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Chapter 3: Exploring Nanotechnology with Traditional Herbal Pharmacology: Nano Carrier-Based Phytochemical Delivery in PCOS Treatment

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Abstract

Polycystic Ovary Syndrome (PCOS) is an important endocrine and metabolic disorder that affects women in their reproductive years. It is characterized by the increase in male hormones, no ovulation, and the formation of many cysts in the ovaries. Standard treatment consists of using oral contraceptives, insulin sensitizers and anti-androgens, among others, which only manage the symptoms and not the underlying causes, besides, they usually have negative side effects and their long-term efficacy is often limited. Moreover, they usually come up with side effects and have limited effectiveness in the long run. On the other hand, the work of bioactive phytochemicals, including flavonoids, polyphenols, alkaloids, terpenoids, and saponins, has provided the hope in the area of treating the disease because they can restore the endocrine system's control, lower the oxidative stress, and enhance the insulin sensitivity. The recent developments in nanocarrier systems, such as polymeric nanoparticles and antibody-conjugated formulations, are having a beneficial impact on the stability, bioavailability, and targeted delivery of the phytochemicals. Furthermore, the understanding of modulation of gut microbiota, functional genomics, and proteomic interactions has paved the way for new therapeutic pathways in the management of PCOS. This chapter presents a discussion on the technical challenges in the usage of nanotechnology and phytochemistry, the translational challenges, and the future of PCOS therapies that are safe, effective, and precision-based.

Keywords: *Polycystic ovary syndrome (PCOS), Endocrine disorder, Bioactive phytochemicals, Herbal therapy, Traditional Chinese Medicine, Nanotechnology, Gut microbiota, PROTACs.*

1. INTRODUCTION

There is no permanent cure of polycystic ovary syndrome (PCOS) and the aim of treatment is to manage the symptoms by lifestyle changes and pharmacological therapy. Loss of weight and exercising become the basis of the treatment, and oral contraceptives are frequently used to control menstrual periods, hirsutism, and acne. Insulin sensitivity and hormonal balance can also be improved using metformin, which may be used in combination with anti-androgens, although other treatments to address acne and hair growth are also used as common way of treating the disease. Ovulation induction medications that include clomiphene and metformin are vital in enhancing success in conception among women with infertility. Poly-cystic ovarian syndrome is a frequent endocrine disorder in all women of reproductive age globally, and its occurrence is estimated to be between 5-20% based on the diagnostic tool used. It is a complicated disorder, and it is defined by hyperandrogenism, menstrual cycle disorders, the presence of polycystic ovaries and other metabolic and psychosocial issues. PCOS has been a significant contributor to infertility due to anovulatory etiology and is also strongly related with type 2 diabetes mellitus (T2DM) at earlier ages that is complicated with cardiovascular diseases and psychiatric disorders. Women with PCOS also face higher risks of pregnancy such as early miscarriage, gestational diabetes, hypertension, preeclampsia and even increased risk of developing endometrial cancer. The estimated prevalence of the condition stands at 11-13 percent of women worldwide, with a huge financial and medical imposition on the healthcare services. Traditionally, management approaches were directed at metabolic dysfunction, reproductive health, androgen excess, and mental well-being. It has been demonstrated that nanoparticles may assist in the more effective delivery of the traditional PCOS therapy, decreasing the inflammatory injury, restoring endocrine activity, and surpassing the pathological changes associated with the disease development. This gives significant potential of applying the nanomaterial-based techniques in the PCOS treatment. Other more recent works emphasize more on the high-quality nanocarrier systems with high biocompatibility, controlled discharging and targeting due to site specific features. The aim of such innovations is not only to improve the therapeutic efficacy but also to reduce the side effects in the system which limits the common therapeutic approaches in most cases. New nanostructures, ligand conjugated nanoparticles and stimuli-responsive release methods are under investigation by the researchers to help identify which combinations of these tools are most appropriate that should be employed in the treatment of PCOS. In addition to this, some new research indicates the possibility of highly customizable nano-delivery platforms, which are more responsive to the heterogeneity of PCOS, which will better target its metabolic, reproductive and hormonal manifestations. Diagnostic Diagnosis of PCOS is typically made when there are two or three of three generally accepted criteria; such as but not limited to polycystic ovarian morphology, irregular or absent

ovulation, and biochemical or clinical evidence of hyperandrogenism. Ultrasonography is the most prevalent forms of visualization of Ovarian cysts, and it is not still easy to interpret because of the spontaneous overlaps with normal ovarian anatomy. Moreover, endocrine disorders such as congenital adrenal hyperplasia, hypothyroidism, or hyperprolactinemia exist, and some of them affect the presentation of symptoms in a manner similar to PCOS, making it more difficult to diagnose it. The intersection underlines the significance of intensive profiling of the hormones and careful differential diagnosis in case a proper identification and adequate treatment were introduced.

