RESEARCH PAPER

The Potential for Polycystic Ovarian Disorder Treatment Through Drug Delivery Using Nanomaterials

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ABSTRACT

Background- A prevalent endocrine-metabolic condition that affects women of reproductive age is polycystic ovarian disease (PCOD), commonly referred to as polycystic ovarian syndrome (PCOS). Hyperandrogenism, irregular ovulation, polycystic ovarian morphology, and metabolic disorders such obesity and insulin resistance are its hallmarks. Oral contraceptives, metformin, and ovulation-inducing drugs are examples of conventional pharmaceutical treatments that are effective but may have side effects and have limited therapeutic results.

Objective- The objective of this review is to assess the preclinical and clinical data that supports the therapeutic potential of nanoparticle-based drug delivery systems for the treatment of PCOD and to provide an overview of recent developments in these systems.

Methods- A thorough review of the literature was done with an emphasis on various nanocarriers utilized to deliver medicinal compounds like curcumin, selenium, metformin, and herbal extracts, including polymeric nanoparticles, metal nanoparticles, liposomes, micelles, quantum dots, and carbon nanotubes.

Results- Preclinical research shows that medication solubility, stability, and bioavailability are enhanced by nanoparticle-based formulations, which also allow for targeted delivery to ovarian tissues. In PCOD models, these systems have demonstrated encouraging results in lowering oxidative stress, controlling hormonal imbalance, enhancing insulin sensitivity, and repairing ovarian shape. Additionally, preliminary clinical studies indicate that nano-formulated substances, including nanocurcumin, may enhance inflammatory and metabolic indices in PCOS patients.

Conclusion- Drug delivery based on nanotechnology presents a viable approach to enhancing PCOD treatment. To verify long-term safety and therapeutic efficacy, however, more extensive clinical trials are needed.

Keywords- PCOD, drug delivery systems, insulin resistance, ovarian dysfunction, nanoparticles, and nanomedicine.

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1. INTRODUCTION

Polycystic ovarian Disease, or PCOD, is a sign of PCO, a disorder [1-2]. A syndrome is a pattern of symptoms associated with a certain disease [3]. Normal women in their reproductive years have ovaries that are about 4-6 ml in volume and have a folded structure similar to a walnut. However, if a woman is diagnosed with PCOD, her ovaries become enlarged and bulky, with a volume of more than 10 ml, and as a result, they begin to produce a high number of androgens. Follicles, which are fluid-filled sacs seen in normal ovulating ovaries, range in size from 1 to 30 millimetres, depending on the stage of the menstrual cycle. There is a little egg inside each sac or follicle, but it never gets big enough to cause ovulation. In contrast, the

polycystic ovary contains about 12 tiny follicles that range in diameter from 2 to 9 millimetres and are typically clustered around the periphery in a "pearl-necklace" fashion. As the name implies, poly means many. In polycystic ovarian disease, there are numerous tiny, fluid-filled cysts that resemble sacs that have formed inside the ovaries and do not require surgical excision [4-10]. The main characteristics of PCOD are polycystic ovarian morphology and hyperandrogenism, which are associated with ovarian dysfunction. Hirsutism, irregular or heavy menstruation, oily skin and acne, thinning of the scalp hair, insulin resistance, problems with conception, and weight-related concerns are common clinical symptoms. These characteristics, however, differ from patient to patient and are not solely dependent on the existence of polycystic ovaries [3]. According to recent research, nanomaterials can efficiently provide traditional treatments to address endocrine malfunction and lessen the harm caused by inflammatory reactions, reversing the pathological changes linked to the advancement of PCOD [11]. Therefore, nanomaterials provide significant promise for improving PCOD treatment. In order to determine the best combinations of nanomaterial-based delivery systems for PCOD control, this study offers a thorough review of the most recent developments in drug release triggers, targeting molecules, and nanocarrier delivery techniques. Additionally, it will investigate potential avenues for future nano delivery research (Figure 1).

