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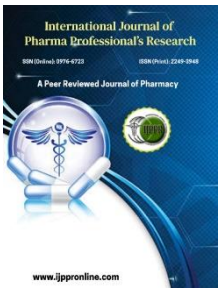

Polyherbal effervescent granules: An abeyant leap in the management of polycystic ovarian syndrome (PCOS)

[1]Payaam Vohra *, [2]Anurag Rane, [3]Sanika Khochare

[1]Department of Pharmacology, Niper Mohali

[2] HKCP, Jogeshwari, Mumbai, India

[3]VIVA Institute OF Pharmacy, Mumbai, India

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Corresponding Author-
Payaam Vohra
payaamvohra@gmail.com
Department of Pharmacology, Niper Mohali

ABSTRACT:
Polycystic ovarian syndrome (PCOS) is a neuroendocrine metabolic disorder characterized by an irregular menstrual cycle. In this current cram, we discuss the significance of herbal remedies in the treatment of PCOS, and the chemical composition, mechanism of action, and therapeutic application of selected herbal drugs against PCOS. Herbal drugs have a promising role in treatment and efficient management of PCOS. We have reviewed various key medicinal herbs and come up with a unique polyherbal formulation and its specialized significance in PCOS management. This evaluation will be of significant use to researchers working on herbal therapies to treat PCOS. Complementary or alternative medicine, such as herbal formulations containing herbal extracts of Turmeric, Aloe Vera, mint, and fenugreek, have been highly regarded as natural sources with low side effects and additional benefits of reducing hyperandrogenism, insulin resistance, and ovarian weight. These plant-based herbal formulations can be effective in this syndrome, which affects serum levels of different hormones and ovarian morphology, representing an opportunity to investigate and discover new bioactive products. Some of the most effective herbs and their formulations that play a critical role in the treatment of PCOS are summarized in this article.

Introduction: The World Health Organization (WHO) stated that PCOS affected over 116 million women worldwide in 2023. One in five Indian women is affected by PCOS.[1] Globally, 1.55 million incident cases of PCOS in women of reproductive age (15–49 years) were reported,

representing an increase in the rate of 4.47% (2.86–6.37%) from 2007 to 2019.[2] PCOS is characterized by clinical and/or biochemical hyperandrogenism and is frequently accompanied by ovulatory dysfunction and polycystic ovaries.[3-5] PCOS is a diagnosis of exclusion, with other androgen excess and related disorders to be excluded. The precise cause of PCOS is unknown, but it is thought to be impacted by both hereditary and environmental factors. Common symptoms include irregular or nonexistent menstrual cycles, high testosterone levels (leading to hirsutism and acne), weight gain or trouble decreasing weight, and probable fertility issues.[6-9]

Why choose Effervescent Granules for PCOS:

The doses are simple to administer. The components (carbonate and acid) act as a pH buffer in the stomach. At 15 minutes, absorption occurs. They can be consumed in liquid form. Patients with swallowing difficulties can readily take these drugs. It is well tolerated in the stomach.CO2 is generated during the effervescent process, which promotes the penetration of active compounds into the paracellular regions.[10-13]

The most common advantages of effervescent pills are:

- Rapid and improved absorption: It dissolves in liquid and the contents are quickly absorbed. Traditional pills disintegrate slowly, resulting in decreased absorption while granules are comparatively faster.
- Excellent compatibility: The effervescent granules have a balanced ratio of acids and carbonates, which form a buffer. It is perfectly compatible with the stomach.
- Increased liquid intake: Effervescent granules provide both the intended medical benefit as well as extra liquid intake. In cases of diarrhea and high temperatures in the summer, drinking effervescent granules with water helps to increase daily liquid intake.
- Benefits for patients with swallowing difficulties: Effervescent granules provide an alternative for these people.
- Easy handling and precise dosing: Effervescent granules dissolve fast, allowing patients to achieve precise dosing.[11-14]

Causes: Recognized four key features of PCOS [15,16]

1) Ovulatory and menstrual dysfunction.
2) Hyperandrogenemia
3) Clinical features of hyperandrogenism.
4) Clinically evident menstrual dysfunction, such as oligomenorrhea or abnormal uterine bleeding, can be observed in a majority of patients with PCOS.

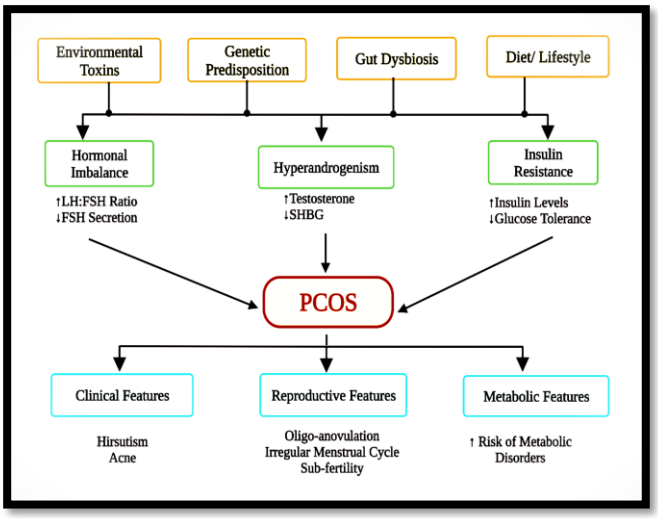

Figure 1: Pathophysiology of PCOS [21]