2. PATHOPHYSIOLOGY OF PCOS AND THERAPEUTIC CHALLENGES

2.1. Pathophysiology

PCOS occurs due to a combination of various factors, and it is difficult to cure. There is no single cause but a combination of hormone changes, ovarian changes, and metabolic changes that result in the syndrome having multiple problems in nature. One of the contributing factors is the insulin resistance whereby the body tissues fail to respond appropriately to insulin. The pancreas responds to this by producing an excessive amount of insulin resulting in a high level of insulin (hyperinsulinemia). This pathway is a connection of PCOS and obesity and is widespread among many women. Excess weight raises insulin resistance, aggravates PCOS symptoms, and predisposes to type 2 diabetes and cardiac disease. Over-secretion of luteinizing hormone (LH) is a hallmark symptom of PCOS and broken balance of LH against follicle-stimulating hormone (FSH). This hormonal disorder disrupts ovulotropic events leading to anovulation and abnormal release of eggs. Consequently, ovarian follicles will not optimally mature and multiple cyst-like structures are formed and can be seen under ultrasonography. These cystic follicles, though not necessarily cysts, are one of the characteristic observations of the syndrome. Androgen excess-especially high testosterone-is another key mechanism in PCOS. It plays a role in this hormone imbalance and is associated with hirsutism, acne and androgenic alopecia as characteristic clinical manifestations of the syndrome. The super-androgens agonize the pilosebaceous units of the skin. This leads to growth of hair in undesired places, and occurrence of sebaceous glands and acne. High androgen production in PCOS women is primarily promoted by elevated luteinizing hormone (LH). LH triggers adrenal glands and ovaries to make additional androgens. Despite the fact that this hormonal imbalance is going to constitute a significant factor in PCOS, it is merely a segment of a much broader puzzle. The pathophysiology of PCOS is complicated. It is a combination of dysfunction of the hypothalamic pituitary ovarian (HPO) axis, malfunction of ovarian steroids, insulin resistance, and other metabolism problems. They are connected problems. The cycle that is created therefore further deteriorates the condition. An example is, the resistance of insulin compels the body to generate

additional insulin. This additional insulin stimulates ovaries to synthesize over androgens. Increased the androgen levels interfere with the follicle formation inhibiting ovulation and leading to distorted cycles. Synchronously, an uncivilized HPO axis continues to secrete more LH into an already super-androgenic milieu. Such endocrine coupled with the metabolic disturbances determine why PCOS manifests differently in every woman and includes hirsutism and acne to obesity, high cholesterol and high probability of developing type 2 diabetes. PCOS is a multifactorial, integrative disorder, so it ought to be considered a systemic condition and not necessarily as a single, reproductive disorder. The diagnosis and treatment of PCOS requires a holistic approach. Hormone levels, metabolism and mental health should be treated to control the symptoms and long-term hazards.

2.2. Therapeutic challenges for PCOS

Poor treatment projections are rife when trying to treat PCOS.

1. **Protracted Diagnosis and Treatment Deficiencies** - There is a high rate of significant delays in diagnosing PCOS and many women are not satisfied with existing therapies. Clinicians do not maintain current information on the aspects of diagnosis and management plans.
2. **Complex and Multifactorial Pathophysiology** - The pathophysiology behind PCOS includes genetic factors, influences of the environment and the effects of transgeneration thus complicating specific treatment.
3. **Variability in Manifestation and Diagnosis** - PCOS is characterized by different symptoms and phenotypes, with malign age- and ethnicity-related differences in the enabling diagnostic criteria, making it difficult to diagnose and treat.
4. **Limited Effectiveness of Lifestyle Interventions** - Although lifestyle modifications have been shown as the first-line intervention, compliance is low, and the availability of evidence-based materials to support the association between the changes and a range of the reproductive outcomes is limited.
5. **Disadvantages of Pharmacological Treatment** - There is no drug dealing with all PCOS symptoms. The primary contraceptive method in the case of hyperandrogenism and irregular cycles is oral contraceptives, whereas metformin does not provide significant improvement in the prevention of metabolic dysfunction and weight. Combinations of therapies are in research.
6. **Mental Health and Quality of Life** - It is associated with higher levels of psychological distress, but mental health support tends to be an inadequately developed treatment strategy that is not prioritized.
7. **Uncertain Long-Term Consequences** - The enduring consequences of PCOS have not been fully comprehended and therefore, impeding in-depth risk counselling.
8. **Obesity and Reactive Prevention** - Morbidity is compounded by the high levels of occurrence of obesity in PCOS. The present condition of early intervention strategy

with at-risk individuals is unsatisfactory, and suggests the necessity of multidisciplinary attention to each individual and additional research.

2.2.3. Global Prevalence Trends of PCOS

It is estimated that 1.55 million new cases emerged among women of reproductive age in the world in 2017 alone and women aged 21 to 30 years in the category contributed to 17.23% of the new cases. Asian-based data, especially in the past three decades, emphasize significant age-standardized incidence rate growths. Indicatively, based on the 2003 criteria used by Rotterdam, China reported that prevalence stood at 10.01 in 2003, which marked one of the highest rates of increase with age-standardized incidence of 73.53 per 100,000 persons that year. The global rates of PCOS prevalence are not equal (6-21), significantly influenced by differences in definitions of the disease, ethnicity, and geography. In addition to reproductive health, there is a high likelihood of co-occurring serious metabolic disturbances with PCOS. About 50 percent of all affected women are obese, and 31.1 percent exhibit impaired glucose metabolism, and 7.5 percent have type 2 diabetes (T2DM). Women with PCOS have more than three times the risk of impaired glucose tolerance (IGT), and approximately three times the risk of T2DM. These are further worsened by obesity where obese PCOS patients exhibit increased occurrence of metabolic syndrome (47.9% vs. 15.9%) and insulin resistance (27.8% vs. 7.1%) than their non-obese counterparts. Subgroup analysis shows that Asian PCOS women are disproportionately at risk as compared to other groups, as they have a 5.2-fold higher risk of IGT and a 4.4-fold increased risk of developing T2DM compared to healthy women. A combination of these results highlights the two-fold issue of increasing prevalence of PCOS and its strong correlation with metabolic dysfunctions, which leaves the urgent concern of developing effective prevention and management interventions in diverse populations.