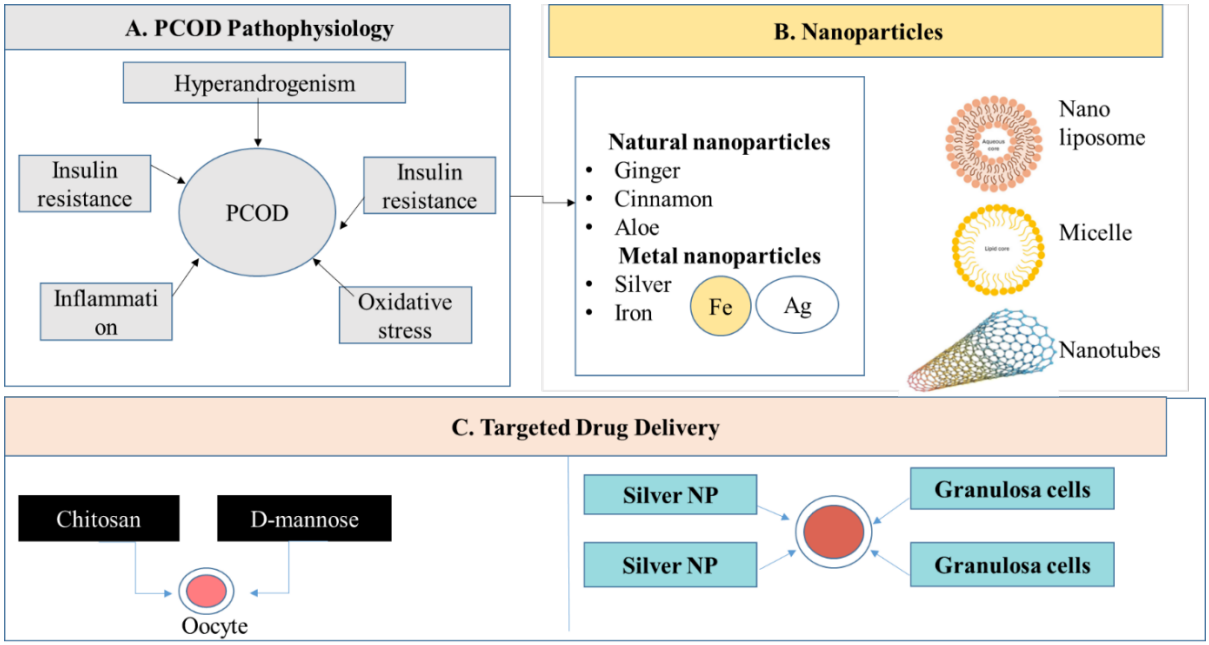

Figure 1: PCOD treatment using targeted ligand–nanomaterial systems (cellular targets and processes)

2. THE PCOD PATHOPHYSIOLOGY

PCOD is a complex disorder characterized by high androgen levels, irregular menstrual cycles, and the presence of polycystic ovaries. The hypothalamic-pituitary-ovarian (HPO) axis dysfunctions that are caused by hyperandrogenism, insulin resistance (IR), poor steroidogenesis, and adipose tissue accumulation are among the pathophysiological mechanisms that underlie PCOD [12]. The regulation of insulin resistance and androgen production depends on the hypothalamic secretion of gonadotropin-releasing hormone (GnRH) in the HPO axis. A disturbance in GnRH secretion can result in an increase in luteinizing hormone (LH) and a decrease in follicle-stimulating hormone (FSH) [13]. According to earlier research, insulin and LH together can increase the production of androgens in follicular membrane cells [14-17]. According to recent studies, the main causes of female reproductive failure are hyperandrogenaemia, insulin resistance, and hyperinsulinemia [18-23].

2.1. Hyperandrogenism

Elevated androgen levels are a defining feature of hyperandrogenaemia, a systemic disease. In those who have been diagnosed, PCOD may be due to impaired endogenous steroidogenesis in ovarian cells [19]. Among the androgens present in women's blood are dehydroepiandrosterone sulphate (DHEAS), testosterone (T), dihydrotestosterone, dehydroepiandrosterone (DHEA), and androstenedione (A) [20]. Therefore, hyperandrogenaemia, which can result from a number of processes that raise androgen levels, is one of the primary underlying causes of the pathophysiology of PCOD.

Moreover, one of the possible causes of IR in PCOD patients is hypothesized to be hyperandrogenaemia. According to research by Paolo et al. [21], people with a hyperandrogenic phenotype showed signs of insulin resistance. It has been proposed that antiandrogenic pharmaceuticals can reduce this population's insulin resistance [22].