Currently available treatments:

- Gjönnaess's laparoscopic ovarian drilling (LOD)
- *Recombinant FSH*
- *Clomiphene citrate*
- The use of Metformin
- New insulin Sensitizers
- Vaginal ovarian drilling [TVOD]
- In-vitro maturation of oocytes [17,18,19]

1. **Turmeric: [Curcumin]**Curcuminoids [turmeric resins] are effective in the treatment of PCOS. They shrink the follicular sheath and promote corpus luteum development and the ovulation process. Curcuminoids also reduce progesterone levels in the blood while increasing estradiol levels in women with

PCOS. Additionally, its estrogenic, antihyperlipidemic, antioxidant, and hypoglycemic in nature and these properties are beneficial in controlling PCOS and avoiding ovarian cell malfunction, hence enhancing ovulation and fertility.[10]

2. **Liquorice: {Mulethi}[Liquiritigenin, isoliquiritigenin, liquiritin, isoliquiritin, glabridin and glabrene]** Liquiritigenin, isoliquiritigenin, liquiritin, isoliquiritin, glabridin, and glabrene are major phytoestrogens found in liquorice and they act as potent anti-androgens, maintain estrogen biosynthesis, and help with PCOS treatment by interacting with estrogenic receptors.Glycyrrhiza flavonoids possess estrogenic activity, anti-androgenic effects, and insulin secretion, aiding in PCOS treatment and reducing blood sugar levels.[14]
3. **Spearmint: [Lutein, Rutin, Rosmarinic acid and Caffeic acid]:** Spearmint reduces atretic follicles and increases graafian follicles in PCOS ovarian cysts. It is anti-inflammatory, anti-diabetic, and anti-cancer. Mentha modulates the LH/FSH blood ratio. It may be effective for the treatment of PCOS based on this modulation of LH/FSH in the blood. Spearmint contains anti-androgen effects, according to several preclinical investigations.[8]
4. **Aloe vera: [Aloe emodin and barbaloin]**: In pre-clinical experiments on rats, aloe vera inhibited not only 3-HSD activity and 17-HSD activity, but also ovary weight, resulting in inhibition of total androgen output and it also stimulated the flow of the steroidogenesis pathway, which enhanced estrogen production. In addition to reducing cholesterol synthesis in the liver, it can restore glucose sensitivity, the estrus cycle, and plasma lipoprotein levels. Aloe vera also regulates blood lipid and glucose levels, making it effective in treating PCOS caused by metabolic abnormalities.[13]
5. **Trigonella foenum-graecum: [*β*-pinene, *β*-caryophyllene, camphor and neryl acetate]:** Reduces cyst size as well as ovary volume in women who got it regularly as a dietary supplement for 90 days. Similarly, it lowers the LH/FSH ratio; substantial menstrual cycle maintenance was seen following oral supplementation. Based on these effects, this herb has the potential to be beneficial and substantial for PCOS.[17]

Material And Methodology:

Materials: The chemicals were procured from Vishal chemicals India and few. Complimentary samples of botanicals were obtained from the nearby resources.

Methodology:

Table 1: Botanicals and their phytoconsituents along with mechanism of action in PCOS

Name of plant	Chemical constituent	Mechanism of action
Aloe Vera	Aloin-Emodin	inhibiting inflammatory reactions by the inhibition of IL-6 and IL-8, the reduction of leukocyte adhesion
Turmeric	Curcumin	attenuating inflammatory response of TNF-α stimulated human endothelial cells by interfering with NF-κB
Liquorice	isoliquiritin, and isoflavones	inhibiting pro-inflammatory cytokines and inflammatory mediators that participate in the MAPK signaling

		pathway and promote immune function.
Fenugreek	Flavonoids, Saponins, Alkaloids	activating of insulin synthesis and its releasing from the pancreatic β-cells
Spearmint	Resins, tannins	prevents the inactivation of cortisol, thereby causing a state of excess mineralocorticoid activity or pseudohyperaldosteronism

Table 2: Herbal ingredients used for the treatment of PCOS

Turmeric Biological source: Rhizomes of Curcuma longa **Family:** Zingiberaceae	
Liquorice Biological Source: Roots and stolons of Glycyrrhiza glabra. **Family:** Leguminosae	
Mentha Biological Source: Fresh dried leaves of mentha spicata **Family:** Lamiaceae	
Fenugreek Biological Source: Trigonella foenum **Family:** Fabaceae	
Aloe Vera Biological Source: Dried latex of leaves of it **Family:** Liliacae	

