IAMJ

INTERNATIONAL AYURVEDIC MEDICAL JOURNAL

Review Article ISSN: 2320-5091 Impact Factor: 6.719

THE COMBINED EFFECT OF NAGAKESARA (MESUA FERREA LINN.) & PUGA (ARECA CATECHU LINN.) IN PCOS (POLYCYSTIC OVARIAN SYNDROME): A COMPREHENSIVE REVIEW

Gupta Priya[1] Panwar Suman[2]

1. PG Scholar, Department of *Dravyaguna Vigyana*
2. HOD & Prof, Department of *Dravyaguna Vigyana*

Shri Dhanwantry Ayurvedic College & Hospital, Sector 46-B, Chandigarh, India- 160047

Corresponding Author: pg.priyagupta98@gmail.com

https://doi.org/10.46607/iamj10p7062023

(Published Online: September 2023)

Open Access

Article Received: 01/08/2023 - **Peer Reviewed:** 05/09/2023 - **Accepted for Publication:** 17/09/2023.

Check for updates

ABSTRACT

Objective- A literary review on the combined effect of *Nagakesara* (*Mesua ferrea* Linn.) and *Puga (Areca catechu Linn.)* possess fertility activity or not by reducing the PCOS induced infertility. **Method-** This study provides a comprehensive review of the available literature on the individual effect of *Nagakesara* & *Puga* from Ayurvedic texts, electronic media and research articles shedding light on their potential synergistic interactions and therapeutic applications for fertility activity. **Result-** Through the available data the combined effect of *Nagakesara* & *Puga* in PCOS (*Pushpagni*) can help resolve infertility problem because of the presence of phytochemicals which reduces PCOS. Hence this review is conducted to know the possible phytochemicals and mode of action through ayurvedic pathophysiology of their combined effect in reducing PCOS symptoms. **Conclusion-** Due to the presence of particular phytochemical like flavonoids, alkaloids, polyphenols & *Rasapanchaka* of both the drugs can help reducing the PCOS symptoms.

Key words: *Nagakesara (Mesua ferrea Linn.), Puga (Areca catechu Linn.),* Phytochemical, Fertility, PCOS (polycystic ovarian syndrome)

INTRODUCTION

***Nagakesara* (*Mesua ferrea* Linn.)**

Mesua ferrea, commonly known as the Ironwood tree or *Nagakesar*, is a species of evergreen tree belonging to the family Guttiferae. It occurs in Himalayas from Nepal eastwards, Bengal, Assam, evergreen rain forests of North Kanara, Konkan, forests of Western Ghats and Andhra Pradesh. It is a slow-growing, medium-sized tree that can reach heights of up to 15-18 meters tall. It has a straight, cylindrical trunk with smooth, Grayish-brown bark. The leaves are simple, glossy, and dark green, arranged in opposite pairs along the branches. The tree produces fragrant, white flowers that are about 5 cm (2 inches) in diameter. The flowers have numerous stamens and a sweet, pleasant fragrance. *Mesua ferrea* is valued for its timber, which is known for its durability and strength. It is commonly used in the construction of buildings, furniture, and boats. The tree also has cultural and religious significance in various Southeast Asian cultures. In India, the flowers of *Mesua ferrea* are used in religious rituals and the tree is associated with Lord Shiva. In traditional medicine, different flowers of the tree are used for their medicinal properties. Various evidence-based research is available where *Nagakesara* is believed to have antioxidant[01], Immunomodulatory Activity [02], Anti-spasmodic activity[03], Hepatoprotective activity[04], Anti-venom activity[05], Anti-ulcer activity[06], Anti-bacterial activity[07], Anti-inflammatory[08], Anti-cancerous[09], Anti-histamine[10], Anti-implantation[11], Fertility Activity[12] etc. In traditional Ayurvedic medicine, various parts of the *Nagakesar* tree are used for their medicinal properties. The dried flowers, flower buds, seeds, roots, leaves and bark are commonly used in herbal remedies. In ayurvedic text it is mentioned as *Amapachana, Kanduhara,* in *Visarpa, Kusthahara, Trishnahara, Vishahara*, in *Bastivikara*, *Vatarakta, Shotha nashaka, Jawarahara, Chardiharan,* in *Kantharoga, Shiraroga, Raktarsha, Charmaroga* etc.

Figure 1.1. *Nagakesara* (*Mesua ferrea* Linn.)

Figure 1.2 *Mesua ferrea* Linn. Flowers (dried)

Mesua ferrea was in Threat status among 242 plant species with high commercial demand (100 Metric Tonne/year) in India with CAMP exercise threat category [State (threat category and year of CAMP exercise)] as Orissa (endangered 2007), Tripura (near threatened 2016), West Bengal (endangered 2007). However, there are efforts to conserve and protect this tree species through measures such as establishing protected areas and promoting sustainable harvesting practices.[13] In the Market of Northern region of India (Punjab, Haryana, Chandigarh), *Calophyllum* species are found and in Southern region of India (Udupi, Bangalore and Mangalore) *Mesua ferrea* flowers (stamens) are available.