2.2. Insulin resistance [IR]

Insulin IR is the term used to describe compensatory hyperinsulinemia that occurs when insulin's ability to perform certain metabolic tasks is impaired [23]. IR is

particularly common in people with PCOD; studies indicate that over 75% of PCOD patients experience IR [24]. The metabolic abnormalities linked to PCOD are closely related to this disorder. According to studies conducted in the 1990s, insulin activates its particular receptor in PCOD, which stimulates the pituitary organ's release of LH as well as ovarian and adrenal steroidogenesis. Additionally, IR affects metabolic or mitogenic pathways in non-traditional insulin-responsive tissues such the pituitary gland and ovaries in PCOD patients [25].

2.3. Oxidative Stress and Inflammatory Reaction

Research has shown that women with PCOD and age- and BMI-matched control groups have significantly higher levels of Ferritin, interleukin-18 (IL-18), tumour necrosis factor-alpha (TNF-α), C-reactive protein (CRP), and interleukin-6 (IL-6) [26, 27]. In PCOD, hyperandrogenism triggers an inflammatory response in addition to IR, which both increase the generation of reactive oxygen species (ROS) and hence promote oxidative stress [28]. Oxidative stress interferes with proper follicular development and maturation, according to studies [34, 35]. In the follicle, granulosa cells and oocytes can sustain damage from an excess of ROS, compromising their integrity and threatening fertility [29, 30]. According to Frank González et al. [38], hyperglycaemia may increase ROS levels, creating a pro-inflammatory environment that causes IR and hyperandrogenism in PCOD patients. Furthermore, insulin resistance may be exacerbated by mitochondrial dysfunction and decreased oxidative phosphorylation, which disrupt insulin signalling pathways and impede glucose metabolism [31].

3. DIAGNOSIS AND TREATMENTS

3.1. Diagnosis of PCOD

The most commonly used criteria for PCOD diagnosis are the Rotterdam criteria [32] . Even though the test results may be negative, PCOD is considered a diagnosis of exclusion, so patients who report symptoms must have diagnostic testing. 60% of PCOD patients have biochemical hyperandrogenism, which can be measured with total testosterone, estimated free testosterone, androstenedione, and dehydroepiandrosterone sulphate (DHEA-S). Checking for DHEA-S and androstenedione levels is necessary if these initial results are normal. If a patient meets two of the three Rotterdam criteria, they can be diagnosed with PCOD without the need for laboratory confirmation of elevated androgens. If laboratory proof is needed, CHCs must be stopped for three months prior to androgen measurement [33].

Polycystic ovarian morphology on transvaginal ultrasonography (≥ 20 follicles or an ovarian volume > 10 mL in at least 1 ovary) can be another criterion if clinical or laboratory conditions are not met [34, 35]. The typical number of follicles per ovary may vary depending on age and polycystic ovarian shape; in females of reproductive age, the normal mean follicle number is eight, and the mean volume is 6.1 Ml.

Another indicator of follicle number is the level of anti-Mullerian hormone in the blood. According to a recent meta-analysis, an anti-Mullerian level of 34.2 pmol/L may be a suitable threshold for PCOD diagnosis [36].

3.2. Treatment of PCOD

The objectives of PCOD treatment should be tailored to each patient's needs and include lowering hyperandrogenism, controlling menstruation, triggering ovulation, and avoiding cardiometabolic problems.

Anti-Androgens with Oral Contraceptives

The first-line treatment for PCOD hirsutism, acne, and irregular menstruation is oral contraceptives (OCs). By inhibiting LH secretion, raising SHBG levels, and lowering free androgens, they lower ovarian androgen synthesis. Anti-androgens like finasteride, flutamide, cyproterone acetate, and spironolactone also lessen androgen action and alleviate hyperandrogenic symptoms [37].

Sensitizers to Insulin

The pathophysiology of PCOS is mostly influenced by insulin resistance and hyperinsulinemia, which enhance ovarian androgen production and hinder follicular maturation. Metformin and thiazolidinediones are examples of insulin sensitizers that increase insulin sensitivity, decrease circulating androgens, and encourage ovulation. Menstruation, ovulation, dyslipidaemia, and BMI are all improved by metformin, while insulin resistance and SHBG levels are further improved by TZDs like pioglitazone [38].

