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DEVELOPMENT AND EVALUATION OF HERBAL GUMMIES CONTAINING LIQUORICE, CINNAMON, TURMERIC, AND VITEX FOR PCOS MANAGEMENT

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1. ABSTRACT

Polycystic Ovarian Syndrome (PCOS) is a highly prevalent endocrine-metabolic disorder affecting 6–20% of women of reproductive age, depending on diagnostic criteria. It is clinically characterized by hyperandrogenism, ovulatory dysfunction, and polycystic ovarian morphology (PCOM), with excess ovarian androgen production recognized as a central pathological feature. Although PCOS frequently originates during adolescence, early detection remains challenging due to overlapping normal pubertal changes and heterogeneous clinical presentation. As a consequence, delayed diagnosis can lead to significant reproductive, metabolic, and psychological complications. Women with PCOS exhibit an increased risk of infertility, pregnancyinduced hypertension, pre-eclampsia, and gestational diabetes mellitus, indicating a lifelong impact on reproductive health. Metabolically, PCOS is associated with insulin resistance, compensatory hyperinsulinemia, dyslipidemia, and obesity, which together drive its cardiometabolic sequelae, including an elevated risk of type 2 diabetes mellitus, cardiovascular disease, and non-alcoholic fatty liver disease. The complexity of PCOS pathogenesis is further compounded by the absence of universally accepted diagnostic criteria and variation in phenotypic expression across different ethnic and age groups. Current management strategies prioritize lifestyle modification, including structured exercise, weight reduction, and dietary interventions, as a crucial first-line therapy to improve metabolic and reproductive outcomes. Pharmacological treatments such as combined oral contraceptives, insulin sensitizers, and anti-androgens are employed based on clinical presentation. Early recognition, individualized treatment, and long-term follow-up are essential to mitigate disease progression and improve quality of life in women with PCOS.

KEYWORDS: Polycystic Ovarian Syndrome (PCOS), Hyperandrogenism, Insulin Resistance, Herbal Gummies, Lifestyle Intervention.

1. INTRODUCTION

Polycystic Ovarian Syndrome (PCOS) is one of the most prevalent endocrine-metabolic disorders in women of reproductive age, affecting approximately 6–20% of the global female population depending on the diagnostic criteria used. It is recognized as a leading cause of anovulatory infertility and is associated with a wide spectrum of reproductive, metabolic, and psychological complications. Despite its high prevalence, the exact etiology and pathophysiology of PCOS remain poorly understood. Current evidence suggests a multifactorial origin involving genetic predisposition, neuroendocrine imbalance, insulin resistance, and environmental influences, all of which contribute to excess ovarian androgen secretion, the hallmark feature of the condition.

PCOS is primarily characterized by hyperandrogenism, ovulatory dysfunction, and polycystic ovarian morphology. Many affected women present with menstrual irregularities, anovulation, hirsutism, acne, or androgenic alopecia. Ultrasound imaging may reveal multiple small fluid-filled follicles arranged peripherally within the ovary. Although PCOS can begin shortly after puberty, its clinical presentation is highly heterogeneous and may evolve with age, making early detection difficult.

The diagnosis of PCOS remains challenging due to the absence of universally accepted criteria. The Rotterdam criteria (2003) are widely used in clinical practice and require the presence of at least two of the following: oligo/anovulation, clinical or biochemical hyperandrogenism, and polycystic ovarian morphology on ultrasound. However, the overlap of PCOS features with other endocrine disorders, such as thyroid dysfunction, hyperprolactinemia, and non-classic congenital adrenal hyperplasia, complicates differential diagnosis. Moreover, women with PCOS frequently exhibit metabolic disturbances, including insulin resistance, central obesity, dyslipidemia, and an increased lifetime risk of type 2 diabetes and cardiovascular disease. Psychological comorbidities such as anxiety, depression, and reduced self-esteem further contribute to disease burden and impair quality of life.

Lifestyle modification, especially weight reduction, dietary intervention, and physical activity, remains the first-line therapeutic strategy and has demonstrated significant benefits in improving metabolic and reproductive outcomes. Pharmacological treatments are individualized based on clinical presentation and fertility goals. However, the lack of targeted therapies and incomplete understanding of disease mechanisms underscore the need for continued research. This mini-review aims to summarize current knowledge on clinical manifestations, diagnostic challenges, and management approaches in PCOS, with an emphasis on emerging therapeutic strategies.

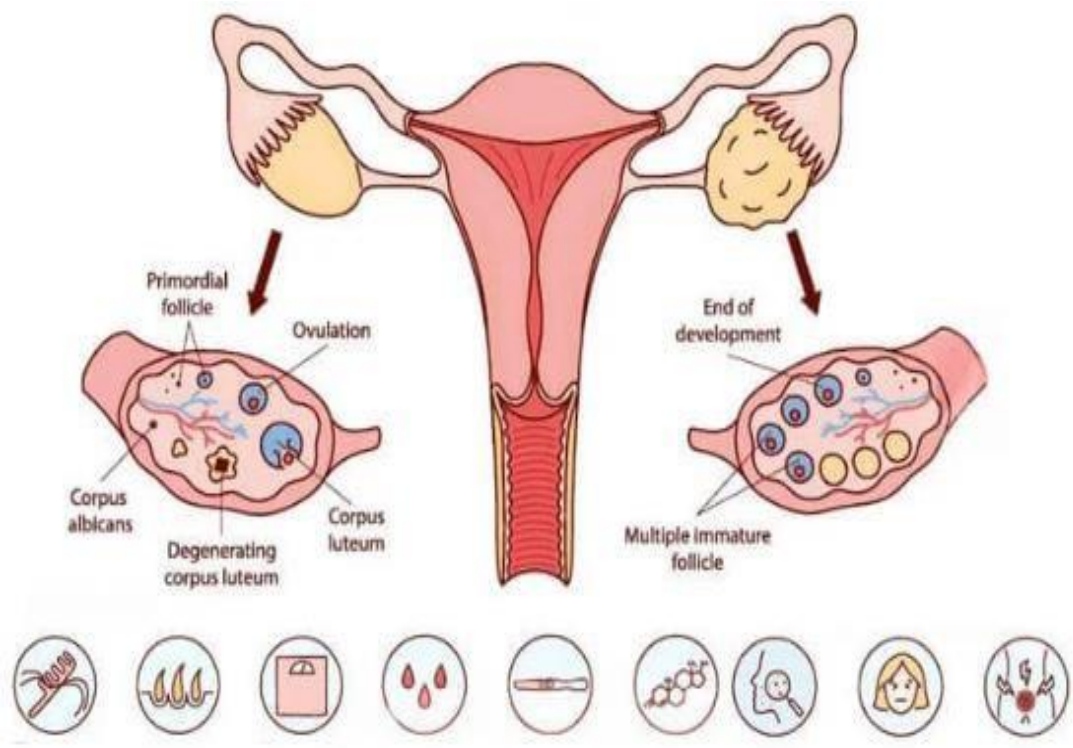


Figure 1.1: Digram Of Pcos Symptoms.