3. PHYTOCHEMICALS IN PCOS MANAGEMENT

Eighteen studies including seventeen randomized controlled trials (RCTs) and one matched clinical study were included in this review. The main findings of the twelve studies, which focused on the phytochemical-based research, are summarized in Table 1. Supplemental analysis in polycystic ovary syndrome (PCOS) [9].

Table 3.1: Impacts of phytochemical-based supplements on PCOS in females (Clinical Trials) [10-13].

Phytochemical Compound	Author/year	PCOS Duration, Sample Size, and Treatment Plan	Significant finding
EGCG	(Tehrani, 2017) (Mombaini, 2017) (Farhadian, 2020)	3 months Overweight and obese women 20–40 years old (n = 60) Tx: One 500 mg green tea tablet per day 45 days Women aged 18–55 years with BMI 20–35 kg/m2 (n = 45) Tx: One 500 mg green tea leaf powder tablet per day 3 months Overweight women 18–35 years old (n = 15) Tx: One 500 mg green tea leaf powder tablet per day	weight reduction decrease in fasting insulin decrease in free testosterone levels significant reduction in weight, BMI, WC, and body fat significant reduction in anthropometric indices such as weight, BMI, and waist and hip circumference
Curcumin	(Jamilian, 2020) (Heshmati, 2020) (Sohaei, 2019) (Gupta et al., 2025)	3 months Women aged 18–40 (n = 60) Tx: 500 mg/day curcumin 3 months Women aged 18–49 (n = 67) Tx: 500 mg curcumin powder in a capsule 3 times/day 6 weeks Women aged 18–40 years old (n = 27) Tx: 500 mg curcumin 2 times/day	significant weight and BMI reduction decrease in fasting glucose decrease in serum insulin improved HOMA-IR (insulin resistance) decrease in total cholesterol and LDL-c Decreased fasting plasma glucose (FPG) Quantitative Insulin Sensitivity Check Index (QUICKI) improved significantly Homeostatic Model Assessment for Insulin Resistance (HOMA-IR) improved marginally

Quercetin	Khorshidi, 2018) Rezvan, 2018)	3 months Women with BMI 25–40 kg/m2, aged 20–40 (n = 27) Tx: 1000 mg quercetin per day 3 months Overweight or obese women, mean age 29 (n = 42) Tx: Two 500 mg capsules	Decreased resistin plasma levels and gene expression Decreased testosterone and LH concentrations FBG, fasting insulin, and insulin The resistance was improved significantly Increased adiponectin receptors (ADIPOR1 and ADIPOR2) _ Enhanced AMPK levels
Resveratrol	(Banaszewska, 2016) (Mansour, 2021)	3 months Overweight women (n = 15) Tx: micronized transresveratrol; 1500 mg/day 3 months Women aged 18–40 (n = 39) Tx: 1000 mg resveratrol/day	significant reduction in ovarian and adrenal androgens, testosterone and DHEAS. improved menstrual cyclicity and hair loss.
Berberine	(Orio, 2013) (An, 2014)	6 months Obese women (n = 50) Tx: 588 mg Berberis aristata and 105 mg of Silybum marianum-1 tablet, 2 times/day 3 months Overweight women (n = 41) Tx: Berberine tablets 500 mg, 3 times/day	improved HOMA-IR and hormonal profiles improved metabolic profile improved HOMA-IR improved response to ovarian stimulation

WC: waist circumference, a measure commonly referred to as a measure of abdominal fat distribution; **LH:** luteinizing hormone, a key regulator in reproductive function; mg: milligrams, a standard unit of measurement for mass in the metric system; n: sample size, which depicts the number of participants or data points in a study; **PCOS:** polycystic ovarian syndrome is a hormonal disorder that is marked by irregular cycles, ovarian cysts, and metabolic abnormalities; **QUICKI:** quantitative insulin sensitivity check index, a formula-based assessment of insulin sensitivity; **Tx:** treatment, the intervention or treatment in question; **AMPK:** AMP-activated protein kinase, enzyme, which is central to energy balance and cellular metabolism; **DHEAS:** dehydroepiandrosterone sulfate: a hormone secreted by the adrenal glands which has functions in androgen and estrogen production; **EGCG:** epigallocatechin-3-gallate, a polyphenol abundant in green tea with antioxidant and metabolic benefits; **FBG:**

fasting blood glucose, the amount of glucose in the lab following some time of fasting, which is used to assess metabolic health; **FPG:** fasting plasma glucose, the other standard test to measure the level of glucose and identify diabetes;