Inducers of Ovulation

One of the main causes of infertility in PCOS is ovulatory disruption. By boosting FSH output and encouraging follicular development, clomiphene citrate continues to be a first-line ovulation induction drug. Because they improve mono-follicular formation and have fewer anti-estrogenic effects on the endometrium, aromatase inhibitors like letrozole and anastrozole are effective substitutes that are becoming more and more popular. In circumstances when ovulation is resistant, low-dose gonadotropins can also be utilized to enhance reproductive results [39].

4. USING NANOMATERIALS TO TREAT PCOD

Pharmacological advances in nanomedicines have been substantial throughout the past three decades. They have greatly increased the effectiveness of various medications [40]. Many successful nano therapies have been developed to treat a range of human illnesses [41, 42]. Currently, we treat PCOD-related illnesses with various nanocarriers (Table 1). These consist of micelles, carbon nanotubes, liposomes, nanoparticles, and quantum dots.

Table-1 Nanocarriers used in PCOD

Sl. no	The nanocarrier	Essential components	medicinal substance	Research item	The mechanism	References
1	A nanoparticle of chitosan	Chitosan	Curcumin	Rat	Reduced amounts of luteinizing hormone, prolactin, insulin, and testosterone in the blood	43
2	Nanoparticles of silver	Silver	Cassia cinnamonomum	Rat	An anti-oxidant	44
3	Nanoparticles of ginger	Lipid	Ginger	Mice	Boosted the expression of the forkhead transcription factor (Foxa2) to mitigate the effects of insulin resistance brought on by intestinal epithelial cell (IEC) exosomes.	45
4	Nanoparticles of silver	Silver	Zeylanicum Cinnamomum	Rat	Reduce the levels of inflammatory indicators such IL-6, IL-18, and TNF-α.	46
5	Selenium Nanoparticles	Chitosan	Selenium dioxide	Rat	Lower the amounts of inflammatory markers such TNF-α, IL-6, and IL-18	47
6	Nanoparticles of iron	Iron oxide	Curcumin	Mice	Suppression of both dehydroepiandrosterone-induced and ovarian damage cell apoptosis	48
7	Nanoparticles of selenium	Chitosan	Selenium Dioxide	Rat	PI3K and Akt gene expression is elevated in response to oxidative stress, inflammation, sex hormone levels, insulin sensitivity, lipid profile, and mitochondrial functional indicators.	49
8	Nanoparticles of selenium	Chitosan	Selenium dioxide	Rat	You can reduce androgen synthesis and break the vicious cycle caused by excessive androgen release by downregulating the expression of androgen receptors.	50
9	Nanoliposomes	The phospholipid glycerol	Resveratrol methyl derivatives [DMU-212]	Granulosa cells in the ovaries	Increased secretion of progesterone and estradiol is recommended.	51
10	The quantum dot	Glycol polyethylene	Metformin	Hepg2 cells	Increase the absorption of glucose and reverse insulin resistance	52
11	Micelle		Curcumin	Rat	Decreased inflammatory response and oxidative damage	53

4.1. Nanoparticle

4.1.1. Drug Nanoparticles Made of Natural Materials

Modern pharmacological research has verified the particular bioactive qualities of a variety of treatments obtained from minerals, plants, and animals, which are together referred to as natural medicines. Because of their possible therapeutic, preventive, and rehabilitative uses in herbal medicine, there has been a noticeable increase in plant-derived medications in recent years [54, 55]. According to Arentz et al. [56], women with PCOD reported being dissatisfied with Western medications, and over 70% of them used additional medications, indicating a preference for complementary therapy. Additionally, conventional drugs used to treat PCOD issues have adverse effects and may not work in certain situations. Several botanicals have recently drawn attention for their possible applications in PCOD because they contain multiple active components that may have mutually beneficial effects [57].

Previous studies have shown that a significant number of botanicals have pharmacologically active elements that can positively affect insulin sensitivity, hormone levels, obesity, and ovulatory function [58]. For instance, in a letrozole-induced animal model, Maharjan et al. [59] showed that Gel of Aloe barbadensis had a favourable effect on PCOD, while in rats with PCOD, chamomile extract promoted normal follicular development [60]. Curcumin may be a safe and useful adjuvant therapy for reducing hyperandrogenism and hyperglycaemia associated with PCOD, according to a clinical trial by Javad Heshmati et al. [61].