***Puga* (*Areca catechu* Linn.)**

Areca catechu, commonly known as the Areca nut palm or betel nut palm, is a species of palm tree native to Southeast Asia. It belongs to the family Palmae and is cultivated for its fruit, which is commonly chewed with betel leaf and other ingredients in many countries for their stimulant and psychoactive effects. Areca catechu is a medium-sized palm tree that can grow up to 20-30 meters (65-100 feet) tall. It has a slender trunk with a crown of large, feathery leaves at the top. The fruit of Areca catechu is commonly referred to as the betel nut or areca nut. It is a large, oval-shaped nut that

grows in clusters at the top of the tree. When ripe, the outer husk turns bright orange or reddish-brown. The betel nut has a long history of cultural and social significance in many parts of Asia. It is commonly chewed along with betel leaf, slaked lime, and sometimes tobacco or other ingredients. Chewing the betel nut mixture produces a stimulant effect and is often used for its mild psychoactive properties. It reduce the severity of symptoms in schizophrenia with reduction in both positive and negative symptoms[14], increases facial skin temperatures[15], increases in blood pressure[16], at modest dosage betel quid consumption affects the sympathetic nervous system but at high dosage, both sympathetic and parasympathetic nerves are activated[17], Two types of piper betle vine leaf are used; the pungent (Mysore) leaf and the non-pungent (Ambadi) leaf and both stimulate pancreatic lipase secretion[18], It is possible that betel leaf extract may affect thyroid function, low doses increasing triiodo thyronine to thyroxine ratios (suggesting increased activation of thyroxine) in rodents while high doses had the reverse effect[19], Antiovulatory and abortifacient effects of Areca catechu (betel nut) in female rats were also seen[20]etc. It's important to note that the use of betel nut and its potential health risks have been a subject of concern and regulation in several countries due to its negative health effects. In ayurvedic text *Puga* is mentioned for *Mohakara, Ruchikara, Abhisyandi, Asyaverasya, Hrideya, Madakaraka, Kledahara, Malaphama, Sankochkara* etc.

Figure 1.3 *Puga* (*Areca catechu* Linn.)

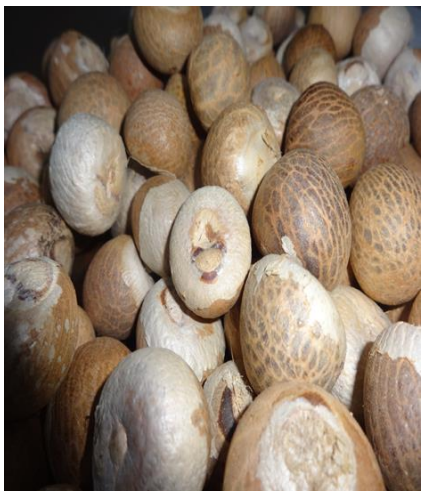

Figure 1.4 *Areca catechu* Linn. Seeds (dried)

In Ayurvedic text a combination of *Nagakesara* and *Puga* treatment modality is found claiming the fertility effect when used together.[21]

Nagakesara Pugaasthichurna Wa Garbhadam Param. (Vangasena Samhita, Strirogadhikara, 145)

Polycystic ovarian syndrome (PCOS) is the most common endocrine disorder in a woman of reproductive age and is primary cause of infertility in women[22] in recent studies hence the effect of combination of *Nagakesara* and *Puga* in reduction of PCOS symptoms is the field of intrust. Female infertility is called *Bandhyatva* in *Āyurveda*.[23] *Pushpagni Revati* in *Kashyapa Samhita* can be corelated with PCOS. It is written as the women who observes fruitless menstruation in appropriate time, has corpulent and hairy cheeks, she is seized with *Pushpagni revati*.[24] *Vritha Pushpam Tu Nari Yathakalam Prapshyati. 33.2 Sthulalomashaganda Wa Pushpaghni Saapi Revati. 34.1 (Kashyapa Samhita, Revatikalpadhyay, 33.2-34.1)*. In Ayurveda, Pathophysiology of PCOS is due to *Kapha* blocking *Vata* and *Pitta*, hence the movement is obstructed, and the transformation process is suppressed. *Kapha dosha*, because of its properties like *Sheet, Manda, Sthir, Guru* causes dimension of digestive fire (*Jathara agni*) and starts affecting the metabolic aspect of the seven tissues called *Dhatu Agni*. [25] The *dhatus* that are affected are:

- *Rasa dhatu* – lymph and plasma

- *Meda dhatu* – adipose tissue and
- *Artava dhatu* – the female reproductive system

Dimension of *Agni*, results in improper digestion and assimilation of *Dhatus* and leads to formation of excessive *Kelda* (*Kledak kapha*). *Kledak kapha* begins to move out of GI tract and enters the channel of the first tissue *Rasa vaha strotas*. This affects the *Rasa dhatu agni* – that is the metabolism of the lymph and plasma in the body. The by-product of *Rasa dhatu* is *Rajah* – that is the menstrual fluid. As there is *Kapha dosha* dominance in the body, the menstrual fluid will also take on the quality of *Kapha* which will in turn begin to block *Apana vayu* in *Artavavaha strotas* and *Rasahavaha strotas* – the channel that supports the functional action of the menstrual fluid. The increased quantity of *Kledak kapha* and *Ama* in the body leads to *Agni mandya*. The increased *Rasa dhatu* coating over cells further leads to decrease in the permeability of the cell membrane thus affecting the cellular intelligence. Due to the decreased cellular permeability, the insulin secreted in the body is unable to engage with the cellular receptors. Thus, insulin begins to build up in the blood stream. Thus, increase in the levels of insulin is present. The increased quantity of *Kledak kapha* and *Ama* in the body also leads to *Dhatu agni mandya*. According to the *Saamanya Vishesh Siddhant*, the *Kledak kapha* and *Ama* affects the *Meda dhatu agni*. The *Meda dhatu agni mandya* leads to *Meda viruddha* leading to obesity. The free androgens moving throughout the body are processed at the level of *Meda dhatu*. Here it takes on the *Guru, Sheet* properties of *Meda dhatu*. This is further expressed as estrogen. Thus, we can see an increase in the levels of estrogen. The *Kapha dosha* and *Ama* created by *Agnimandya* also cause *Stroto dushti* in the *Artavavaha strotas*. The *Apana vayu* in *Artavavaha strotas* becomes stagnant – that is *Sanga* of *Apana vayu* - blocking the channel impeding the flow of *Vata* in the ovarian cycle. The blocking of channels of *Apana vayu* leads to disturbances in the outflow of menstrual fluid. Thus, menstrual disturbances like oligomenorrhoea, amenorrhoea is present. Menstrual problems manifest due to the aggravation of all three *doshas* but mainly *Apana vayu*. The main property of *Artava dhatu* is *Agneyatva*. The blocked *Artava dhatu* leads to aggravation of *Pitta dosha*. *Pitta* aggravation at the level of *Bhrajaka pitta* and *Ranjaka pitta* manifests as acne and increased body hair seen.