Research indicates that quercetin demonstrates significant therapeutic advantages in the management of PCOS. Quercetin exerts diverse effects by influencing many pathways, thereby regulating metabolic, endocrine, and molecular processes, which eventually alleviates symptoms and enhances quality of life (Jyoti *, Sonia, Chennu M. M. Prasada Rao, 2025). Another study thoroughly records the development of bioactive phytochemicals, including flavonoids, polyphenols, and alkaloids, from TCM and medicinal plants in the treatment of PCOS. The literature claims that these beneficial phytochemicals showed anti-inflammatory, anti-oxidative, hormone-disorder and insulin-resistant (IR)-improving, and hyperinsulinemia-relieving therapeutic actions in PCOS, which were backed by in vitro and in vivo studies (E. D. Luo et al., 2023). Nowadays, drugs used to treat PCOS can have negative side effects, like impairing fertility and raising the risk of venous thrombosis. PCOS is now being treated with drug delivery methods that include nanomaterials, which are distinguished by their extended half-life, precise distribution, improved bioavailability, and decreased toxicity. Many medicinal plants are deemed especially useful in relieving the complication of PCOS since they have therapeutic benefits and in many cases, have hypoglycemic effects which aid in the regulation of blood sugar and facilitate the balance of hormones [16]. In conjunction with these remedies, lifestyle changes, such as dietary and general health care changes are very important in ensuring stable levels of PCOS. Some new approaches are also being considered--one of them is an innovative nanotechnology-based approach that is becoming increasingly popular as an improved and dependable way of improving drug performance in treatment [3].

4. NANO CARRIER SYSTEM FOR PHYTOCHEMICAL DELIVERY

4.1.1 Using nanomedicine to diagnose PCOS: Henry Rhodes: 4.1.1. Nanomedicine to diagnose PCOS: Early and accurate diagnosis of polycystic ovary syndrome (PCOS) is essential in a way that patients will access faithful preventive care early and keep alive their fertility levels as well as reduce chances of cardiovascular, metabolic and reproductive complications later in life. Conventional PCOS testing, which primarily includes imaging, hormonal testing, and biochemistry screening, commonly has high cost, long turnaround time, little sensitivity, and unreliable accuracy across the different populations [17]. FSH-LH-testosterone hormone test can provide helpful information, but most often fails to capture the free, active form of androgens. The role of sex hormone-binding globulin (SHBG) has gained increased significance, since fluctuations of SHBG better reflect the quantities of the functional testosterone and enhance the accuracy of the diagnosis of PCOS-related hyperandrogenism. Nanotechnology can remedy these. Researchers can detect SHBG and other markers

using biosensors or diagnostic tools constructed with nanomaterials with greater sensitivity, reduced results, and reduced cost than other labs. The optical and electrical properties of gold nanoparticles, quantum dots and polymer-based nanosystems can be bound to biomolecules in a highly specific manner. Such properties enhance signal-strength, decrease the detection-limits, and reduce cross-reactivity thus they are the best candidates of next-generation PCOS diagnostics [18]. Hence, nanomedicine application to the diagnostics of PCOS could transform the way people detect it early and facilitate point-of care tests that are inexpensive, fast, and precise, which will eventually result in better patient outcomes and decision-making by making the system less overloaded.

4.1.2 Using nanomedicine to treat PCOS

Nanotechnology is a field of rapid growth in the context of diagnosis and treatment of polycystic ovarian syndrome (PCOS) (Fig. 1). The conventional drugs are not very effective and are accompanied by numerous side effects and that has led the researchers to consider even better methods. Nanomedicine has come out as one of these promising ones. Herbal-derived nanosystems, lipid-based nanocarriers, and metallic nanoparticles, including selenium and silver, are under trial as possible treatments, as either alone or in combination with standard medicines. As an example, silver nanoparticles obtained by extraction of Cinnamomum zeylanicum have been shown to be effective in lowering inflammatory markers in animal models and can be effectively used in the treatment of PCOS-induced inflammation. The other interesting bioactive substance being studied is curcumin, which is an antioxidant and anti-inflammatory agent. Curcumin supplementation has been associated with better insulin resistance, hyperlipidemia, hyperglycemia and hyperandrogenism in women with PCOS. Regrettably, its clinical potential is still restricted due to low bioavailability and low solubility in physiological pH. In order to address these obstacles, nano-formulated curcumin has been designed. The biocompatible variant is more polar, orally absorbed, has an increased uptake rate by the system orally, and is more bioavailable, making it a better choice in the treatment of PCOS. This suggests that nano-delivery of curcumin may present a viable treatment avenue to PCOS patients. Besides these new tactics, metformin remains among the most commonly prescribed medications used in PCOS. Its advantages are it can restore ovulation, decrease body weight, reduce circulating testosterone levels, and reduce the risk of miscarriage and type 2 diabetes. Metformin is not perfect, however. It has a short half-life, has limited oral bioavailability, and its side effects are worsened by the need to use high doses regularly, and since it has some adverse effects on the gastrointestinal tract, these effects include nausea, bloating, abdominal pain, diarrhoea, and a lingering metallic taste. This is an indication of the importance of selecting delivery systems that are specific to nanomedicine. They may

provide a better method to take medicine, but more significantly, they can relax the restrictions of the current treatments of PCOS.

