<sup>[15]</sup> synergistically maintains the health of *Artavavaha srotas*.

### Role of *Kapha Dushti* in Causing *Dhatugata Vikara*

*Rasa dhatu* shares qualities similar to *Kapha dosha*, as both exhibit a predominance of the *Jala* and *Prithvi mahabhuta*. During the formation of *Rasa dhatu*, *Kapha* is produced as *Mala*<sup>[16]</sup> which is one of the essential components in the process of maintaining tissue physiology. Adequate release of *Dhatu mala* ensures the physiological outcome related to *dhatu*s and *Dhatwagni* function. However, deviations from normal dietary or lifestyle habits can significantly impact the quality of *Dhatu*s and *Dhatu mala*. Due to *Dhatu mala dushti*, the *Srotas* can suffer from *Atipravritti*, *sang*, or *Vimarga gamana* depending on the type of vitiation<sup>[17]</sup>. *Artava vaha sroto sang* caused by the vitiation of *Kapha* can lead to irregular menstrual cycle and similar symptoms are observed in PCOS condition. The *kapha* vitiation can affect the function of *Uttarotara srotases* affecting corresponding *Dhatu*s. *Rasa dhatu dushti* and *Kapha prakopa* due to *Ukta nidana sevana* disturbs the function of respective *Dhatwagni* and subsequent *Dhatu*s including *Rasa*, *Rakta*, *Mamasa*, *Meda* upto the level of *Shukra*. The woman with such complex vitiation of *Dhatu*s suffers varied symptoms which are evidently present in complex disease like PCOS.

### Analysis on Etiopathogenesis of PCOS -An Ayurvedic Perspective

*Acharya Vagbhata* explains that most of the diseases arise out of *Mandagi*.<sup>[18]</sup> Genetic, sedentary lifestyle, faulty diet, inflammatory conditions and stress are the common etiological factors of PCOS. *Acharya Charaka* explains *Mithya ahara* and *Vihara*, *Pradushta artava*, and *Daiva* as the cause of *Yoni vyapad*<sup>[19]</sup> other causes are *Viruddha ahara*, *Asatmya bhojana*, *Adhyashana* leads to *Agni dushti*.

*Acharya Charaka* explains *Rasa pradoshaja rogas* such as *Ashradha*, *Aruchi*, *Asyavairasya*, *Ayathakala Valaya* (premature wrinkling), *Palita* (grey hair) and *Sroto rodha*. *Rasa dhatwagni mandhya* causes *Srotorodha* due to the vitiation of *Kapha* (*Rasa dhatu mala*). Hence the *Kapha prakopa lakshanas* like *Aruchi*, *Gaurava*, *Tandra*, *Sroto rodha* are mostly present in PCOS women along with other *Rasa dushti lakshana*<sup>[20]</sup>.

The next level of vitiation affects *Artava* which is the immediate byproduct of *Rasa*. *Kapha dushti* leads to *Artavavaha srotorodha* causing *Sanga* in the *Srotas* thereby affecting the normal *Gati* of *Apana vata* causing conditions like *Artava kshaya*. Some of the

clinical symptoms like *ammenorrhea* (*Yathochita kala Adarshana*), *Alpata* and *Yoni vedana*<sup>[21]</sup> corresponds to the symptoms of PCOS women. The condition *Nashtarhava* described by *Acharya Susruta* involves *Kapha* or *Vata* alone or *Kapha vata* together may cause *Aavarana* (obstruction) to *Arthavavaha srotas*.<sup>[22]</sup> *Kaphavrita vata* causing *Sanga* in the *Srotas* causes menstrual irregularities in such women. The *Rasa dhatu dushti* is followed by *Rakta dhatu* vitiation that affects its *Dhatu mala - pitta*. In this process, *Raktagata dhatwagni dushti* causes *Twak vikara* causing *Mukha dushika* (acne) and *Karshnya* (acanthosis nigricans, features of PCOS). In Ayurveda, *Mukhadushika* is one of the *Kshudra kushta* affecting the skin. *Mukhadushika* is caused due to *Pitta pradhana tridosha prakopa* and *Rasa* and *Rakta dushti*.<sup>[23]</sup>