2. Pathophysiology

The pathophysiology of polycystic ovarian syndrome (PCOS) is complex and remains incompletely understood, but it is widely accepted to involve a multifactorial interplay between neuroendocrine, metabolic, and intrinsic ovarian dysfunction. One of the fundamental abnormalities lies in the hypothalamic–pituitary–ovarian (HPO) axis, where increased frequency and amplitude of gonadotropin-releasing hormone (GnRH) pulses preferentially stimulate luteinizing hormone (LH) secretion over follicle stimulating hormone (FSH). The resulting elevation in the LH:FSH ratio drives excess androgen synthesis by ovarian theca cells, while inadequate FSH levels impair follicular maturation, ultimately leading to chronic anovulation.

Hyperandrogenism is central to PCOS pathophysiology, contributing not only to clinical manifestations such as hirsutism, acne, and androgenic alopecia but also to abnormal folliculogenesis. Parallel to neuroendocrine alterations, insulin resistance and compensatory hyperinsulinemia—present in up to 75% of women with PCOS, including those with normal BMI—play a critical pathological role. Insulin acts synergistically with LH to enhance androgen production and simultaneously suppresses hepatic synthesis of sex hormone–binding globulin (SHBG), resulting in elevated levels of free circulating androgens. This establishes a self-reinforcing cycle in which androgen excess further aggravates metabolic dysfunction.

Another important contributor is the persistently elevated concentration of antiMüllerian hormone (AMH) in PCOS patients. AMH inhibits FSH-mediated follicle selection, thereby promoting follicular arrest and accumulation of multiple immature follicles. This process is responsible for the characteristic polycystic ovarian morphology (PCOM) observed via ultrasonography. Additionally, disrupted feedback regulation of estrogen and progesterone on the hypothalamus perpetuates abnormal GnRH pulsatility and chronic anovulation.

Collectively, current evidence suggests that PCOS arises from the convergence of neuroendocrine dysregulation, hyperandrogenism, insulin resistance, and ovarian dysfunction, which together explain its heterogeneous clinical presentation and variable metabolic risk profile. Understanding these interrelated mechanisms remains essential for the development of targeted therapeutic strategies.

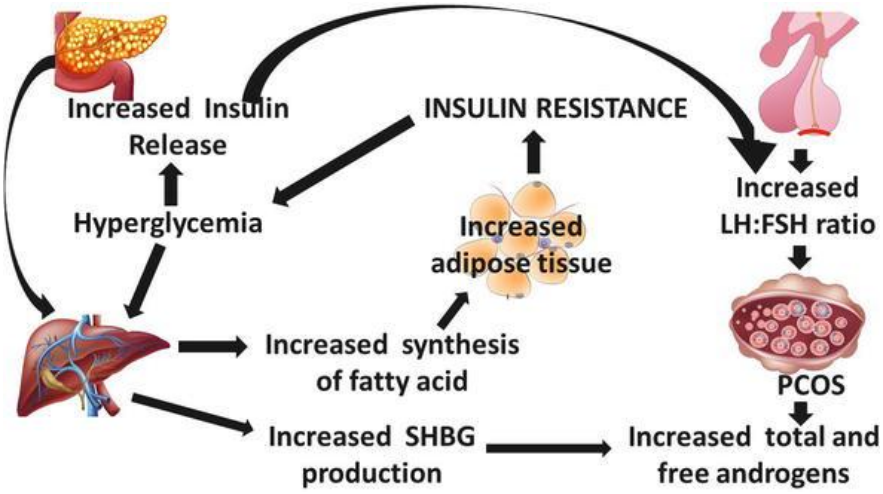


Figure 1.2: pathophysiology of PCOS.

4.

Metabolic Conditions

Metabolic dysfunction is a key component of polycystic ovarian syndrome (PCOS), with insulin resistance and compensatory hyperinsulinemia serving as central pathological features. Insulin resistance is present in 50–75% of women with PCOS, regardless of body weight, and contributes to enhanced ovarian androgen production and reduced hepatic synthesis of sex hormone–binding globulin (SHBG), thereby increasing free circulating androgens. Women with PCOS frequently exhibit central (visceral) obesity, dyslipidemia (elevated triglycerides and LDL, reduced HDL), and impaired glucose tolerance, placing them at significantly higher risk of type 2 diabetes mellitus, metabolic syndrome, and cardiovascular disease compared to the general female population. In addition, the prevalence of non-alcoholic fatty liver disease (NAFLD) and systemic low-grade inflammation is markedly increased in PCOS. These metabolic abnormalities not only worsen reproductive dysfunction but also contribute to long-term morbidity, making early identification and lifestyle intervention essential.

Table 1.1: Contain Features That Can Be Found In Insulin Resistance And Cardiovascular Disease

Feature	Insulin Resistance	Cardiovascular Disease
Prevalence	50-75% PCOS women	Risk increases with age
Key Mechanism	Reduced tissue sensitivity to insulin leading Hyperinsulinemia	Dyslipidemia, inflammation, endothelial dysfunction
Major impact	↑ Androgen, ↓ SHBG, ↑ Diabetes risk	↑ Risk of metabolic syndrome, Hypertension, stroke
Seen in Lean PCOS?	Yes	Yes, even without obesity
Management	Lifestyle modification, metformin	Risk screening, lipid/glucose control

i. Insulin Resistance

Insulin resistance (IR) is considered the core metabolic abnormality in polycystic ovarian syndrome and is present in approximately 50–75% of affected women, including those with normal body mass index (BMI). The defect is partly intrinsic, as studies show impaired insulin signaling at the post-receptor level in skeletal muscle and adipose tissue of PCOS patients. Hyperinsulinemia develops as a compensatory response to IR and plays a critical role in disease pathogenesis by acting synergistically with luteinizing hormone (LH) to stimulate ovarian theca cells to produce excess

androgens. Insulin also suppresses hepatic synthesis of sex hormone–binding globulin (SHBG), leading to increased levels of bioavailable testosterone and worsening hyperandrogenic symptoms.

In addition to reproductive effects, insulin resistance contributes to visceral adiposity, impaired glucose tolerance, and early-onset type 2 diabetes mellitus, with estimates showing a five- to tenfold increased risk of diabetes in women with PCOS compared to healthy controls. The severity of insulin resistance is greater in obese PCOS patients, but even lean phenotypes exhibit significant metabolic dysfunction, highlighting that IR is not solely weight-dependent. This makes early metabolic screening and lifestyle intervention crucial for all PCOS phenotypes.

ii. Cardiovascular Disease

Women with PCOS display multiple cardiometabolic abnormalities that significantly elevate their long-term risk of cardiovascular disease (CVD). Insulin resistance, chronic low-grade inflammation, oxidative stress, and endothelial dysfunction create a proatherogenic environment. Dyslipidemia is highly prevalent, characterized by increased triglycerides and LDL cholesterol, decreased HDL cholesterol, and qualitative LDL changes that promote plaque formation. Central obesity, frequently observed in PCOS, further aggravates the inflammatory and metabolic burden.