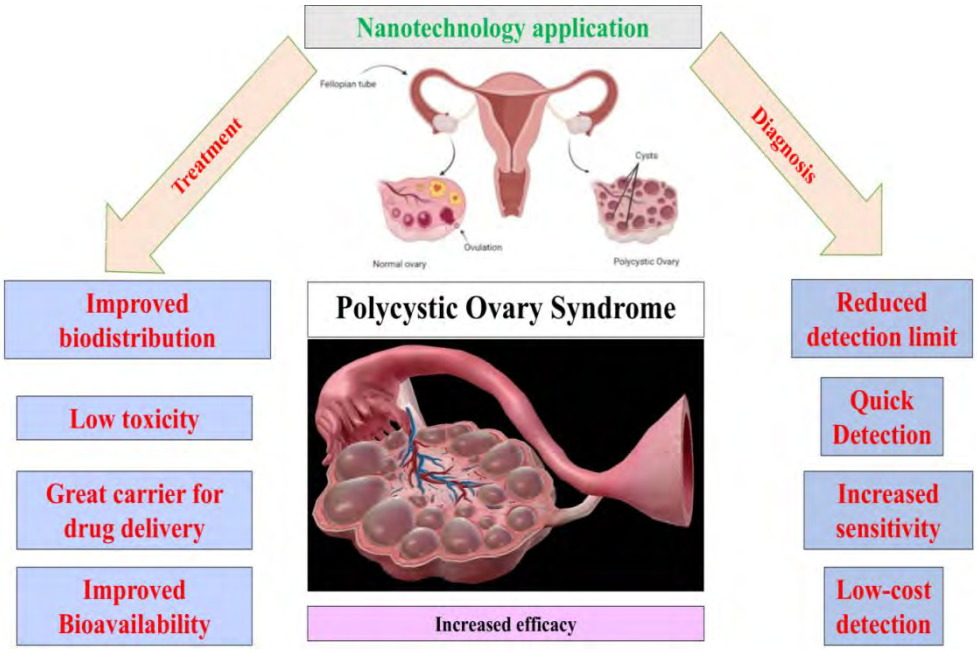

Figure 3.1: Nanotechnology for the treatment of PCOS

4.1.3 Polymeric Nanoparticles (PNs)

Current research lists using bioactive phytochemicals in pragmatic relationship with clomiphene citrate to treat polycystic ovary syndrome (PCOS) as adjuvant therapy. This is a promising combination to restore hormonal balance and improve the structure of the ovarian. These results indicate the diversified therapeutic application of phytochemical-carried delivery systems in contemporary medicine. Plastic nanoparticles (PNs) are already becoming popular in the biomedical sector. Their benefits, such as low toxicity, great biocompatibility, an easy method of production, and easy functionalization of surfaces rank them as the best drug delivery vehicles. Adding phytonutrients to PNs is an extensive debate in the field of breast cancer treatment, a tactic that proposes patient-centered and targeted therapy. The phytochemicals may get covalently attached to the backbone of the polymer, or be enclosed in the nanoparticle core, based on the formulation design. Artificial polymers (PLA, PGA, PLGA, poly anhydride and PSBMA) play a crucial role in the construction of polymeric nanostructures. They offer better control of the material breaking down process and strength.

Researchers employ various traditional methods of fabrication to prepare phytochemical-integrated polymeric nanoparticles (PNs). These consist of

nanoprecipitation, ionic gelation, layerbylayer assembly and evaporation by emulsions. All of them have their own advantages when it comes to particle size, stability, and encapsulation efficiency. This enables PNs to be tailored to therapeutic requirements.

A promising development has been the addition of bioactive phytochemicals to these nanosystems. It does not only enhance the therapeutic effect, but also forms synergies with several compounds. Indicatively, when co-encapsulated antioxidants and anti-inflammatory phytochemicals have the potential to interact with each other to enhance overall effects. A notable area of use is in reproductive health. Phytochemical mixtures in PNs have been able to balance hormones, stabilizing estradiol and progesterone. This proves that phytochemical-integrated PNs are not mere carriers. They can be used as a sophisticated multi-faceted platform that has the ability to deliver drugs in a controlled, sustained and targeted manner that can open new possibilities of managing the complex disease such as PCOS.

4.1.4 Nanomaterials in PCOS Treatment

Nanomedicines have advanced over the past three decades in the field of pharmacology. They have contributed greatly to the utility of certain medicines. There were many useful nano therapies developed in different human diseases. In PCOS treatment, recently, nanotechnology has been observed to make progress. These processes can be intervened by nanomaterial-based therapy in several ways. To treat these diseases, nano carriers are used as vehicles to deliver drugs in the body. Currently, we are using several Nano carriers in PCOS related conditions. They are nanoparticles, liposomes, carbon nanotubes, quantum dots and micelles. Their advantages, difficulties related to PCOS, and mechanisms of drug administration are as follows.

Table 3.2: List of nanocarriers with key drugs and their research objectives

Nano carrier	Key Ingredient	Therapeutic Agent	Research Objective	Reference
Chitosan nanoparticles	Chitosan	Curcumin	Rat	(Raja et al., 2021)
Ginger nanoparticles	Lipid	Ginger	Mice	(A. Kumar et al., 2022)
Silver nanoparticles	Silver	Cinnamomum cassia	Rat	(Kouame et al., 2019)
Silver nanoparticles	Silver	Cinnamomum zeylanicum	Rat	(Alwan & Al-Saeed, 2023)
Iron nanoparticles	Iron oxide	Curcumin	Mice	(Fatemi

				Abhari et al., 2020)
Selenium nanoparticles	Chitosan	Selenium dioxide	Rat	(Abdallah et al., 2023)
Selenium nanoparticles	Chitosan	Selenium dioxide	Rat	(Rabah et al., 2023)
Liposomes	Glycerol phospholipid	Methoxy derivatives of resveratrol (DMU-212)	Ovarian Granulosa cells	(Józkowiak et al., 2023)
Carbon nanotubes	Silkworm powder	Nitrogen-doped carbon nanorods (N-CNR)	Mice	(M. Park et al., 2022)
Quantum dot	Polyethylene glycol (PEG)	Metformin	Hepg2 cells	(Sarkar et al., 2024)

4.1.5 Enhanced Phytochemical Administration Techniques: Numerous plant-derived secondary metabolites demonstrate poor solubility and inadequate stability, hence limiting their application in medicinal research. Phenolic phytoconstituents exhibit significant antioxidant properties; nonetheless, they are unstable in experimental conditions. Moreover, despite their significant potential efficacy, bioactive substances like paclitaxel and curcumin exhibit poor solubility and bioavailability, necessitating the employment of toxic solvents. **Fig. 3.2** illustrates diverse categories of nanocarriers along with their characteristics.