In modern Although the specific pathological mechanism of PCOS remains unclear, numerous studies have shown that oxidative stress, insulin resistance, and androgen excess play an essential role in the occurrence and development of polycystic ovarian syndrome. PCOS can be considered a state of oxidative stress. Specifically, the antioxidant function in the human body cannot deal with excessive reactive oxygen species, which further exacerbates the clinicopathologic features of PCOS, such as chronic oligo-anovulation or anovulation, clinical or biochemical signs of hyperandrogenism, and polycystic ovarian morphology in women. Meanwhile, high levels aggravate the oxidative stress reaction and are often accompanied by insulin resistance, worsening PCOS symptoms. In addition, many factors, such as the maternal environment and genetics, have influenced the evolution of PCOS. Namely, high prenatal maternal androgen levels cause PCOS in female infants. Moreover, recent studies disclose that multiple genes are highly related to PCOS, and data analysis shows that 241 gene mutations are involved in the etiology of PCOS. These pathological factors indicate that PCOS is a comprehensive disease referring to multiple signalling pathways and targets.

Recent studies have found that the process of chronic inflammation plays an essential role in the pathogenesis of PCOS. The higher activity of proinflammatory processes in adipocytes is related to insulin resistance. Therefore, obesity, inflammatory factors, and insulin resistance will jointly affect the occurrence and development of PCOS. Obesity is a symptom most PCOS patients face, and overweight and obese women have lower ovulation rates, conception rates, pregnancy rates, and live birth rates. Moreover, obesity can promote the molecular mechanism of androgen expression, which may be the cause of obesity leading to PCOS. In addition, the latest studies have revealed that the gut microbiota is also connected with the pathogenesis of PCOS. Studies have shown that the abundance of Firmicutes and Bacteroides in the gut

microbiota of PCOS patients is changed. As beneficial bacteria, Lactobacilli and Bifidobacterial can regulate the levels of sex hormones, manage the synthesis and secretion of insulin, and reduce the production of pro-inflammatory cytokines. All these studies prove that restoring the abundance of some gut microbiota can be used as a new strategy to relieve PCOS symptoms. There is a close relationship between hormonal alterations and bone metabolism in PCOS. For example, an increase in androgen leads to an increase in inflammatory factors and impairs bone formation. Estrogen is mainly used to maintain the development of female bones, while the decrease in estrogen in PCOS will cause some damage to bones. Other hormonal alterations, such as changes in LH, FSH, and insulin levels, also affect bone formation and development[26.]

METHOD

From above literature data was analysed for both drugs i.e., *Nagakesara* (*Mesua ferrea* Linn.) & *Puga* (*Areca catechu* Linn.) acting in reducing the symptoms of PCOS or not through modern and ayurvedic perspective. Over the years, several different approaches have been proposed to alleviate PCOS symptoms. Supplementation with natural molecules such as inositols, resveratrol, flavonoids and flavones, vitamin C, vitamin E and vitamin D, and omega-3 fatty acids may contribute to overcoming PCOS pathological features, including the presence of immature oocyte, Insulin Resistance (IR), hyperandrogenism, oxidative stress and inflammation.[31] Bioactive phytochemicals isolated from traditional Chinese medicine and medicinal plants in treating PCOS, including flavonoids, polyphenols, and alkaloids. These phytochemicals show therapeutic effects on PCOS supported by in vivo and in vitro studies, mainly depending on anti-inflammatory, antioxidation, improvement of hormone disorder and IR, and alleviation of hyperinsulinemia.[26] *Mesua ferrea* showed wide range of various phytochemical constituents, which are responsible for different medicinal properties. *Mesua ferrea* seed oil is a typical triacylglycerol, consists of fatty acid and glycerol moieties. The major compositions of the fatty acids are myristic acid (2.13%), palmitic acid (10.87%), linoleic acid (13.68%), oleic acid (55.93%), stearic acid (14.19%), and arachidic acid (2.92%). The bark oil is rich in (E)-α bisabolene (31.3%) and α-selinene (12.2%). The predominant components in the oils of tender and mature leaves are α-copaene (19.3%and9.9%) and β-caryophyllene (18.8%and26.0%). The bud and flower oils also contained α-copaene (28.7%and20.2%, respectively) and in addition germacrene D (19.0% and16.1%, respectively). Seed oils are used as an alternative biofuel in the diesel and compression ignition engines and paint industries.

Phytochemical screening of *Mesua ferrea* and reported the presence of alkaloids, glycosides, reducing sugars, tannins, phenolics, coumarins, sterols, flavonoids, saponins, and volatile oils. Polyphenolics, coumarins, xanthones, and terpenoids were the major phytochemicals isolated from the plant stem, stem bark, leaves, root, root bark, and f lowers of Mesua ferrea. The stem bark and heartwood yielded 4-alkylcoumarins, viz., ferruol A and ferruol B, a luepol-type terpenoid guttiferol, mesuaxanthone A and mesuaxanthone B, ferraxanthone 1,7-dihydroxyxantone, 1,5 dihydroxy-3-xanthonem 1, 2, 6-trihydroxyxanthone, 1,5-dihydroxyxnthone, 1-hydroxy-7-methxyxahtnone, and β-sitosterol. α-and β-amyrin, β-sitosterol, biflavonoids such as mesuaferrone A and mesuaferrone B, mesuanic acid, 1,5-dihydroxanthone, and euxnathone-7-methyl ether were isolated from stamens. Varied coumarins were also isolated from seed oil of *Mesua ferrea* plant. Seeds contain about 75% of oil, and linoleic, oleic, stearic, and arachidic acids were major fatty acids. Chemical compounds including mesuol, mesuagin, mammeisin, mammeigin, and mesuone were also extracted from seeds.[27]