PCOS is strongly associated with metabolic syndrome, with affected women having a two- to threefold higher prevalence compared to age-matched controls. Studies also report increased carotid intima–media thickness, arterial stiffness, impaired flowmediated vasodilation, and subclinical atherosclerosis. These abnormalities are often present even in young women before overt CVD becomes clinically evident. While PCOS is not yet officially classified as a cardiovascular risk equivalent like diabetes, growing evidence suggests that the disorder contributes to an elevated lifetime risk of hypertension, ischemic heart disease, and stroke. Therefore, long-term monitoring of lipid profile, blood pressure, and glucose metabolism is strongly recommended in PCOS management guidelines.

5. Genetic Factor

The genetic contribution of PCOS plays a major role in its pathogenesis. Studies suggest that the loci identified by genome-wide association studies (GWAS) account for less than 10% of its high heritability.However, it has been consistently demonstrated that daughters of women with PCOS have a significantly higher risk of developing the condition compared to daughters of unaffected women. For example, a large Swedish cohort study involving more than 29,000 participants found that daughters of PCOS mothers had five-fold higher risk of developing PCOS compared to controls.

PCOS represents a highly heterogeneous and complex condition, with genetic backgrounds varying both across and within families, yet converging on related biological pathways. It is recognized as a polygenic disorder influenced by multiple susceptibility genes. Genes encoding enzymes involved in the steroidogenic pathway are strong candidates, including CYP11A, CYP17, and CYP19. Specifically, CYP11A encodes the cytochrome P450 side-chain cleavage enzymes, CYP17 encodes cytochrome P450 17-hydroxylase/17,20-desmolase, and CYP19 encodes aromatase. These genes are implicated in the altered steroidogenesis observed in PCOS. In addition, theca cells in the ovaries of women with PCOS exhibit elevated enzyme activity, leading to increased androgen production. This results in higher testosterone levels and disruption of the LH/FSH ratio, further contributing to the syndrome's pathophysiology.

Beyond candidate genes, GWAS have identified specific susceptibility loci in different populations. In Korean women, the strongest association was found on chromosome 8q24.2, with additional signals at 4q35.2,16p13.3,4p12,3q26.33,9q21.32,11p13, and 1p22. The strongest signal was located upstream of KHDRBS3, a gene linked to telomerase activity, which may be involved in PCOS development. In European women, novel loci were mapped to chromosome 8p23.1 and 11p14.1, along with a significant association at 9q22.32. In Han Chinese women, robust associations were observed with three loci: 2p16.3,2p21, and 9q33.3.

These findings provide new insight into the pathogenesis of PCOS, highlighting the strong role of genetic factors and offering evidence of common as well as populationsspecific susceptibility loci.

1. Family History

- First-degree relatives (mother, sister) often have PCOS.
- Risk is **5–10 times higher** in women with affected relatives.
- Suggests autosomal dominant pattern with variable expression.

2. Genes Related to Gonadotropin Regulation

These genes affect how ovaries respond to hormones.

Gene	Role
FSHR (Follicle Stimulating Hormone Receptor)	Alters ovarian response to FSH → anovulation
LHCGR (Luteinizing Hormone/Choriogonadotropin Receptor)	Increases androgen production

3. Genes Related to Insulin Resistance These contribute to metabolic features:

Gene	Role
INSR (Insulin Receptor Gene)	Reduced insulin sensitivity → hyperinsulinemia
PPAR-γ gene	Controls lipid metabolism → obesity risk
IRS-1 / IRS-2 (Insulin receptor substrate genes)	Impaired insulin signaling

4. Genes Controlling Androgen Production These lead to excess male hormones:

Gene	Role
CYP17A1	Increases androgen synthesis
CYP11A1	Affects steroid hormone pathway
AR Gene (Androgen Receptor)	Affects androgen sensitivity → hirsutism severity

5. Genes Related to Inflammation

PCOS is associated with chronic low-grade inflammation.

Gene	Role
TNF-α	Increased inflammation → insulin resistance
IL-6	Systemic inflammation

6. Genetic Variants Identified by Genome-Wide Association Studies (GWAS)

Modern studies show involvement of.

- **DENND1A** (involved in androgen production)
- **THADA** (energy metabolism)
- **FSHB** (gonadotropin regulation)
- **YAP1** (ovarian follicle development)

These genes are consistently linked to PCOS in multiple populations.

6. Age Group Factor

Polycystic Ovarian Syndrome (PCOS) is primarily a reproductive-age disorder, with most symptoms appearing at the onset of menstruation or during adolescence. In adolescence, the clinical features often overlap with normal pubertal changes,such as irregular menstrual cycles, acne, and weight fluctuation, which complicates early diagnosis. To better understand PCOS across age groups, studies measuring androgen concentrations in women have shown that those aged 18-29 years exhibit higher androgen secretion and present with clinical features such as acne, hirsutism, and alopecia more frequently. In contrast, women above 30 years display lower androgen levels and reduced prevalence of these features. This highlights hyperandrogenism as a cornerstone of PCOS and emphasizes the role of age in influencing its clinical and biochemical manifestations.

However, the decline in hyperandrogenic features after 30 years does not fully explain the increased prevalence of infertility and abdominal obesity in women aged 30-40 years. In this age group, infertility risk is compounded by both advancing maternal age and persistent ovulatory dysfunction. Furthermore, metabolic complication—including insulin resistance, dyslipidemia and cardiovascular disorders–becomes more prominent. Beyond the reproductive years,during perimenopause and postmenopause, menstrual irregularities naturally diminish, but the long-term cardiometabolic risks associated with PCOS, such as hypertension, type 2 diabetes, and coronary artery disease, persist or even worsen. Chronic anovulation also predisposes women to endometrial hyperplasia and, in severe cases, endometrial carcinoma.

Across all age groups, PCOS significantly affects psychological well-being. Adolescents often face self-esteem issues due to visible features like acne, hirsutism, or alopecia, while adult women may struggle with depression, anxiety, and reduced quality of life due to infertility, weight gain, and chronic health concerns. Taken together, these findings demonstrate that PCOS is a dynamic condition, with its clinical, metabolic, and psychosocial manifestations evolving with age–shifting from reproductive and cosmetic concerns in adolescence to fertility challenges in adulthood and metabolic risks in later life.