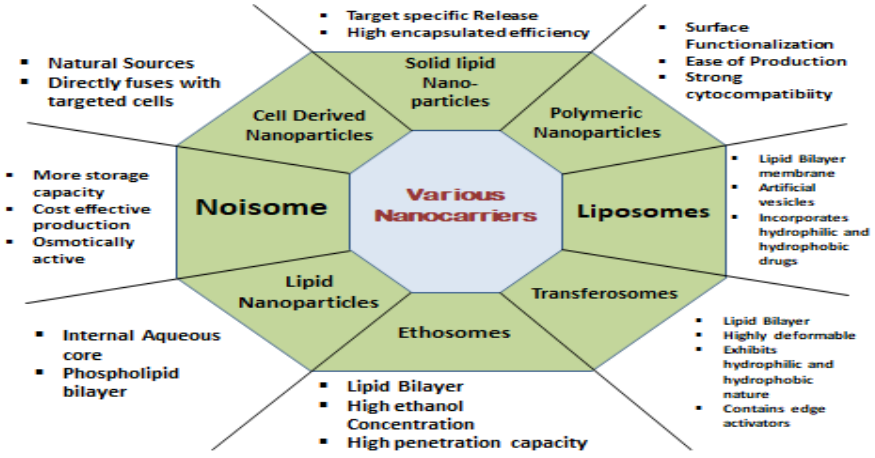

Figure 3.2: Categories of nanocarriers together with their attributes.

4.1.6 Natural-Based Drug Nanoparticles:

Such clinical studies as that conducted by Javad Heshmati et al. have noted that curcumin supplementation may serve as a safe and effective adjunctive treatment to diminish hyperandrogenism and high blood sugar levels typically linked to PCOS. Such like other experiments also have shown the benefit of herbal extracts in PCOS therapy- as in Aloe barbadensis gel giving restorative effects to the letrozole-induced animal models, with chamomile extract stimulating normal follicular development among the rats used. Though this is encouraging, the standard PCOS medication has side effects and not all people can respond to these medications. There has been increased interest in herbal medicines since plant compounds are able to interrelate and enhance the actions of others. Most plants have compounds that enhance insulin pampering, aid in the management of weight, control hormones and aid in ovulation. This has led to a lot of consideration being attributed to herbs as an alternative or complementary alternative or therapy. Natural therapy incorporates botanical, mineral or animal sources whose particular biological actions have been demonstrated scientifically. Plant-based medicine is employed in contemporary health care, particularly rehabilitation, prevention and treatment. According to a survey by Arentz et al, over 70 percent of PCOS women treated by conventional medicine transition to complementary medicines due to lack of satisfaction with conventional medicine. This continues to imply that less invasive and all-encompassing interventions are required. Doxorubicin is a working drug in breast-cancer are administered which produces SOS. Doxorubicin-induced cardiotoxicity is caused by these toxic molecules that damage heart tissue. A way is to add the doxorubicin to quercetin, which is a flavonoid, which is natural and exists in a large number of fruits and vegetables. Quercetin is an active antioxidant, which has the ability of neutralizing excess ROS and protecting heart tissue. This synergistic alternative is a ray of hope since it is determining a better future through better cancer treatment and lesser heart side effects which makes the treatment more promising and worth retaining by lesser heart effects and side effects which are otherwise fatal to patients. Natural drug nanoparticles have attracted a great interest during the past years. Their surface charge is comparable and they have a size similar to mammalian extracellular microbubbles. Such biomimetic nanocarriers carry drugs in vesicle-like constructs and conform to biological structures and functions, and are applicable in clinical practice. This similarity causes them to be potent rivals to the next generation biomedical technological procedures especially on the drug delivery platforms that they can tailor ad-hoc based on urgent clinical demands. An example of these natural molecules is curcumin, the plant-based phenolic compound which has been successfully identified as an antioxidant and anti-inflammatory agent and has been found to reduce the insulin resistance, hyperglycemia, and high levels of androgens in PCOS patients. However, low solubility of water and stability in various PHs undermine its therapeutic effect. To overcome these challenges scientists have turned to biocompatible polymeric nanoparticles such as chitosan (CS) that is a polysaccharide that has the characteristic to dissolve easily and is fairly easy to