Areca nut (seed) contains gum, gallic acid, tannin, alkaloids (namely, arecaine, arecoline, arecaidine, guvacine, guvacoline, and choline), and several minerals such as copper, calcium, phosphorus, and iron. *Areca catechu* is the only one of 54 different *Areca* species identified to contain alkaloids. The Arecaine is the chief constituent of the Areca nut. The chief constituent of *A. catechu* is tannins. Tannins (also termed as tannic acid) are water-soluble polyphenols that are found abundantly in many plant foods. These

compounds are responsible for reductions in feed intake, feed efficiency, growth rate, net metabolic energy, and protein metabolism in experimental animals. Consequently, foods rich in tannins are thought to be of low nutritional value. Tannins containing food components act by inhibiting enzymes such as hyaluronidase and 5-lipoxygenase, which constitute the action as anti-inflammatories, keratolytic agents, and antimicrobials. Tannins do not function exclusively as primary antioxidants (i.e., they donate electrons or hydrogen atom), but they also function as secondary antioxidants. These therapeutic properties are assumed to be ascribed to the ability of tannins to show properties of free radical scavengers by activating antioxidant enzymes. Areca nut comprises key biochemical complexes like fat (15%), polyphenol (20%), alkaloids (0.5%), and starch (20%). More than 59 different constituents have been identified and isolated from this plant. Polyphenols- The polyphenols, typically flavanols, comprise about 12% of (+)-leucocyanidin, 2.5% epicatechin, and 10% of (+)-catechin, and the remaining fraction comprises complex flavonoids in erratic degrees of polymerization. A diverse series of tetrameric, trimeric, and dimeric procyanidins have been separated from the seeds of *A. catechu*. Flavonoids - The flavonoids isolated from *A. catechu* include isorhamnetin, chrysoeriol, luteolin, quercetin, 4′,5′-dihydroxy-3′,5′,7′-trimethoxyflavone, 5,7,4′-trihydroxy-3′,5′-dimethoxyflavanone, liquiritigenin, and jacareubin. Alkaloids - *Areca catechu* is the only herbal-origin plant comprising alkaloids of the family Arecaceae. The four most important alkaloids that have been isolated from the areca nut are arecaidine (1.5 mg/g weight), arecoline (7.5 mg/g weight), guvacine (2.9 mg/g weight), and guvacoline (2.0 mg/g weight). All these isolated alkaloids are related chemically; among them, arecoline is volatile and colourless in nature resembling chemical nicotine.

Fat- Areca nut consists of numerous fatty acids consisting of 46.2% myristic acid, 19.5% lauric acid, 1.6% stearic acid, 12.7% palmitic acid, 6.2% oleic acid, 0.3% decanoic acid, 5.4% dodecenoic acid, 7.2% hexadecenoic acid, and 0.3% tetradecenoic acid.

Tannins- Tannins are one more distinctive constituent of *A. catechu*, and the foremost types that are found in areca are condensed tannins also termed as proanthocyanidins. The important types of tannins in *A. catechu* are the catechins and epicatechin. The specific tannin compounds of *A. catechu* include procyanidin B1, procyanidin A1, procyanidin B2, areca tannin B1, areca tannin A1, areca tannin A2, areca tannin C1, areca tannin B2, and areca tannin A3.

Mineral content- The mineral matter includes calcium (0.05%), phosphorus (0.13%), and iron (1.5 mg/100 g). It also contains vitamin C (416.2 mg) and vitamin B6 (286.9 mg).[28.]

Various synonyms along with their properties and actions given for the *Nagakesara* (*Mesua ferrea* Linn.) from different *Acharyas* in various Ayurvedic textbooks are the following tables which can directly or indirectly considered for fertility action:

Table 1.1 *Nagakesara* (*Mesua ferrea* Linn.) Synonyms

S. No.	Synonyms	*BN[29]	*RN[30]	*MN[31]	*DN[32]	*KN[33]	*SL. N[34]	*SN[35]	*PN[36]	*SD. N[37]
1.	*Nagapushpa*	+	+	+	+			+		
2.	*Naga*	+		+	+			+		
3.	*Kesara*	+	+	+	+	+	+	+	+	+
4.	*Nagakesara*	+					+	+	+	+
5.	*Champeya*	+	+	+	+	+	+	+		
6.	*Nagakinjalaka*	+	+		+	+		+		
7.	*Kanchnavyah*	+	+							
8.	*Nagahva*					+				+
9.	*Ahipushpa*					+				
10	*Devapushpa*					+				
11.	*Nagapushpaka*					+				

12	*Hemabha*					+				
13	*Kanaka*				+	+				
14	*Ibh*					+				+
15.	*Duroha*					+				
16.	*Nagareruka*					+				
17.	*Hemakanchanam*				+					
18	*Gaja*			+						
19	*Kinjilaka*		+							
20	*Nagiya*		+							
21	*Kanchan*		+						+	
22	*Suvarna*		+							
23	*Hemakinjilaka*		+							
24	*Rukam*		+							
25	*Hema*		+					+		+
26	*Pinjara*		+							
27	*Phanikeshara*		+							
28	*Punnaga Kesara*		+							
29	*Rajapushpa*						+			
30.	*Phalaka*						+			
31	*Swaraghatana*						+			
32	*Nata*							+		