7. Management

The management of Polycystic Ovary Syndrome (PCOS) is comprehensive and individualized, targeting metabolic, reproductive, dermatological, and psychological components of the disorder. The cornerstone of therapy is lifestyle modification**,** including calorie-controlled diets, regular aerobic and resistance exercise, and weight reduction, which improve insulin sensitivity, restore ovulation, reduce androgen levels, and prevent long-term metabolic complications. Pharmacological interventions are tailored to specific symptoms: combined oral contraceptive pills are the first-line treatment for menstrual irregularities, acne, and hirsutism; they regulate the menstrual cycle, lower androgen levels, and protect against endometrial hyperplasia. Metformin, an insulin-sensitizer, is widely used in overweight or insulin-resistant women to improve glucose tolerance, induce ovulation, support weight loss, and reduce cardiovascular risk. For infertility, ovulation induction agents such as letrozole (first line) or clomiphene citrate are used, and in resistant cases, gonadotropin**s** or IVF may be required. Hyperandrogenic symptoms like hirsutism and acne may be addressed with anti-androgens (spironolactone, finasteride) in combination with OCPs, while dermatologic methods such as laser hair removal or topical therapies provide additional support. Weight-loss

medications (e.g., orlistat, GLP-1 agonists) and bariatric surgery may be considered in severe obesity with metabolic complications. Mental health is a key component of management, as PCOS is strongly associated with anxiety, depression, body-image issues, and reduced quality of life. Psychological support, behavioral therapy, and stress-reduction practices are therefore essential. Supplements like myo-inositol**,** D-chiro inositol**,** and vitamin D have shown benefits in improving insulin sensitivity and menstrual regularity. Ultimately, PCOS management requires a multidisciplinary approach involving gynecologists, endocrinologists, dermatologists, dieticians, and mental-health professionals to address both immediate symptoms and long-term risks such as diabetes, dyslipidemia, cardiovascular disease, and endometrial carcinoma. Continuous follow-up, patient education, and personalized long-term strategies are crucial to achieving optimal health outcomes.

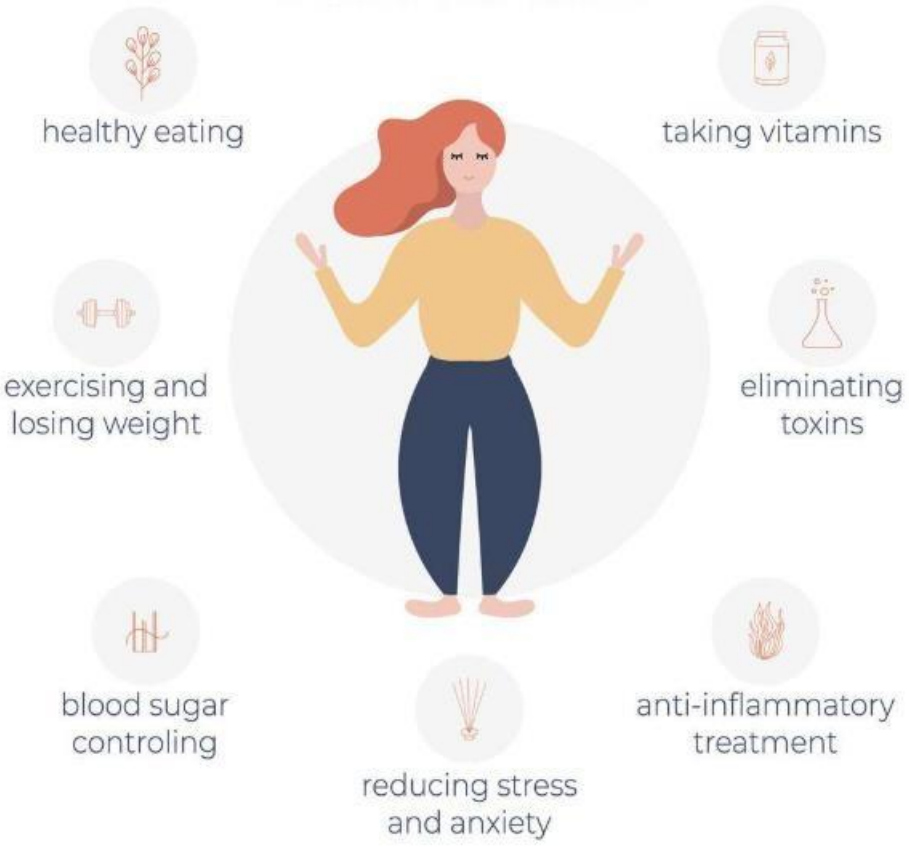


Figure 1.3: Pcos Healing Cycle.

8. Life Style Intervention

The most effective and first-line treatment approach for PCOS is lifestyle intervention, as patients often experience physiological and psychological challenges that compromise the quality and normalcy of day-to-day life.

Women with PCOS have more prevalence of overweight and obesity and higher rate of longitudinal weight gain; therefore,lifestyle management through exercise and diet is essential to prevent further progression of the condition. Obesity in PCOS women can be the cause of worsened condition, so managing weight or weight loss is an important step for managing metabolic, hormonal, reproductive, cardiovascular and psychological features. Lifestyle intervention includes appetite regulation and energy expenditure, fatigue and sleep disorder management, Psychological management includes self-management, Depression and body image distress,health literacy, working on this factor for the improvement of psychological health is helpful for treatment.

i. Diet management include

Transitioning from an unbalanced diet to a structured meal plan with balanced macronutrient distribution—approximately 40% carbohydrates, 30% protein, and 30% healthy fats—plays a vital role in improving insulin sensitivity and maintaining metabolic homeostasis. A controlled carbohydrate intake helps prevent postprandial glucose spikes, while adequate protein supports satiety, muscle maintenance, and metabolic rate. Healthy fats contribute to hormonal balance and reduce inflammation.

In addition to macronutrient composition, consistent meal timing is crucial for regulating appetite hormones such as insulin, leptin and ghrelin. Avoiding prolonged fasting or irregular eating patterns prevents fluctuations in blood glucose levels and promotes stable energy

metabolism. Together, these dietary strategies support weight regulation, reduce hyperinsulinemia, and improve long-term metabolic outcomes in individuals with PCOS

ii. Physical activity

Physical activity serves as a cornerstone in the management of PCOS, particularly due to its profound impact on metabolic function and hormonal regulation. Regular exercise helps improve insulin sensitivity, which reduces compensatory hyperinsulinemia and subsequently decreases ovarian androgen production.

Aerobic activities such as walking, running, swimming, and cycling enhance cardiovascular health and promote glucose utilization, reducing the risk of obesity and type 2 diabetes. Incorporating resistance training supports the development of lean body mass, increases resting energy expenditure, and further improves insulin action at the cellular level.

Mind–body exercises, especially yoga and stretching, have shown additional benefits by lowering cortisol, alleviating stress, improving autonomic balance, and supporting menstrual regulation—factors that play a significant role in PCOS-related hormonal imbalance.

Evidence suggests that a structured routine combining aerobic training (minimum 150 minutes per week), strength training (2–3 sessions), and flexibility or relaxation-based practices offers the most comprehensive benefits in controlling metabolic disturbances, improving ovulatory function, and enhancing overall quality of life.

iii. Sleep hygiene

Sleep disturbances are highly prevalent among women with PCOS and are often associated with insulin resistance, mood dysregulation, daytime fatigue, and altered circadian rhythms. Poor sleep quality further aggravates hormonal imbalance by increasing cortisol levels and worsening metabolic dysfunction. Common issues include insomnia, delayed sleep onset, and obstructive sleep apnoea (OSA), especially in overweight and obese women with PCOS.