*Acharya Vagbhata* has mentioned the role of *Meda* in the pathology of *Mukhadushika* which resembles the modern theory of sebum in the pathogenesis of acne. *Medogarbhavta*<sup>[24]</sup> (filling *Meda* inside the *Pidika*) or acne is said to be one of the symptoms of the disease PCOS. In *Sharangadhara Samhita*, it has been mentioned that acne is caused due to *Shukradhatumala* (by products during semen formation).<sup>[25]</sup> *Pindika* or *Mukhadooshika* can be considered as one among the *Shukra dhathu Malas*. *Shukra dhathu* will be active only when the person attains puberty and skin conditions like pimples manifest due to over activity of sebaceous gland during this phase. Testosterone increases the secretory activity of sebaceous gland. At the time of puberty, when body is exposed to sudden increase in testosterone secretion, the excess secretion of sebum leads to development of acne on the face. Hence *Dushti* of *Shukra dhatu* and *Shukradhatwagni* can be considered as one of the pathogenesis causing symptoms of PCOS like acne or *Mukhadushika*.

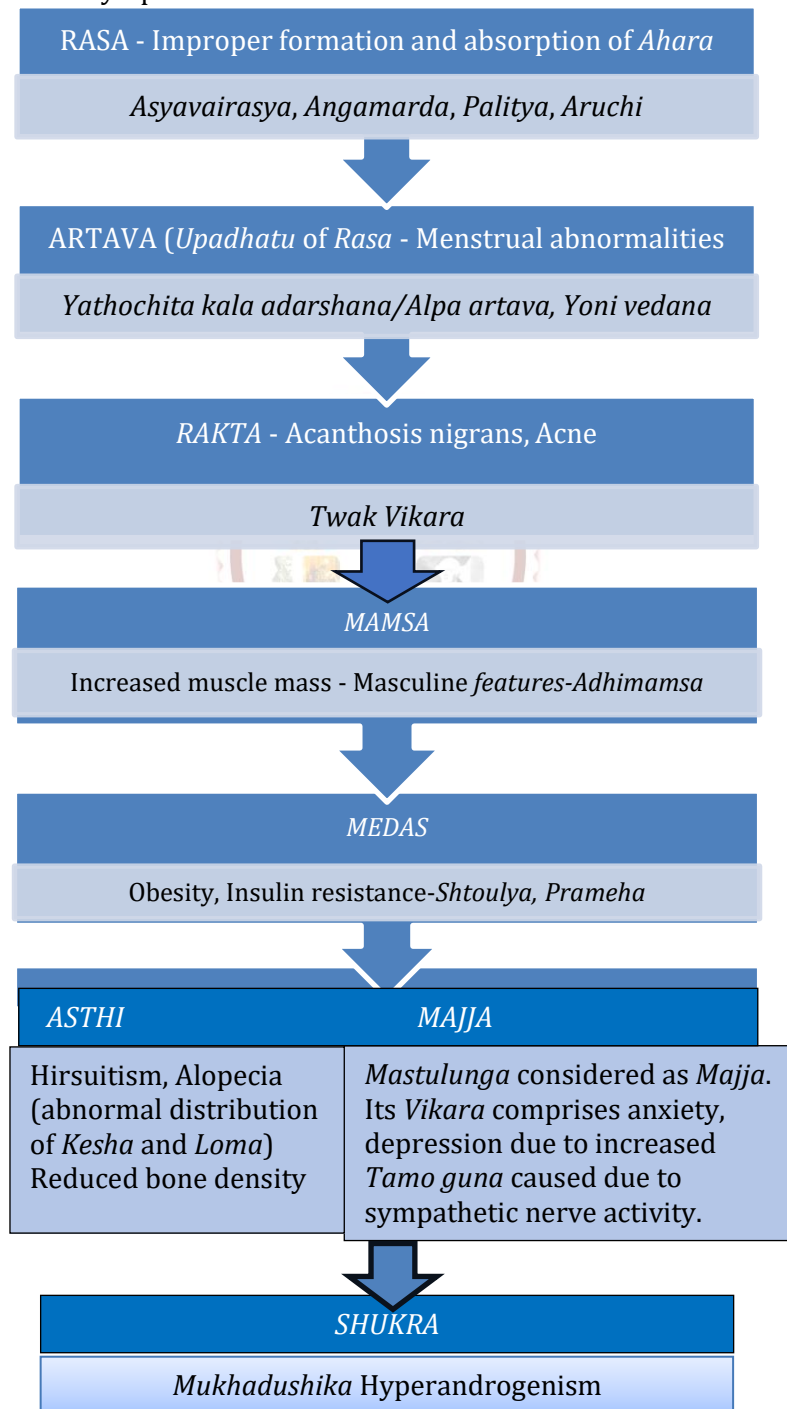
The vitiation of *Mamsa dhatu* and *Mamsadhatwagni* in a PCOS woman contributes to increased body mass which is expressed as the male pattern of muscle mass. Hence the *Mamsavaha sroto dushti lakshana* like *Adhimamsa* can be understood. Subsequently, the next level *Dhatu Medas dushti* leads to *Sthoulya* and *Prameha*. Obesity and insulin resistance are the common features which suggest metabolic dysfunction in PCOS woman.