[*Abbrevations: *Bhavaprakash Nighantu- BN; Raja Nighantu- RN; Madanpal Nighantu- MN; Dhanwantry Nighantu- DN; Kaeydeva Nighantu- KN; Shaligram Nighantu- SL.N; Shodhal Nighantu- SN; Priya Nighantu- PN; Shadarasa Nighantu- SD.N; Maoushadha Nighantu-Mo.N.*] Explaining the corelation of different synonyms of both the drugs w.r.t. its properties, action, identification etc. from *Amarkosa.*[38] '*Nagapushpa'* synonyms when studies in deep by separating *Naga+Pushpa*, where '*Naga'* means superior / snake name/ elephant name/ mirror name & '*Pushpa'* apart from being a flower it is also known for menstrual blood. '*Naga*' name was given to denote its Snake shaped stamens. *'Kesara*' & *'Kinjilika*' is used for stamens of *Kamala.* Five names of *Nagakesara* are given in *Amarkosha* i.e., *Punnaga, Purush, Tunga, Kesara, Devavallabha, Champeya, Nagakesara, Kanchnawyah.* Another name of *Bakula, Maulashiri* tree is *Kesara* and *Bakula. 'Champeya'* apart from given in the names of *Nagakesara, Champa* flowers are also known as *champeya*. '*Ahi'* is one of the 25 names given to *Sarpa*. '*Deva*' is one of the 26 names given to *Devata* & also is used for the synonym of *Raja* as *Deva* & *Bhattraka*. *'Kanaka, Rukam, Rukam, Kanchana'* is the name given to Suvarna. *'Ibh'* and '*Gaja'* is one of the names given to Elephant among 15 different names. *Pinjara* is used for *napunshaka linga*. Through this a summary could be made that this drug must be acting on disorder related with menstruation weather it is oligomenorrhoea or amenorrhoea and due to its bright stamens, which are compared with gold indicating the useful part of this plant.

Table 1.2 *Nagakesara* (*Mesua ferrea* Linn.) *Rasapanchaka* & Properties

S. No.	Properties	*BN[29]	*RN[30]	*MN[31]	*DN[32]	*KN[33]	*SL. N[34]	*SN[35]	*PN[36]	*SD. N[37]	*Mo. N[39]
1.	*Kashya Rasa*	+				+			+		
2.	*Tikta Rasa*		+		+						
3.	*Ushna Virya*	+		+		+			+		+
4.	*Alpa Ushna Virya*		+		+						
3.	*Ruksha Guna*	+		+		+					+
4.	*Laghu Guna*	+	+	+	+	+			+		+
5.	*Tikshna Guna*					+					+
Dosa Karma											
1.	*Vatahara*		+								+
2.	*Kaphahara*	+	+	+	+	+		+			+
3.	*Pittahara*	+		+		+		+			
4.	*Vata anu-bandhi pitta*								+		
Roga Karma											
1.	*Amapacha-na*	+		+		+					
2.	*Vamana*					+					
3.	*Kandu*	+			+	+					
4.	*Visarpa*	+		+		+					
5.	*Sweda*	+				+		+			
6.	*Durgandha*	+		+		+		+			
7.	*Kusta*	+		+		+		+			
8.	*Trishna*	+				+		+	+		
9.	*Visha*	+		+	+	+			+		+
10.	*Bastivikara*		+		+						
11	*Vatarakta*				+						
12.	*Shothanas-haka*				+						
13	*Jwara*	+							+		
14	*Chardi*	+				+					
15	*Hallasa*	+				+		+			
16.	*Kantha- roga*		+								
17.	*Shira Roga*		+								
18.	*Raktarsha*							+	+		
19.	*Adho-rak-tapitta*								+		
20.	*Charmaro-ga*								+		
21.	*Rochaka*										+
22.	*Mukhadur-ghandh*										+
23.	*Agnivardh-aka*										+

Table 1.3 *Puga* (*Areca catechu* Linn.) Synonyms

S. No.	Synonyms	*BN[40]	*RN[41]	*MN[42]	*DN[43]	*KN[44]	*SL. N[45]	*SN[46]	*PN[47]	*SD. N[48]	*Mo. N[49]
1.	*Ghontaph-ala*				+	+		+		+	+
2.	*Pugaphala*			+	+	+	+	+			
3.	*Udvega*				+	+		+			+
4.	*Kathina*							+			
5.	*Chikkana*		+		+			+			+
6.	*Sarasa*							+			
7.	*Chikka*				+	+		+			
8.	*Tauvara*							+			
9.	*Harita*							+			
10.	*Guvaka*	+			+		+	+	+		+
11.	*Varttula*							+			
12.	*Sthula*							+			
13.	*Kashaya*							+			
14.	*Kalasha*							+			
15.	*Guru*						+	+			
16.	*Puga*	+	+	+		+			+	+	+
17.	*Pugavrik-sha*		+								
18	*Kramuka*	+	+	+		+	+			+	+
19.	*Dirghap-ada*		+								
20.	*Valkataru*		+								
21.	*Kshadvalka*		+								
22.	*Ghoranta*	+									
23.	*Pugi*	+					+				+
24.	*Kebuka*					+					
25.	*Kashaya phala-push-paka*					+					
26.	*Stranshi*				+	+				+	
27.	*Chikkan*				+	+				+	+
28.	*Khrpura*				+		+				
29.	*Kramooka*			+							
30.	*Tambula*										+
31.	*Pugiphala*						+				

Explaining the corelation of different synonyms of both the drugs w.r.t. its properties, action, identification etc. from *Amarkosha*[38.] It is called *Ghontaphala* because its fruits look like the fruits of *Badara* i.e., when ripped, big and oval shaped; also following names are being used for denoting *Puga* tree i.e *Ghontaphala, Udvega, Guvaka, Kramuka, Puga. Kathina, Chikkana, Harita,* and *Sthula* are some of the names describing the fruit appearance of

Puga tree. Due to the presence of *Kashaya rasa*, it is called *Kasaya*, *Kasayaphalapushpaka* and *Guru* due to the presence of *Guru guna.*