Proper sleep management is essential and can significantly improve hormonal balance, mental well-being, and overall quality of life. Key approaches include.

1. Sleep Hygiene Techniques (First-Line Non-Pharmacological Management)

a. Maintaining a fixed sleep–wake cycle (going to bed and waking up at the same time daily)
b. Avoiding screen exposure (blue light) at least 1 hour before bedtime
c. Limiting caffeine and heavy meals at night
d. Keeping the bedroom environment dark, cool, and quiet
e. Restricting daytime naps, especially in late afternoon
f. These behavioral adjustments are considered the most commonly recommended treatment for sleep issues in PCOS.

2. Relaxation and Mind-Body Practices

a. Yoga, meditation, and deep breathing reduce sympathetic overactivity and cortisol levels
b. Progressive muscle relaxation helps induce sleep
c. Mindfulness-based stress reduction (MBSR) supports emotional balance and improves sleep quality

3. Natural Sleep promoting Remedies

Herbal teas such as chamomile, lavender, acts as a mild anxiolytic and promote sleep.

4. Medical Suppport Professional

a. Consultation with a physician to screen for sleep apnea, restless leg syndrome, or mood disorders
b. Cognitive Behavioral Therapy for Insomnia (CBT-I) — considered the most evidence-based treatment for chronic insomnia.
c. In severe cases, short-term use of sleep medications may be considered under strict medical supervision.

Psychological health

Polycystic Ovary Syndrome (PCOS) significantly impacts the overall physiological health of affected women due to its complex interplay of hormonal, metabolic, and reproductive dysfunctions. The condition is characterized by chronic anovulation, hyperandrogenism, and polycystic ovarian morphology, which together disrupt normal reproductive physiology and lead to irregular menstrual cycles, infertility, and abnormal endometrial growth. Elevated androgen levels influence skin and hair physiology, resulting in acne, hirsutism, and androgenic alopecia. Metabolically, PCOS is strongly linked with insulin resistance, compensatory hyperinsulinemia, and increased visceral fat deposition, predisposing women to obesity, type 2 diabetes, dyslipidemia, and hypertension. These metabolic alterations also increase long-term cardiovascular risks. Additionally, low-grade systemic inflammation, oxidative stress, and dysregulated adipokines further impair endocrine and metabolic homeostasis. PCOS also influences psychological physiology, with higher rates of anxiety, depression, body-image disturbances, and sleep abnormalities like obstructive sleep apnea. Overall, the physiological health burden in PCOS extends far beyond reproductive issues, involving multiple organ systems and contributing to long-term chronic disease risk.

9. Medical intervention

Medical intervention, alongside lifestyle intervention is essential to prevent further deterioration of condition. Pharmacological or medical intervention used in the treatment includes oral contraceptives (OCs), Metformin, TZDs, Insulin sensitizing agents, Anti-androgen agents, GLP-1 Receptor agonists , Antioxidants.

1. Oral Contraceptives, Metformin,TZDs, Insulin sensitizing agents,
GLP-1 Receptor agonists
Oral contraceptives are tailored according to the patient's need, containing estrogen and progesterone hormone combination for balancing hormone level in the body also to minimise the secretion of androgen, in case of Hyperandrogenism.

Metformin and TZDs are used for patient with insulin insensitivity, it enhances the insulin sensitivity and controlling the excess androgen level, AS for Metformin it is primary medication for the treatment of insulin insensitivity and for mitigating Hyperandrogenism and Thalizolidines(TZDs) has same properly as Metformin but it's used is Restricted because of side effect like weight gain,obesity,increased risk of Hypoglycemia and potential of cardiovascular risk. GLP-1 receptor agonists present a novel therapeutic approach for PCOS management, facilitating weight loss, improving insulin sensitivity, and regulating glucose metabolism. Emerging evidence indicates their potential effectiveness for obese patients with PCOS. Antiandrogen like spironolactone and cyproterone acetate used for reducing the Excess androgen level and also alleviate symptoms like hirsutism and acne but, its long term use without proper Medical intervention can lead to side effects like breast tenderness,breast enlargement and liver toxicity.

2. Antioxidants
Antioxidants shows promising results in reducing oxidative stress along with improving the ovarian environment, promoting follicular maturation and increasing the number of oocytes, but also regulate lipid and glucose metabolism, as well as vascular endothelial cell function which helps in obesity and chronic complication in PCOS women.

Table 1.2: Medical Intervention Used For The Pcos Treatment.

Intervention Type	Medications / Examples	Primary Purpose	When It Is Used
1. Hormonal Therapy	Combined Oral Contraceptive Pills (OCPs)	Regulate periods, reduce androgen levels (acne, facial hair), protect endometrium	Irregular cycles, acne, hirsutism, non-pregnancy planning
	Progesterone therapy (cyclic or continuous)	Induces withdrawal bleeding, prevents endometrial hyperplasia	Women who cannot take OCPs
2. InsulinSensitizing Agents	**Metformin**	Improves insulin resistance, helps weight control, regulates periods	Overweight patients, insulin resistance, irregular cycles
3. Ovulation Induction Drugs	**Letrozole** (first line)	Stimulates ovulation for pregnancy	Women trying to conceive
	Clomiphene citrate	Helps ovulation	Alternative to letrozole
	Gonadotropins	Strong ovulation induction	If oral drugs fail
4. AntiAndrogen Drugs	**Spironolactone**	Reduces hirsutism, acne	If OCPs are insufficient; not used in pregnancy
	Finasteride / Flutamide	Reduce excess hair growth	Specialistprescribed
5. Weight-Loss Medications	Orlistat, GLP-1 agonists (e.g., Liraglutide)	Supports weight reduction, improves cycles & metabolic health	In obese or overweight PCOS with difficulty losing weight
Intervention Type	**Medications / Examples**	**Primary Purpose**	**When It Is Used**
6. Dermatology Treatments	Topical retinoids, antibiotics, laser hair removal	Treat acne & excessive hair	For cosmetic symptoms
7. Metabolic Management	Statins	Lower high cholesterol	PCOS with dyslipidemia
8. Infertility Advanced Treatment	IVF, controlled ovarian stimulation	Helps pregnancy	When ovulation drugs fail
9. Surgical Intervention	**Laparoscopic Ovarian Drilling (LOD)**	Reduces androgen production, induces ovulation	Used rarely; resistance to medications
10. Supportive Supplements	Myo-inositol, Dchiro inositol, Vitamin D	Improve insulin sensitivity, cycle regulation	As supportive therapy

❖ FORMULATION

➢ Materials

Fresh herbal constituent of liquorice, cinnamon, turmeric and vitex (to be collected from the Gandhinagar region of Gujrat.

➢ Methods

1. Collection and authentication of the liquorice, cinnamon, turmeric and vitex
2. Extraction of the liquorice, cinnamon, turmeric and vitex components by the Soxhlet extraction method
3. Identification of phytoconstituents using preliminary methods
4. Phytochemical screening using quantitative, qualitative, and chromatographic analysis
5. Formulation and evaluation of herbal gummies
6. Biological evaluation using in vitro evaluation techniques
7. Analyse the data using statistical software

➢ Chemicals and reagents

Table 1.3: list of chemicals and reagents used.