Table 3: Formulation Table

Ingredients	**Quantity**
Citric acid	2.5gm
Sodium Bicarbonate	3.5gm
Sodium Sulphate	2.0 gm
Tartaric acid	1.5gm
Turmeric	150mg
Liquorice	50mg
Aloe Vera	100mg
Mint	40mg
Fenugreek	250mg

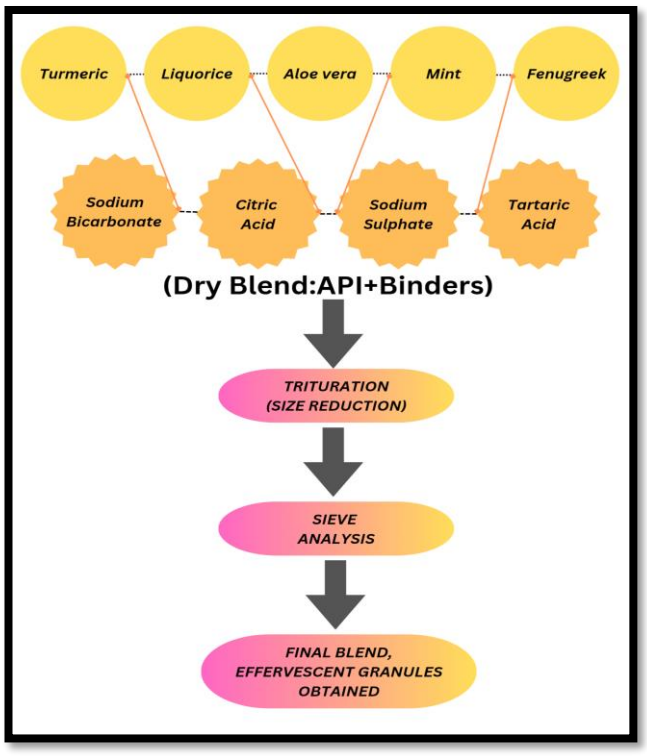

Figure 2: Preparation of Polyherbal mixture into granules [22-24]

Figure 3: Glimpse of Effervescent Granules Preparation

[Front]

[Back]

Figure 4: Product Sachet

Characterization:

1. Tapped Density: The tapped density is a higher bulk density obtained by mechanically tapping a container containing a powder sample. The found tapped density was 660 kg/m3
2. Bulk Density: The bulk density of a substance is the mass-to-volume (including interparticulate void volume) ratio of an untapped powder sample. The found bulk density was 600 kg/m3.

Figure 5: Measurement using Tapped density apparatus

3. Angle of Repose: Through a funnel pass some amount of powder on a graph paper and note the flow rate. Now as shown in figure make the diameters such that they do not pass through a common point and note the radius of each diameter. Calculate the average and apply in the formula

   Tan θ= h/r

   Where h=height of pile of powder

   r=radius of pile

   θ **=25.7**

   This indicates an excellent flow.

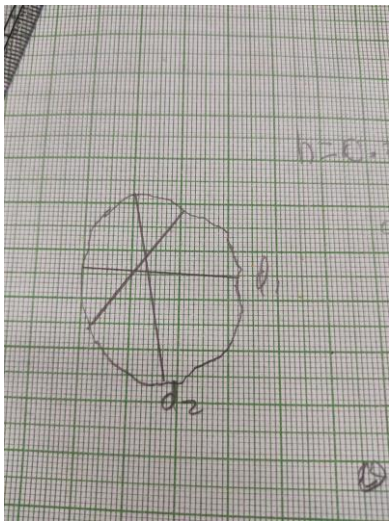

Figure 6: Calculation and Measurement of Angle of Repose

4. Hausner's ratio: The ratio of a powder's tapped bulk density to its poured (loose) bulk density is known as the Hausner ratio. This ratio can be used to determine a powder's flow characteristics. Here, H = tapped density/bulk density = 660/600 = 1.1
5. Carr's Index: Indication of the compressibility of powder. Here, CI = (Tapped Density - Bulk Density/ Tapped Density*100) = 660-600/660*100 = 9.1
6. Effervescence time:

   Take a **specific amount** of the Granules and add it to 150 ml of water and the effervescence time was determined. The effervescent time was 38 seconds
7. Effervescence pH:

   Take a **specific amount** of the Granules and add a few ml of water and measured its Ph using Litmus Paper.pH was found to be slightly acidic.
8. Stability Studies: The sachet pouch was kept in the stability chamber at 75 Relative Humidity and 45 degree Celsius for 1 month. No significant changes were observed.

Figure 7: Accelerated stability studies in the stability chamber

Conclusion: PCOS is the most common hormonal illness in women from adolescence to pre-menopause, with a variety of complications, including infertility, metabolic and cardiovascular issues and long-term health issues that can last a lifetime. Synthetic medications have shown excellent management for the treatment of PCOS, but substantial adverse drug reactions make their value for long-term cure questionable. The current work provides a thorough review of amalgamation herbs that are beneficial for PCOS and related complications. This formulation can bring a paradigm shift in management of PCOS. Hence, more pre-clinical and clinical studies are required to explore the effectiveness of herbal medicines in PCOS.

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