Table 1.4 *Puga* (*Areca catechu* Linn.) *Rasapanchaka* & Properties

S. No.	Properties	*BN*[38]	*RN*[39]	*MN*[40]	*DN*[41]	*KN*[42]	**SL. N*[43]	**SN*[44]	**PN*[45]	**SD. N*[46]	**Mo. N*[47]
1.	*Kashaya rasa*	+				+		+	+		+
2.	*Hima rasa*		+								
3.	*Madhura rasa*					+					
4.	*Guru guna*	+	+			+		+			+
5.	*Ruksha guna*	+				+		+	+		+
6.	*Vikashi guna*								+		
7.	*Sheeta virya*	+									+
8.	*Ushna virya*		+								
9.	*Amla vipaka*		+								
10.	*Snigdha*					+					
Dosa Karma											
1.	*Kaphahara*	+				+		+			+
2.	*Pittahara*	+				+		+			+
3.	*Pittavardhaka*		+								
4.	*Vatahara*		+								
5.	*Vatahara (pakwa)*							+			
6.	*Tridosahara (swinna)*	+				+		+			+
7.	*Dhhatukheenakara*								+		
8.	*Saraka*							+	+		
Roga Karma											
1.	*Moha kara*	+	+			+					+
2.	*Dipana*	+									+
3.	*Ruchikara*	+									+
4.	*Asyaverasya*	+									+
5.	*Abhishyandi (aadra)*	+						+			+
6.	*Kshariya*		+								
7.	*Rochana*					+					
8.	*Hrideya*					+					
9.	*Dawrgangha*					+					
10.	*Abhishyandi*					+					
11.	*Agnimadyakrita (aadra)*					+					
12.	*Madakarka*								+		
13.	*Sankochkara*								+		
14.	*Kledahara*							+			
15.	*Malaphama*							+			

DISCUSSION

In brief, flavonoids reduce androgen levels and improve hyperandrogenism mainly by inhibiting the activities of 3βHSD, 17β-HSD, and aromatase, thereby

inhibiting androgen conversion. For example, quercetin decreases the activities of 3β-HSD and 17β-HSD to reduce testosterone and oestradiol levels. Due to their phenolic groups, polyphenols have redox properties, which are responsible for antioxidant effects in treating PCOS. In addition, polyphenols also reduce the release of inflammatory factors by downregulating NF-κB, thereby achieving anti-inflammatory effects. For alkaloids, berberine increases insulin sensitivity and alleviates IR by regulating IRS-1 and activating the PI3K/Akt pathway. Nevertheless, other valuable alkaloids have received less attention in treating PCOS. According to the literature, a detection of those flavonoids and polyphenols accounted for most PCOS therapies, compared to a minor proportion of alkaloids. Continuous investment and attention to flavonoids and polyphenols will benefit the discovery of new drugs for PCOS. Some of the phytochemicals can directly or indirectly affect bone metabolism. For example, quercetin and curcumin can specifically mediate bone metabolism and osteoclast-related pathologies; soy isoflavones can directly participate in bone metabolism and maintain the development of bones; resveratrol can stimulate the proliferation and differentiation of Osteoblast cells or inhibit the osteoclastic resorption; and berberine can not only directly participate in bone metabolism, but also reduce the production of adipocytes. Compounds like Quercetin, Soy isoflavones, Naringenin, Apigenin, Luteolin, Resveratrol have Anti-androgenic activity. As a result, these phytochemicals can potentially treat PCOS by affecting hormone and bone metabolism. This conjecture needs to be validated by abundant experiments.[50]

The combined effect of *Nagakesara* (*Mesua ferrea* Linn.) & *Puga* (*Areca catechu* Linn.) can help in the above said physiology through a lot of ways which can be deduced from the table 1.2 & 1.4 given above:

Agni deepan property of *Nagakesara* can reduce the PCOS symptoms as *Agni mandya* is the basic cause that leads to PCOS, *Agnideepan* treatment plays an important role in the management. *Ama pachan* property of *Nagakesara* is another important factor helping reduce PCOS. Thus, *Amapachan* property gives better result in the treatment plan. *Kapha nashana* action of the selected drugs are the major factor responsible for improving symptoms. *Lekhan karma* of *Laghu guna* in *Nagakesara* for *Kapha dosha* and *Ama* leading to *Strotorodha,* hence *Lekhana* treatment is to be given.

The *Guru guna* of *Nagakesara* is responsible for *Shoshana, Sthambana* which are *Vatahara* and *Kaphakara* in nature. *Laghu guna* of *Nagakesara* is responsible for *Langhana karma* which causes *Utsaha, Lekhana* and *Ropana karma* which is *Agnivatakara* and *Kaphaghna*. *Tikshna guna* of *Nagakesara* is responsible for *Shamana karma* which is *Kaphahara*. The *Guru guna* of *Puga* is responsible for *Vatahara,* and *Rukshna guna* is for *Kaphahara* which leads to *Shoshana* action which is *Sthambhana* in nature. *Snigdha guna* of *Puga* is responsible for *Vatahara* which further leads to *Varnya*. *Saraka* is responsible for *Kaphahara* which is for *Daha-paka-strava Nashaka. Ushna veerya* of both the drugs help in resolving problems occurring due to increases *Kapha dosa.*

Both the drugs comes under *Soumya Varga* due to the presence of *Kasaya Rasa* which is responsible for *Kaphanashana, Sthambhana Karma*. *Kashaya rasas* include *Ruksha, Sheeta* and *Guru guna* which is *Vayu* and *Prithvi Mahabhuta Pradhana*. *Tikta rasa* of *Nagakesara* is having *Ruksha, Sheeta* and *Laghu guna* and *Madhura Rasa* of *Puga* (*Areca catechu* Linn.) also comes under *Somya Varga* responsible for *Snehana, Tarpana* with the *Snigdha, Sheeta, Guru guna*. Hence from the above data the combination of *Nagakesara* (*Mesua ferrea* Linn.) & *Puga* (*Areca catechu* Linn.) must possess fertility activity and can be used as treatment modality for *Bandhyatva* due to the presence of phytoconstituents and their mode of action.