S.NO	Name of chemicals	Manufacture/supplier
1	Hexane	Merck
2	Ethyl acetate	SD fine/LR
3	Acetone	Avantor performance materials
4	Chloroform	Rankem
5	HCL	ACS Grade
6	NaOH	Finar Chemicals Limited
7	Agar-Agar	RCFL limited
8	Glycerol	LOBA Chemie
9	Sodium benzoate	LOBA Chemie
10	Citric acid	LOBA Chemie
11	Dimethyl sulfoxide (DMSO)	Sigma-Aldrich (Merck)
12	Hydrogen peroxide	Evonik Industries
13	DPPH (2,2-Diphenyl-1-picrylhydrazyl)	Thermo Fisher Scientific
14	Ethanol	Merck (Sigma-Aldrich)
15	Ascorbic acid	Muby Chemicals
16	Dichlorofluorescein Diacetate	Biotium
17	DMEM (Dulbecco's Modified Eagle Medium)	Biosera
18	Fetal bovine serum	Atlanta Biologicals
19	EDTA	Central drug house (P) LTD
20	N-acetylcysteine (NAC)	Cayman Chemical
21	MTT (3,4,5 Dimethylthiazol 2-yl)-2,5-diphenyltetrazolium bromide) reagent	Biotium
22	Alsever solution	Krebs Biochemicals & Pharmaceuticals
23	Pectin	K. K. Agarwal & Co.
24	Sorbitol	Roquette India Pvt. Ltd.
25	Honey	Dabur India Ltd
26	TLC silica gel 60 F254	Merck (Sigma-Aldrich)

➢ Instrumentation

Table 1.4: list of instruments used.

S. No.	Name of equipment	Manufacturer/supplier
1.	HPTLC	CAMAAG
2	LCMS	Agilent Technologies
3	UV-VIS Spectrometer	Shimadzu UV-1800
4	Water bath	Samarath Electronics
5	Hot air oven	SICO
6	Rotary evaporator	RotevaMedica instrument
7	TLC chamber	Merck (MilliporeSigma)
8	UV chamber	Spectroline (Spectronics Corporation)
9	Centrifuge	Thermo Fisher Scientific
10	Heating mantle	Prefit India

➢ **Pharmacognostical studies**

The organoleptic characteristics of the fresh herbal constituent of liquorice, cinnamon, turmeric and vitex, including taste, odour, color, and texture, were assessed through repeated observations as necessary and systematically recorded.

➢ **Collection and Authentication of Plant**

The plant is collected from the Gandhinagar region of the Gujrat, and the plant is authenticated by the Botanical Survey of India, western Regional Centre, Gujrat, India.

Figure 1.4: Liquorice, Cinnamon, Turmeric, Vitex.

➢ **Drying and Crushing of liquorice, cinnamon, turmeric and vitex**

The herbal constituent liquorice, cinnamon, turmeric and vitex were initially subjected to shade drying at room temperature to preserve their phytoconstituents and prevent degradation due to direct sunlight, as shown in (Figure 5.1). Once thoroughly dried, the herbal constituent was mechanically ground using a suitable grinder to obtain a fine powder, which was then stored in an airtight container for further pharmacognostical and phytochemical analysis.

➢ **Macroscopy and Microscopy evaluation**

Macroscopic examination involves observing the physical properties of various plant parts, including their size, shape, colour, and texture. These characteristics are necessary for the preliminary identification and evaluation of plant material. The cellular arrangement and structure are examined under a microscope, which reveals minute characteristics like trichomes, vascular bundles, and stomatal patterns. To guarantee the potency and purity of the plant material used in medical medicines, this level of examination is essential.

➢ **Physicochemical Analysis of liquorice, cinnamon, turmeric and vitex herbal constituent**

Physicochemical qualities, such as total ash, water, and alcohol soluble extractive, and loss upon drying at 105°C, were examined in triplicate using the Indian Pharmacopeia recommended Standard procedures.[69] Loss in drying: The crude liquorice, cinnamon, turmeric and vitex sample was weighed, placed in a crucible for the night, and the reading was taken. The guidelines issued by the WHO serve as the basis for this method. Water soluble extractive value: The polarity of the given sample was used to determine its extractive value. The sample was carefully weighed, placed in a conical flask, and stired continuously for the whole night. Alcohol soluble extractive value: The polarity of the given sample was used to determine its extractive value. The sample was carefully weighed, placed in a conical flask, and stirred continuously for the whole night. (All these procedures are given as per WHO guidelines).

❖ **Phytochemical Tests**

➢ **Phytochemical Tests of herbal constituent Extract**

This plant was subjected to a phytochemical analysis to identify its active constituents, which include alkaloids, protein, saponin, resin, tannin, carbohydrates, flavonoids, and steroids.

➢ **Tests for alkaloids**

- **Mayer's test:** A solution containing potassium mercury iodide (mayer's reagent) was added to the filtered extracts. If alkaloids were present, a yellow precipate would form.
- **Wagner's Test:** A solution containing iodine in potassium iodide (Wagner's reagent) was added to the filtered ectracts. A brown or reedish precipitate would indicate the presence of alkaloids.
- **Dragendorff's Test:** Another specific reagent solution containing potassium bismuth iodide (Dragendorff's reagent) was added to the filtered extracts. A red precipitate would signal the presence of alkaloids.
- **Hager's test:** In a test tube containing 1 ml of extract, a few drops of Hager's reagent were added. Appearance of yellow color or buff coloured precipitate indicates the presence of alkaloids.

➢ **Tests for Flavonoids**

- **Shinoda test:** Add a few drops of dilute HCI to 1 mL of the ethyl acetate extract; the appearance of a red colour indicates the presence of flavonoids.
- **Vanillin HCl test:** Add 2 mL of Vanillin-HCI reagent to 1 mL of the ethyl acetate extract; a pink or red colour indicates the presence of flavonoids.
- **Ammonia test:** Add a few drops of dilute ammonia solution to 1 mL of the ethyl acetate extract; the formation of yellow precipitates indicates the presence of flavonoids.

➢ **Tests for Steroid**

- **Salkowski test:** Add 2 mL of the plant extract to a test tube and carefully add 2 mL of concentrated sulfuric acid (HOSO) along the sides of the tube; the

formation of a reddish-brown colour at the interface indicate the presence of steroids.

➢ **Tests for Cardiac Glycosides**

- **Baljet test:** Add a solution of the ethyl acetate extract solution into sodium piecrate solution; the formation of a yellow to orange colour indicates the presence of cardiac glycoside

➢ **Test for Reducing Sugars**

- **Fehlings's reagent:** Add 2ml of the test sample to a test tube and mix with 2 mL of Fehling's reagent; the formulation of a red precipitate indicates the presence of reducing sugars.