manipulate and is relatively simple to manipulate that is a naturally occurring polysaccharide. CS can be dissolved heavily in water, though functionalisation by chemistry can be performed to allow it to trap a wide set of active agents to improve their pharmacokinetics. The cationic nature of its nanoparticles also makes the use of CS nanoparticles ideal in loading antimicrobials, analgesics and anti-inflammatory drugs. Raja et al. ready made curcumin-conjugated CS nanoparticles through a one-novie study, and were alkylated with coccobacillus arginine and N-acetylhistidine. They showed that serum insulin, LH, prolactin, and testosterone in a PCOS rat model were reduced significantly, which shows nanoparticles as a potent system to deliver curcumin. Another plant that has significant therapeutic relevance is Zingiber officinale, better known as ginger. The rhizome of it possesses a large range of bioactive molecules, such as phenolic derivatives, terpenes, and essential oils. Among all these, the primary bioactive ingredient is 6-gingerol that not only gives ginger its typical pungent taste but also has a metabolic impact. It is also discovered that 6-gingerol decreases insulin concentration in blood and improves their insulin potential, and due to this reason, it is an ideal material that one can contemplate in treating insulin-departing metabolic syndrome and PCOS. This was also confirmed in a report by Anil Kumar et al. who concluded that nanoparticles of ginger also inhibit insulin resistance by potentially promoting the expression of Foxa2 and interfering with insulin resistance signaling through exosome delivery by intestinal epithelial cells (IECs). The synergistic roles of ginger claim and its nanoparticles increase its application in usage as a food supplement and nanorice as an agent of delivery of nanomedicines. Light-brown cinnamon was used worldwide as a food additive, as a medication, and presented its virtues in aromatherapy over centuries. It belongs to the genus of spices, with numerous bioactive compounds: cinnamaldehyde, eugenol, iron, manganese, calcium, dietary fiber, among other trace elements, which has preconditioned the involvement of this product in the role of therapeutics. Recent scientific researches have analyzed the usefulness of cinnamon in the treatment process of PCOS in animal models and win clinical therapies. Findings indicate that cinnamon supplementation was able to re-establish normal estrous cycles in mice, reduce insulin and testosterone, and elevate luteinizing hormone(LH). The results complement the use cinnamon has throughout history as a natural medicine, and its position as a complementary medication to treat endocrine and metabolic diseases associated with PCOS.

5. ITS APPLICATIONS IN PCOS: CURRENT EVIDENCE

The effectiveness of treating PCOS patients has improved due to the elusive delivery of drugs in a more controlled manner. Scientists say that the development of delivery systems targeted to specific locations can be of immense benefit. To achieve this, the selective ligands can be subdivided into two broad categories including those, which bind receptors on the oocytes and those, which bind to receptors on the granulosa cells. This division assists scientists in creating drugs that get to the specific place of work.

The unique feature of nanoparticle drug carriers is that targeting ligands can be coated on the surfaces. This coating allows the drug to go directly to the target cell, enhancing precision and reducing undesired side effects. This targeting option is not implemented at traditional carriers, which typically provide less efficient treatment and increase their risk of side effects. Through the advantages of nanoparticle systems researchers are able to produce more selective and effective drugs and present new possibilities to better manage PCOS. Nanomaterials enhance gastrointestinal absorption and dissolution of drug, causing higher absorption into the systemic circulation. We increase bioavailability by covering drugs with nanoparticles: the drugs become more stable and have lower chances of being digested by enzymes, as well as more visible to the immune system. Nanoparticles also affect vital Vital pharmacokinetic processes, which include absorption, distribution, metabolism, and excretion processes. Because of this, drugs remain in the body longer and are eliminated slower. The extended circulation both enhances therapeutic effect and reduces unwanted side effects. Cell membranes and tissue barriers permeated more easily by nanoparticles as they are very small. It enables a greater amount of drug to be delivered to the area of action and avoids healthy tissue. Some of the experimental results emphasize these advantages. An example is the popular metformin that is used to treat insulin resistance in PCOS, which has demonstrated a prolonged half-life and enhanced accessibility when encased in nanoparticles. Similarly, first-line ovulation inducing medication, such as clomiphene citrate (CC), frequently impairs endometrial receptivity, which can impair fertility. A lean carried out by Marziyeh Ajdary and others revealed that a new formulation (Phosal-based formulation PBF) containing CC and released through nanoparticles enhanced the targeted delivery of the drug and reduced the adverse effect of the drug on the endometrium.

Enhancing Comprehension of the Etiological Mechanism of Polycystic Ovary Syndrome

More often, genetic, epigenetic, gut microbiota, corticolimbic brain activity, and metabolomic factors associated with PCOS have been identified (Figure 3) [32]. This development has been catalyzed by recent developments in molecular genetics, next-generation sequencing, transcriptomics, and proteomics.