CONCLUSION

Due to the presence of flavonoids, alkaloids, polyphenols and *Rasa, Guna, Veerya, Vipaka, Prabhava* of both the drugs a conclusion can be made that both the drugs i.e., *Nagakesara* (*Mesua ferrea* Linn.) & *Puga* (*Areca catechu* Linn.) are having those compounds which are responsible for reducing the symptoms occur due to PCOS and can further improve the fertility profile. In terms of their medicinal applications, both

Nagakesara (*Mesua ferrea* Linn.) & *Puga* (*Areca catechu* Linn.) have demonstrated potential benefits and can be used for fertility activity in different formulations in combined form. Future research should focus on identifying the active compounds responsible for the synergistic effects and conducting rigorous clinical trials to validate their combined therapeutic potential w.r.t fertility action. Despite the promising findings, there is still a dearth of scientific literature elucidating the precise mechanisms of action and optimal dosage regimens for the combined use of *Nagakesara* (*Mesua ferrea* Linn.) & *Puga* (*Areca catechu* Linn.). Further research is warranted to fully understand the mechanisms underlying their synergistic interactions, paving the way for the development of novel phototherapeutic formulations and improved healthcare interventions.

REFERENCES

1. Garg S, Kameshwar S, Rajeev R, Pankaj A, Parshuram M. In-vivo Antioxidant activity and hepatoprotective effects of methanolic extracts of Mesua ferrea L. Int J Pharmatechnol Res, 2009; 1:1692-96.
2. Chahar MK, Kumar DS, Lokesh T, Manohara KP. In-vivo antioxidant and immunomodulatory activity of mesuol isolated from *Mesua ferrea* L. seed oil. International immunopharmacology. 2012 Aug 1;13(4):386-91.
3. Garg S, Kameshwar S, Rajeev R, Pankaj A, Parshuram M. In-vivo Antioxidant activity and hepatoprotective effects of methanolic extracts of Mesua ferrea L. Int J Pharmatechnol Res, 2009; 1:1692-96.
4. Garg S, Kameshwar S, Rajeev R, Pankaj A, Parshuram M. In-vivo Antioxidant activity and hepatoprotective effects of methanolic extracts of Mesua ferrea L. Int J Pharmatechnol Res, 2009; 1:1692-96.
5. Uawonggul N, Chaveerach N, Thammasirirak N, Arkaravichien T, Chuachan C, Daduang S. Screening of plants acting against Heterometrus laoticus scorpion venom activity on fibroblast cell lysis. J Ethnopharmacol, 2006; 103: 201-07.
6. Gopalakrishnan C, Shankarnarayanan D, Nazimudeen SK, Viswanathan S, Kameswaran L. Anti-inflamatory and CNS depressant activities of xanthones from Calophyllum inophyllum and Mesua ferrea. Ind J Pharmacol, 1980; 12: 181-91.
7. Aruldass CA, Marimuthu MM, Ramanathan S, Mansor SM, Murugaiyah V. Effects of Mesua ferrea leaf and fruit extracts on growth and morphology of Staphylococcus aureus. Microsc Microanal, 2013; 19(1): 254-60.
8. Tiwari P, Nandy S. Screening of antiinflammatory activity of *Mesua ferrea* Linn flower. International Journal of Biomedical Research. 2012;3(5):245-52.
9. Rana AYKM, Khanam JA, Asad-Ud-Daula M. Antineoplastic Screening of Some Medicinal Plants against Ehrlich Ascites Carcinoma in Mice. J Med Sci, 2004; 4: 142-145.
10. Bhide MB, Naik PY, Joshi RS. STUDIES ON ANTI-ASTHMATIC ACTIVITY OF MESUA-FERREA. Bulletin of Haffkine Institute. 1977 Jan 1;5(1):27-30.
11. Sharma S, Sharma AK. Female Anti-Fertility Screening of Plants Mucuna prurita, *Mesua ferrea* and Punica granatum on Rats. Int. J. Pharmaceut. Chem. Res. 2017;3(3).
12. Naik NR, Malleswari D, Indira P. Effect of *Mesua ferrea* flower and Carica papaya seed extracts on estrous cycle of female albino rats for fertility and anti-fertility activity. Biolife. 2015; 3:730-4.
13. Gowthami R, Sharma N, Pandey R, Agrawal A. Status and consolidated list of threatened medicinal plants of India. Genetic Resources and Crop Evolution. 2021 Aug;68(6):2235-63.
14. Sullivan RJ, Allen JS, Otto C, Tiobech J, Nero K. Effects of chewing betelnut (Areca catechu) on the symptoms of people with schizophrenia in Palau, Micronesia. Br J Psychiatry 2000; 177:1748.
15. Chu NS. Betel chewing increases the skin temperature: effects of atropine and propanolol. Neu rosci Lett 1995; 194:1302.
16. Chu NS. Cardiovascular responses to betel chew ing. J Formos Med Assoc 1993; 92:8357.
17. Chu NS. Effect of betel chewing on RR interval variation. J Formos Med Assoc 1995; 94:10610.
18. Prabhu MS, Platel K, Saraswathi G, Srinivasan K. Effect of orally administered betel leaf (Piper betle Linn.) on digestive enzymes of pancreas and intestinal mucosa and on bile production in rats. Indian J Exp Biol 1995; 33:7526.
19. Panda S, Kar A. A dual role of betel leaf extract on thyroid function in male mice. Pharmacol Res 1998; 38:4936.
20. Shrestha J, Shanbhag T, Shenoy S, Amuthan A, Prabhu K, Sharma S, Banerjee S, Kafle S. Antiovulatory and abortifacient effects of Areca catechu (betel nut) in female rats. Indian Journal of pharmacology. 2010 Oct;42(5):306.
21. Roy R.K. *Vaṅgasena Saṃhitā.* Varanasi. *Prachya Prakashan*. 1983. *Strīrogādhikara/*145. 666.
22. Mehreen TS, Ranjani H, Kamalesh R, Ram U, Anjana RM, Mohan V. Prevalence of polycystic ovarian syndrome among adolescents and young women in India. J Diabetol 2021; 12:319-25.
23. Pandey Jaymini. *Hārīta Saṃhitā.* Varanasi. *Chaukhambh*a Publication. 2010. *Tṛtīya Sthāna.* 48/1-4. 463.