➢ **Test for Tannins**

- **Ferric chloride test**: Add a few drops of 1% ferric chloride (FeCI) solution to 2 mL of the test sample; the appearance of a brownish-green or blue-black colour indicates the presence of tannins.

➢ **Test for Carbohydrates**

- **Benedict's reagent test:** Add 2 mL of Benedict's reagent to 2 mL of the test sample and heat the mixture in a boiling water bath for 2-5 minutes; the formation of a green, yellow, or brick-red precipitate indicates the presence of reducing carbohydrates.

➢ **Test for Saponins**

- **Saponin test:** Add 1 mL of the extract solution to 19 mL of distilled water to make a total volume of 20 mL; the formation of stable foam upon shaking indicates the presence of saponins.

❖ **Thin Layer Chromatography**

Thin Layer Chromatography (TLC) is a simple and effective technique used to serrate and identify the different compounds present in a plant extract. For liquorice, cinnamon, turmeric and vitex, detecting the medicinal plant known for its therapeutic properties, TLC helps in presence of bioactive constituents. of the plant. To perform the test, a small amount thin extract is spotted near the bottom of a TLC plate, which is coated with a layer of silica gel. The plate is then placed in a developing chamber containing a suitable solvent. As the solvent rises the plate by capillary action, it carries the components of the extract along with it. Each compound travels at a different rate depending on its interaction with the stationary phase (silica gel) and the mobile phase (solvent), leading to the formation of distinct spots. After the solvent front reaches an appropriate height, the plate is removed, dried, and observed under UV light or treated with a visualizing agent. The different mobile phases are used detect the presence of bioactive constituents.

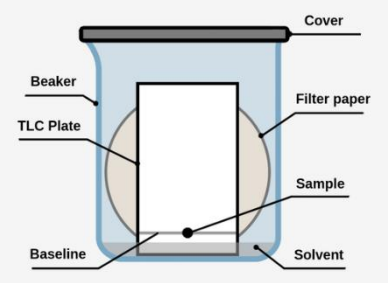


Figure 1.5: Thin Layer Chromatography.

➢ **UHPLC-QTOF-MS Analysis**

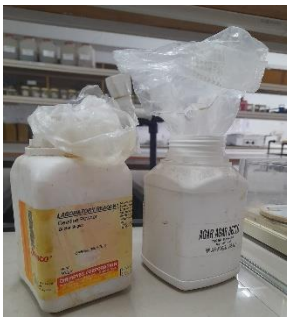
UHPLC-QTOF-MS analysis is a modern technique used to identify and study the chemical compounds present in plant extracts like liquorice, cinnamon, turmeric and vitex. First, the plant extract is injected into an ultra-high-performance liquid chromatography (UHPLC) system, which separates the different compounds based on how they move through a special column. Then, these separated compounds enter the quadrupole time-of-flight mass spectrometer (QTOF-MS), which measures the exact mass of each compound with very high accuracy. This helps scientists determine the molecular structure and composition of the compounds in the extract. Together, UHPLC-QTOF-MS provides detailed information about the complex mixture of bioactive molecules in liquorice, cinnamon, turmeric and vitex, supporting in understanding the medicinal properties. The following are the features of the instrument: 320°C gas temperature, 12 l/min gas flow, 40 psig nebuliser, and 350 sheath gas temperature with 11 sheath gas flow. With zero collision energy, the scan source parameters are set to VCap 4000 V, Nozzle Voltage 1000 V, Fragmentor 175, Skimmer1 65, and Octopole RF Peak 750 V.

➢ **Formulation of Gummies**

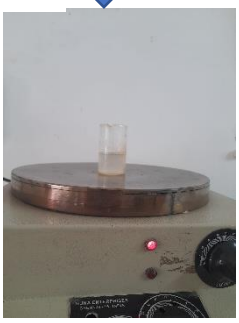
The liquorice, cinnamon, turmeric and vitex extract were prepared using Soxhlet extraction with ethyl acetate as the solvent. The extract obtained was filtered and then concentrated under reduced pressure to yield a semisolid mass suitable for formulation. For the Tulsi (Ocimum sanctum) extract, a hydroalcoholic extraction was performed using the Soxhlet extraction technique. The Liquorice (Glycyrrhiza glabra), cinnamon (cinnamomum verum), turmeric (curcuma longa), vitex decoction was prepared by boiling 10 grams of coarsely powdered herbal constituent in 100 mL of distilled water until the volume was reduced to approximately 50 mL; the decoction was then filtered using a muslin cloth. For natural colouring, fresh beetroot was crushed and filtered to obtain beetroot juice, which was used as a natural and safe colouring agent in the gummy formulation. In a clean beaker, add 2.5 g of pectin and 4 g of agar-agar to approximately 20 mL of distilled water. The mixture was heated to 70-80°C with constant stirring until both gelling agents were completely dissolved. Further 6.0 g of honey and 2.5 g of sorbitol were added to the hot gel base and stirred continuously to obtain a homogenous sweetened gel. Cooling of mixture was done around 40-

45°C to avoid degradation of actives. Now add 290 mg of liquorice, cinnamon, turmeric and vitex extract, 239 mg of Tulsi extract, and a measured quantity of 2 mL of the prepared liquorice decoction. 4 mL of beetroot extract (used as a natural colouring agent) was added to the cooled gummy base. Additionally, 0.05 mL of ginger oil and 0.05 mL of cinnamon oil were incorporated to add flavour, enhance therapeutic value, and provide mild antimicrobial action. The mixture was then stirred thoroughly to ensure uniform distribution of all the active herbal components and excipients throughout the formulation. The warm mixture was poured into pre-sterilized silicone gummy moulds and refrigerate at 4-8°C for 30-60 minutes after cooling. The set gummies were allowed to dry under laboratory conditions at room temperature (approximately 25±2°C) for a period of 24-48 hours and stored in airtight, light-resistant containers to preserve shelf life and potency.

Take the chemicals for the test



Take gelatine, agar agar for gummie base



Add active constituent in the mixture

Place the mixture into the gummies mold

➢ **In vitro Studies**

In vitro, studies of liquorice, cinnamon, turmeric and vitex involve testing the plant extracts and compounds petri in controlled dishes. laboratory conditions outside a living organism, such as in test tubes or its antioxidant, these studies help to evaluate the biological activities of the plant, like antimicrobial, anti-inflammatory, or cytotoxic effects. By using in vitro methods, we can better understand how liquorice, cinnamon, turmeric and vitex works at a cellular or molecular level before moving to animal or human studies. This approach is important for identifying potential medicinal uses and the safety of the plant extract.

➢ **DPdH Assay**

100 pl of varied concentrations of sample and standard were mixed with 900 µf of After incubation, the absorbance was measured using a UV-visible

spectrophotometer 0.004% DPPH solution (w/v, in methanol) and left to react in the dark for 15 min. at 517 nm. Ascorbic acid was used as a standard reference. The following equation.