*Asthivaha srotodushti* in PCOS woman can be explained by the appearance of abnormal distribution of *Kesha* and *Loma* in the body. Such woman suffers from male pattern of alopecia and male pattern of hair distribution all over the body and faces which is termed as hirsutism. According to *Sharngadhar*, *Kesh* is the *Updhatu* of *Majja Dhatu*<sup>[26]</sup> but according to other scholars *Kesha* is *Updhatu* of *Asthi*. *Kesha* is considered to be the intermediate byproduct of *Asthi* and *Majja*<sup>[27]</sup>.

In the order of dhatu involvement *Majja dhatu* involvement can be understood as follows. *Mastulunga* is *Majja Dhatu*<sup>[28]</sup>. Chakrapani also described "*Mastishkam sirahstho majja*"<sup>[29]</sup>. *Majjavaha Srotas* are aligned with neural circuits and pathways influenced by CSF. *Shiras* is the *Sthana* for *Tarpaka kapha*<sup>[30]</sup>. Vitiating of *Majja* and *Kapha* can lead to disorders like anxiety, depression, and schizophrenia reflect imbalances in these systems. Studies show higher rates of depression and anxiety in PCOS than women in the general population.<sup>[31]</sup> Many factors associated with polycystic ovary syndrome (PCOS) are also associated with increased activity in the sympathetic nervous

system<sup>[32]</sup>. The involvement of sympathetic nervous system in PCOS pathology is supported by the greater density of catecholaminergic nerve fibres in polycystic ovaries (PCO)<sup>[33]</sup>. Increased ovarian sympathetic nerve activity might contribute to PCOS by stimulating androgen secretion.<sup>[34]</sup>

The involvement of *Saptadhatu* in PCOS woman causes metabolic disorders like insulin resistance, obesity, hyperandrogenism, cardiovascular diseases along with the disturbance in menstrual pattern. Studies shows hirsutism was associated with lower psychological quality of life<sup>[35]</sup>.



## DISCUSSION

Acharya Charaka mentioned *Mithya ahara* and *Vihara* are the causes of diseases in women. *Agni dushti* followed by *Rasa dushti* leads to the vitiation of *Rasa* and subsequent *Dhatu*s involving respective *Dhatwagnis* resulting in severe metabolic derangement of various organs and systems of the body. *Acharya Charaka* explains *Rasavaha sroto dushti* causes *Srotosanga* resulting in impotence, tiredness (*Angavasada*).<sup>[36]</sup> Women with PCOS often present with these symptoms along with menstrual irregularities, anovulatory cycles, anorexia, heaviness of body and drowsiness. Such women experience concerns related to fertility and sexual disturbances. The physiological function of *Rasa dhatu* and *Uttarotara dhatu*s can be restored by correction of *Agni* that can be achieved by following basic principles of Ayurveda. Administration of *Shodhana*, *Shamana* and *Pathya* helps restore the menstrual cycle, ovulation, corrects the metabolic dysfunction, hyperandrogenism and obesity. PCOS women should be thoroughly analysed for the involvement of *Dhatu* and *Dhatwagni* responsible for the manifestation of pathogenesis and plan to provide a sustainable and long-lasting cure at *Dhatugata* level.

## CONCLUSION

PCOS is a multifactorial disease and involves various hormonal pathways resulting in metabolic dysfunction and menstrual irregularities affecting adolescents and reproductive women. Ayurvedic concepts explain the involvement of *Saptadhatu* and respective *Dhatwagni* in the manifestation of the disease PCOS and based on the severity, the symptoms are seen, Ayurveda provides a sustainable treatment plan and preventive measures to overcome and manage this condition.

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