24. Dr. Priti Singh Verma. AYURVEDIC MANAGEMENT OF PCOS- A REVIEW. 2018. Volume 7, Issue 7, 236-244.
25. Mishra Amrita, Mhatre Priyanka. AN OVERVIEW OF AYURVEDIC ASPECT OF POLYCYSTIC OVARIAN DISEASE: A CONCEPTUAL APPROACH. 2017,4(7), 274-276.
26. Krishnan, A., and Muthusami, S. (2017). Hormonal alterations in PCOS and its influence on bone metabolism. J. Endocrinol. 232 (2), R99–R113. doi:10.1530/joe16-0405
27. Kshirsagar, P.R., Patil, S.M. (2019). Phytochemistry and Pharmacology of *Mesua ferrea* L. In: Murthy, H., Bapat, V. (eds) Bioactive Compounds in Underutilized Fruits and Nuts. Reference Series in Phytochemistry. Springer, Cham. https://doi.org/10.1007/978-3-030-06120-3_16-1
28. Ansari A, Mahmood T, Bagga P, et al. Areca catechu: A phytopharmacological legwork. Food Frontiers. 2021; 2:163–183. https://doi.org/10.1002/fft2.70
29. K.C Chunekar. *Bhavaprakasha Nighantu*. Varanasi. *Chaukhambha* Bharati Academy. 2013. *Karpuradi Varga*/28. 219.
30. Dr. Indradev Tripathi. *Raja Nighantu*. Varanasi. Chowkhamba Krishnadas Academy. 2010. *Pippalyadi Varga*/176-178. 170
31. Dr. Gyanedra Pandey. *Madanpal Nighantu*. Varanasi. Chowkhamba Orientalia. 2012. *Karpooradi varga*/30. 296.
32. Jharkhande Ojha, Umapati Mishra. *Dhanwantry Nighantu*. 2004. *Shatapushpadi Dwitiya varga* 22/480-49.105.
33. PV Sharma. *Kaideva Nighantu*. Delhi. Chaukhambha Orientalia. 1979. *Aushadhi varga* 413/1345-1347. 249.
34. Kshemraj Shrikrishnadas Sresthina. *Shaligram Nighantu*. Shrudhitwa Prakashita. *Saptamobhaga*. 1980. *Karpuradi varga.* 40.
35. Dr. Gyanendra Pandey. *Shodhal Nighantu.* Varanasi. Chaukhamba Surbharti Prakashan. 2009.
36. Acharya PV Sharma. *Priya Nighantu.* Varanasi. Chaukhambha Surbharati Prakashan. 1995. *Haritkyadi Varga*/95-99. 23.
37. Dr. Goli Penchala. *Sadrasa Nighantu*. Varanasi. Chowkhamba Sanskrit Series Office. 2009. *Katudravya skandha*/5. 84.
38. Shri Manna Lal 'Abhimanyu'. The Amara Kosha of Shri Amara Sinha. 1999. Varanasi. Chowkhambha Vidyabhawan.
39. Arya Daskumarsing. *Mahoushadha Nighantu.* 2006. *Sankhya varga*/13-14.204.
40. K.C Chunekar. *Bhavaprakasha Nighantu.* Varanasi. *Chaukhambha* Bharati Academy. 2013. *Amradi Varga*/45-51. 550.
41. Dr. Indradev Tripathi. *Raja Nighantu*. Varanasi. Chowkhamba Krishnadas Academy. 2010. *Amradi Varga*/233-245. 388
42. Dr. Gyanedra Pandey. *Madanpal Nighantu*. Varanasi. Chowkhamba Orientalia. 2012. *Phaladi Varga*/98-101. 491.
43. Jharkhande Ojha, Umapati Mishra. *Dhanwantry Nighantu*. 2004. *Chandanadi Triteya varga* 19/37-38.132.
44. PV Sharma. *Kaideva Nighantu*. Delhi. Chaukhambha Orientalia. 1979. *Aushadhi varga* 128/514-519. 94.
45. Kshemraj Shrikrishnadas Sresthina. *Shaligram Nighantu*. Shrudhitwa Prakashita. *Saptamobhaga*. 1980. *Amradiphala Varga*. 457.
46. Shodhal Nighantu
47. Acharya PV Sharma. *Priya Nighantu.* Varanasi. Chaukhambha Surbharati Prakashan. 1995. *Haritkyadi Varga*/249. 54.
48. Dr. Goli Penchala. *Sadrasa Nighantu*. Varanasi. Chowkhamba Sanskrit Series Office. 2009. *Kashayadravya skandha*/28. 115.
49. Arya Daskumarsing. *Mahoushadha Nighantu.* 2006. *Swarnadi varga*/48-50.197.
50. Luo ED, Jiang HM, Chen W, Wang Y, Tang M, Guo WM, Diao HY, Cai NY, Yang X, Bian Y, Xing SS. Advancements in lead therapeutic phytochemicals polycystic ovary syndrome: A review. Frontiers in Pharmacology. 2023 Jan 9; 13:1065243.

Source of Support: Nil
Conflict of Interest: None Declared

How to cite this URL:Gupta Priya & Panwar Suman: The combined effect of nagakesara (mesua ferrea linn.) & puga (areca catechu linn.) In pcos (polycystic ovary syndrome): a comprehensive review. International Ayurvedic Medical Journal {online} 2023 {cited September 2023} Available from: http://www.iamj.in/posts/images/upload/560_572.pdf