% DPPH radical scavenging =

$$\frac{\text{O. D. (Control)} - \text{O.D.(Standard/Test)} \times 100}{\text{O.D (Control)}}$$

Where O.D. (control) is the absorbance of the control and O.D. (standard/test) is the absorbance of the standard/sample. The f value was calculated to express the free radical scavenging activity of the sample, showing the effective concentration of the sampleused to scavenge 50% of DPPH radicals. The lower the ICovalue more will be the scavenging ability.

- **Egg Albumin Denaturation Assay**

To prepare the reaction mixture (total volume: 5 mL), 0.2 mL of egg albumin solution, 2 mL of the test extract or standard drug (Diclofenac sodium) at different concentrations, and 2.8 mL of phosphate-buffered saline (PBS, pH 7.4) were combined. For the control setup, 2 mL of triple-distilled water was mixed with 0.2 mL of the egg albumin solution and 2.8 mL of phosphate-buffered saline to make a final volume of 5 mL. All prepared mixtures were incubated at 37±2°C for 30 minutes, followed by heating at 70±2°C in a water bath for 15 minutes. After the heating step, the samples were allowed to cool to room temperature. The absorbance of each mixture was then recorded at 280 nm using a UV-Visible spectrophotometer, with triple-distilled water serving as the blank. The percentage inhibition ROAD ofG.T protein denaturation was calculated using the following formula.

% inhibition= 100×(At/Ac-1)

Where At = absorbance of test sample and Ac= absorbance of control

ICso value was calculated to express the % inhibition activity of the sample, showing the effective concentration of the sample used to inhibit 50% of denaturation. The lower the IC50 value more will be the inhibitory ability.

- **Human Red Blood Cell Membrane Stabilization Assay (HRBC Assay)**

Assay mixture by adding 0.5 ml of HRBC suspension, 0.5 ml of phosphate buffer(0.15 M pH 7.2), 2 ml hyposaline (0.36 %), and 1 ml of various concentrations of extract/drug. The assay mixture was incubated at 37°C for 30 minutes and centrifugedat 3000 RPM for 20 minutes, and absorbance of supernatant was measured at 560 nm. Diclofenac sodium was used as reference standard, and HRBC suspension as control. The following equation was used to compute the percent stabilization activity:

% stabilization =

$$\frac{\text{O. D. (Control)} - \text{O. D. (Standard/Test)} \times 100}{\text{O. D. (Control)}}$$

Where O.D. (control) is the absorbance of the control, and O.D. (standard/test) is the absorbance of the standard/sample. The ICso value was calculated to express the percent stabilization activity of sample. The lower the ICs0 value more will be the stabilization ability.

- **Cellular Viability Evaluation**

Cell viability was evaluated using the MTT test according to standard protocol (120). Initially, RAW 264.7 cells were cultured in a specialised 96-well plate. The cells were subjected to several doses of extract 1, 5, 10, 20, 40, 60, 80, and 100 µM over 24 hours in a humidified incubator after they had reached a particular density (about 70% confluency). Following this procedure, an MTT solution (5 mg/mL) was added to each well after the liquid containing the cells was removed. After that, the cells were treated once again for three hours at 37°C. To evaluate cell viability, a device known as a microplate reader was used to measure a certain light intensity (optical density) a a wavelength of 570 nm. ROS 2025 was analyzed by Adherent Cell Microplate Assay. Approximately 50000 cells were seeded in a 96-well plate in DMEM media and cultured overnight at 37°C and 5% CO2. The media was aspirated and added 100µl per well of freshly prepared Ix assay buffer. Aspirated the 1x assay buffer, then added 100µl per well of freshly prepared 20µM H2DCFDA solution. Incubated in the dark for 45 minutes at 37°C. Aspirated the H2DCFDA working solution and washed with 1x assay buffer. Added 100µl per well of 1x assay buffer containing various concentrations of sample and incubated for 1-2 hours. H2 O2 was used as Positive control, and NAC is used as an antioxidant control. Measured the microplate in a microplate reader (excitation at 485nm and emission at 535nm). % ROS Level was calculated as:

% ROS Level = (Corrected Fluorescence of Sample / Corrected Fluorescence of Control) × 100

10. CONCLUSION

PCOS represents a lifelong health concern that affects women physically, metabolically, and psychologically. The cumulative risk of diabetes, obesity, hypertension, dyslipidemia, and endometrial cancer highlights the need for long-term screening and preventive care. Empowering patients through education, encouraging sustainable lifestyle interventions, and ensuring access to appropriate medical treatment will help reduce complications and improve quality of life. A shift from symptom-based treatment to comprehensive, preventative healthcare is essential in managing PCOS effectively.

11. RESULT

i. Appearance evaluation

The prepared herbal gummies were evaluated for their physical appearance including color, odor, texture, and shape. The formulation showed acceptable organoleptic properties comparable to the standard marketed gummy formulation.

Parameter	Formulated herbal gummies	Standard gummies
Color	Light orange	Orange
Odor	Pleasant herbal odor	Fruity odor
Shape	Uniform bear shape	Uniform
Texture	Smooth and elastic	Smooth
Surface appearance	Non-sticky	Non-sticky

Interpretation: the formulated gummies exhibited a smooth texture, uniform appearance, and acceptable elasticity without stickiness, indicating successful formulation development.

ii. Weight variation test

Twenty gummies were individually weighed and the average weight was calculated

Sample no	Weight of formulated gummies (g)	Standard gummies (g)
1	3.02	3.01
2	2.52	2.96
3	2.85	3.00
4	3.00	3.02
5	2.99	3.01
Average weight	2.96	3.01

Interpretation: the weight variation of herbal gummies was within acceptable pharmacopoeial limits, indicating uniformity in formulation and molding process.

iii. Elasticity test

Parameter	Formulated gummies	Standard gummies
Elasticity/flexibility	Good	Excellent
Stickiness	Slightly sticky	Non-sticky
Chewability	Acceptable	Good
Texture recovery	moderate	Good

Interpretation: the herbal gummies exhibited satisfactory elasticity and chewable texture suitable for oral administration.

iv. pH determination

Formulation	Observed pH	Standard pH range
Herbal gummies	5.9	5.5-6.5

Interpretation: the pH of gummies was within acceptable range and suitable for oral consumption.

v. In-Vitro dissolution study

Conditions

- Medium: phosphate buffer pH 6.8
- Temperature: 37 C

Time (min)	% drug release-formulate gummies	% drug release-standard
5	18%	20%
10	36%	40%
15	55%	58%
20	71%	74%
25	86%	88%
30	92%	98%

Interpretation: the formulated gummies showed gradual and effective release of herbal constituents comparable to standard formulation

vi. Stability studies

Storage condition

- Temperature: 40*C
- Relative humidity: 75% RH
- Duration: 1 months

Parameter	initial	After 15 day	After 1 month
Appearance	Smooth	Slight dullness	No major change
Colour	Orange	Stable	Stable
Odour	Pleasant	Pleasant	Pleasant
Texture	Soft	Slightly firm	Firm
pH	5.9	5.8	5.8
Drug release (%)	92%	91%	90%

Interpretation: the herbal gummies remained stable throughout the study period with no significant change in appearance, pH, or drug release profile.

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