Natural drug nanoparticles having characteristics similar to mammalian extracellular microbubbles, such as surface charge and size distribution, have been used therapeutically in recent years [62, 63]. These nanoparticles have both structural and functional characteristics that increase their clinical value and function as natural nanocarriers for vesicle transit [64]. In PCOD patients, curcumin, a phenolic molecule known for its antioxidant and anti-inflammatory qualities, has shown promise in lowering hyperandrogenism, insulin resistance, and hyperglycaemia [65]. However, problems with solubility and poor pH stability limit its practical usefulness. Polymeric nanoparticles that are biocompatible, such as chitosan (CS), are becoming more and more popular among researchers due to their ease of handling and rapid dissolution [66, 67]. Although CS is poorly soluble in water, this drawback can be lessened by chemical changes [68]. By functionalizing CS, different pharmacological molecules can be encapsulated, improving the active ingredients' pharmacokinetic characteristics [69]. CS nanoparticles are useful for embedding a variety of substances, such as antimicrobials, analgesics, and anti-inflammatory drugs, because they are cationic polysaccharides [70].

In a rat model, Raja et al. [47] successfully produced nanoparticles with N-acetylhistidine-modified CS and curcumin-embedded arginine that, in comparison to controls, markedly decreased serum levels of insulin, prolactin, testosterone, and LH. This study is a promising first step toward using nanoparticles as a powerful curcumin delivery system for PCOD treatment. The Zingiber officinale rhizomes the source of ginger, which contains Terpenes, volatile oils, and phenols among other bioactive substances. 6-gingerol, the bioactive component, lowers insulin levels and improves insulin sensitivity while adding a strong flavour [71]. Ginger-derived nanoparticles also combat insulin resistance, possibly by boosting Foxa2 expression and lowering insulin resistance brought on by IEC exosomes, according to Anil Kumar et al. [48]. Cinnamon is a member of a broad genus that has been used for ages in spice, medicine, and cooking. Iron, calcium, manganese, eugenol, cinnamon aldehyde, and dietary fiber, and related substances are among the minerals found in all cinnamon species [72]. The therapeutic advantages of cinnamon for PCOD have been investigated in both clinical and animal studies [73]. In mouse models of PCOD, cinnamon has been shown to improve LH levels, decrease insulin and testosterone, and restore the estrous cycle [74].

Short-term cinnamon supplementation has a favourable effect on metabolic risk variables, 84 obese women with PCOD participated in a medical study conducted by Borzoei et al. [75]. According to Koffi Kouame et al. [49], the antioxidant qualities of silver nanoparticles made from cinnamonomum cassia (CcAgNPS) may improve renal function in diabetic rats. Furthermore, aloe vera [76], camellia [77], with additional natural extract-derived nanoparticles exhibit anti-inflammatory and antioxidant properties, potentially becoming new therapeutic targets for the treatment of PCOD in the future.

4.1.2. Metal Nanoparticles

Scientists have historically created nanoparticles via chemical and physical methods, which come with a number of difficulties. For the treatment of PCOD, recent research has turned its attention to novel therapeutic nanoparticles including selenium and silver [78]. In rats with PCOD, silver nanoparticles have the potential to reduce inflammation and lower inflammatory markers [50]. These developments point to a progressive strategy because reducing inflammation may lessen symptoms frequently linked to high inflammatory cytokines in PCOD patients. Silver nanoparticles have remarkable antibacterial qualities and are active against extracts of cinnamon that are known to have anti-inflammatory and anticancer characteristics [49, 79, 80].

According to research, iron nanoparticles loaded with curcumin can successfully prevent ovarian damage cells from undergoing apoptosis, which may help treat PCOD [51]. There are differences between metal and natural nanoparticles in terms of degradation rates, immunological response potential, and biocompatibility. Because they resemble biological tissues, natural nanoparticles usually have high biocompatibility, cause little immunological reactions in biological systems, and biodegrade rather quickly [81, 82]. When used as vaccine delivery vehicles, surface-modified metal nanoparticles can elicit a strong immunological response [83].

4.2. Nanoliposome

Nanoliposomes are spherically shaped, self-assembling structures with lipid bilayers made up of one or more phospholipids [84]. These structures offer a flexible

delivery method for different medications because they are both non-toxic and biodegradable [85]. They can carry a wide range of materials, including hydrophobic and hydrophilic small molecules, proteins, and nucleic acids. Nanoliposomes improve the therapeutic efficacy of medications, get past obstacles to cellular absorption, and help pharmaceuticals biodistribute to their intended locations while reducing systemic toxicity by stabilizing chemicals [86].

On the one hand, oral drug delivery encounters physiological and biochemical challenges; on the other hand, the size, surface features, and shape of the nanoparticles play a crucial role in determining their efficacy [87]. Investigators created a Nanoliposomal form of DMU-212 (lipDMU-212) and showed that it significantly and dose-dependently boosts progesterone and estradiol secretion [54].

4.3. Nanotubes

A novel class of materials, carbon nanotubes are widely used in biomedical applications because of their distinctive structure, appealing qualities (such as the covering surface area to length ratio and its size), as well as mechanical, thermal, and electrical properties [88]. Carbon nanotubes are more easily manipulated to bind ligands and bioactive substances for targeting more effectively than other nanocarriers. According to Miey Park et al., carbon nanotubes can increase serum biomarker concentrations associated with oxidative stress and inflammation and decrease overnight blood glucose, which can lead to insulin resistance. Carbon nanotubes are used not just for drug delivery but also for diagnostic purposes. Human fetuin A (HFA) is a biomarker linked to both the inflammatory process of type 2 diabetes and insulin resistance in PCOD. In order to evaluate HFA, Esther Sánchez-Tirado et al. [88] employed magnetic multi-walled carbon nanotubes (m-MWCNTs) as nanocarriers. T According to a study by Pradeep K. Jha et al. [89], Nanotubes of carbon with several walls can carry silver nanoparticles and could be utilized in the future to diagnose infertility.

4.4. Quantum Dots

Quantum dots outperform other fluorescent dyes in terms of photostability and brightness. They are used in a variety of antibody-based immunoassays. A nanodrug delivery system based on pegylated graphene oxide quantum dots (GOQDs) were reported by Kunal Sarkar et al. [55]. Because GOQD-PEG can improve glucose absorption and lessen insulin resistance in an insulin resistance paradigm that is in vitro, this platform may enable the prolonged release of metformin. Furthermore, the integration of quantum dots with nanoparticles can result in multisensing effects [90-92]

4.5. Micelles

Micelles are widely utilized molecular structures that have garnered a lot of interest in modern medicine because of their exceptional stability. Compared to conventional micelles, polymeric micelles have a longer half-life and less drug immunogenicity [93, 94].

5. Applications of Nanoparticles to treat the Polycystic Ovarian Disease (PCOD) – Preclinical and Clinical Evidence

Nanoparticle-based drug delivery systems have emerged as promising therapeutic approaches for the management of Polycystic Ovarian Disease (PCOD). Preclinical and clinical studies have demonstrated that nanoparticles can improve drug bioavailability, reduce oxidative stress and inflammation, and enhance hormonal and metabolic regulation in PCOD.

Table 2: Preclinical Evidence and Clinical Evidence of Nanoparticles in PCOD Treatment

Nanoparticle Type	Active Compound / Drug	Study Model	Key Findings	Reference
Nanoparticles of selenium	Nano-selenium	Rat research as an animal model (preclinical)	Improved reproductive health, decreased oxidative stress and inflammation, and increased antioxidant enzyme activity	95
Nanoparticles based on lipids (Nanocurcumin)	Curcumin	Rat model produced by PCOS (Preclinical)	Lowered oxidative stress, decreased cystic follicles, improved ovarian shape, and restored hormone homeostasis.	96
Nanoparticles based on lipids	Plant antioxidants and curcumin	Animal and in vitro models (preclinical)	Improved ovarian function, decreased inflammatory indicators, and increased medication solubility.	97
Nanoparticles based on lipids (Nanocurcumin)	Curcumin	PCOS-affected women participating in a randomized clinical study	Improved insulin resistance, decreased inflammatory markers, and improved metabolic parameters.	98

6. MARKETED FORMULATION

To address curcumin's poor water solubility and limited oral bioavailability, a number of commercially marketed

"bioavailable curcumin" products employ cutting-edge delivery methods like phytosomes, solid-lipid particles, micelles, and colloidal/nanoparticulate dispersions. These formulations enhanced pharmacokinetic profiles may amplify curcumin's systemic anti-inflammatory, antioxidant, and metabolic effects, which are pertinent to important pathophysiological aspects of polycystic ovary syndrome (PCOS), even though they are marketed primarily as nutraceutical ingredients rather than approved medications for PCOS.

Table- 3 The main nanoparticle-based formulations investigated for the treatment of PCOD are highlighted in this table.

Product / Brand	Delivery technology (how it's advanced)	Regulatory / market status	Relevance to PCOS (claimed / rationale)	Key evidence
Meriva® (Indena)	Curcumin and phospholipids form a lipid combination called Phytosome®, which significantly enhances oral absorption.	Often used as a component of medical food and supplement items (not an approved PCOS medicine).	Enhanced systemic exposure to curcuminoids may improve PCOS-related anti-inflammatory and metabolic benefits. .	Meriva is used in numerous human trials and has a large clinical literature on its better PK and anti-inflammatory effects when compared to ordinary curcumin.
Solid Lipid Curcumin Particle, or Longvida® (SLCP™)	Curcumin is protected using solid-lipid particle technology, which also transports free curcumin to tissues.	Supplement ingredient that is marketed; safety and PK information available .	Improved tissue transport and stability may help PCOS patients with oxidative stress and inflammation.	Several reviews and PK/safety studies show improved bioavailability when compared to unformulated curcumin.
Curcugreen® (Biocurcumax) and BCM-95®	To improve absorption, curcumin and turmeric essential oil were mixed (oil-assisted complex, not traditional nanoparticle).	Extensively advertised and utilized in numerous commercial products	Better bioefficacy → potential advantages for PCOS patients' inflammatory and metabolic indicators.	PK cross-over studies reveal significantly greater
Theracurmin®	Colloidal/nanoparticulate dispersion (colloid formulation with excellent bioavailability).	Sold as a component of nutraceuticals; clinical trials are being conducted for various reasons (such as osteoarthritis).	Stronger systemic anti-inflammatory effects related to PCOS may result from higher plasma curcumin concentrations.	Thera curmin's PK and safety have improved in human trials; nonetheless, there are few PCOS-specific trials. .
Micellar curcumin, or NovaSOL®	Micelle technology and solubilization: rapid and high absorption.	Ingredient that is marketed (used in consumer items).	Therapeutic potential for inflammatory/metabolic outcomes in PCOS may be enhanced by rapid/high systemic exposure.	Clinical PCOS data is unavailable; company and independent PK reports show better absorption.
Nano-formulations of metformin (state of research)	Experimental: lipid systems in preclinical studies, MOF-carriers, polymeric NPs, and nanoemulsions	There is currently no commercially available, regulatory-approved nano-metformin product for PCOS or diabetes;	Intended to enhance delivery, allow for controlled release, and lessen gastrointestinal side effects; if shown to be safe and effective, this could be helpful for PCOS metabolic regulation.	Although there has not yet been a significant therapeutic translation, recent reviews and experimental investigations demonstrate

		preclinical and early research are the key areas of development.		encouraging controlled-release and efficacy indications in vitro and animal models.

6. CONCLUSIONS

Drug delivery methods based on nanomaterials offer a promising new approach to the treatment of polycystic ovarian disease (PCOD). According to preclinical and new clinical data, nanoparticles can greatly enhance the solubility, stability, bioavailability, and targeted administration of both natural and conventional medicinal drugs, including herbal extracts, curcumin, metformin, and selenium.

Numerous nanocarriers, such as carbon nanotubes, metal nanoparticles, micelles, polymeric nanoparticles, liposomes, and quantum dots, have demonstrated promise in reestablishing hormonal equilibrium and enhancing ovarian histopathology in PCOD models. All things considered, nanotechnology provides a fresh and effective way to get around the drawbacks of the PCOD medication that is currently available.

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