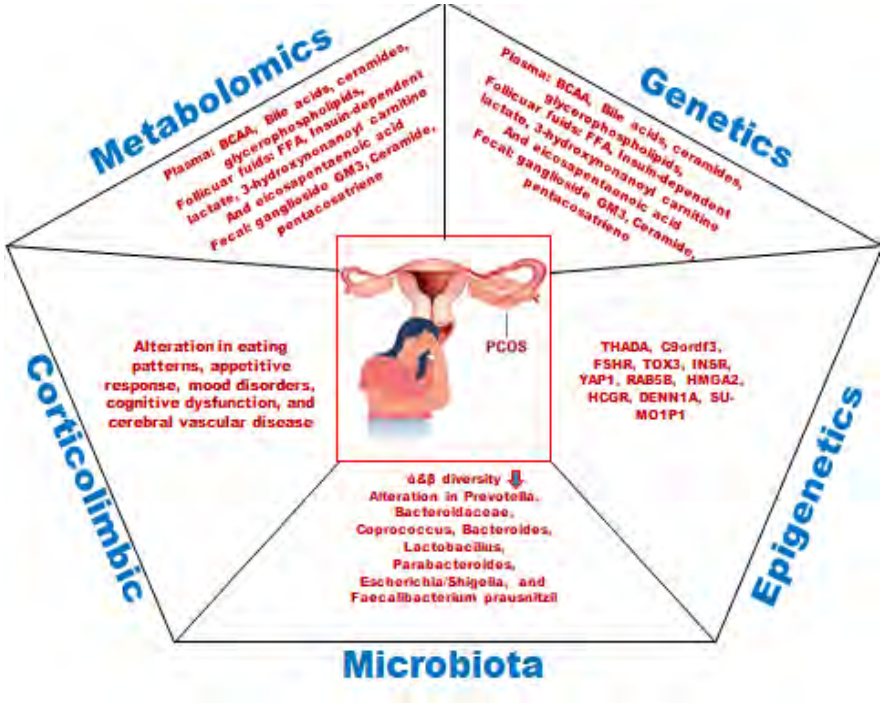

Figure 3.3: The causes of PCOS have been substantially identified, and insights have been found in the fields of genetics, epigenetics, the microbiome, corticolimbic brain activity, and metabolomics. The pathophysiology of the polycystic ovary syndrome is multifactorial.

BCCA- branched -chain amino acid; DNA -deoxyribonucleic acid; **DNMT3A -DNA** methyltransferase 3A; **FFA** -free fatty acid, **FSHR** -follicle-stimulating hormone receptor; INSR -insulin receptor ;**PCOS** -polycystic ovary syndrome; **TET** -ten-eleven translocation methylcytosine dioxygenases.

5. THERAPEUTIC CONUNDRUM IN POLYCYSTIC OVARY SYNDROME

The challenge to healthcare and population intervention in the future is that it would eliminate the intergenerational health risks associated with PCOS. Transmission of metabolic health issues to a series of generations presents a threat not only to the long-term health of a specific family unit, but also that of the entire society. This is the reason why it is a medical and socio-economic issue. In animal and human studies, there are numerous studies which consistently demonstrate that children on women with PCOS tend to develop a range of metabolic issues.As an example, mice subjected to prenatal androgen excess have been found to exhibit impaired glucose tolerance, abnormal accumulation of visceral fat, increased triglyceride in the circulation, structural cardiac changes including left ventricular hypertrophy, impaired liver fat production and exaggerated hepatic fat accumulation. These results are reflective of the increased health hazards in human populations. The risk of PCOS being passed on to daughters of PCOS women is significantly high. According to Risal and colleagues,

they had nearly five times the risk of developing PCOS. Large Swedish registry studies and Chilean case-control studies have confirmed this finding. The Finnish national birth registry demonstrated evident correlations between maternal PCOS and long-term health risks of children. Young children were 1.58 times more predisposed to become obese in childhood and 1.37 times to become obese in adolescence and greater than twice as likely to become type 2 diabetic when they were young adults. The research done by Zhang and the colleagues reported that a prospective study of the Ningbo birth cohort in China demonstrated comparable growth and metabolism patterns when the Ningbo birth cohort generation was matched to those of children born to PCOS mothers. Combined, these results suggest that the children of PCOS women have a higher risk of early metabolic complications. They have also significant risks to their reproduction, and that reflects an enormous intergenerational transmission of risks associated with PCOS. The implication is clear: not only are metabolic and reproductive dysfunctions inherited by members of the same generation, but survivors of one generation propagate them, which, correspondingly, preconditions the existence of a vicious circle of diseases that spread (**Fig. 3.4**).

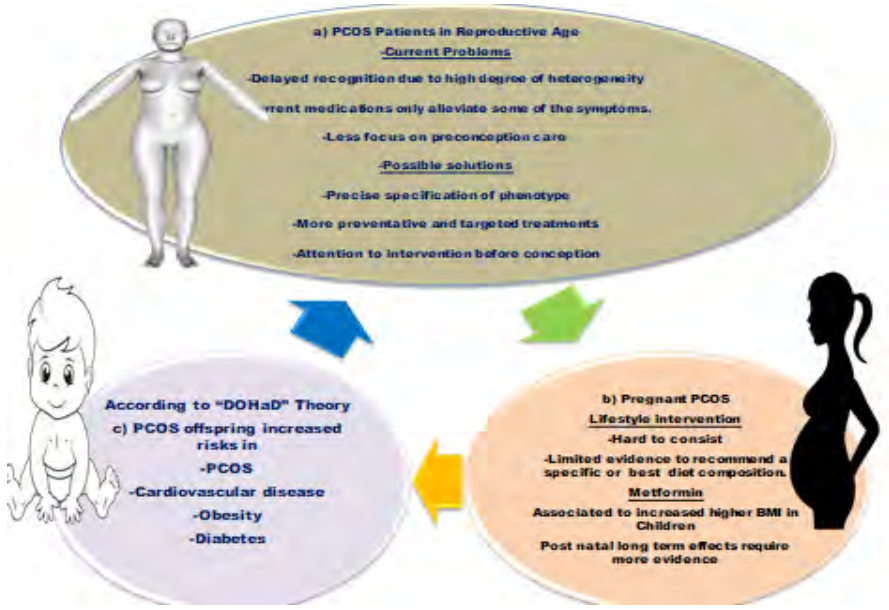

Figure 3.4: Timing in (a) One of the most pressing problems of the future is to eliminate this ongoing cycle. PCOS still has several diagnostic and treatment complications that pose the risk of missing timely intervention in people of reproductive age who have this medical condition. Besides the reproduction challenges, multimorphic metabolic derangements linked to PCOS also puts both the expectant mother and her infant at risk of health complications, therefore reinforcing the multigenerational-influencing effects.

(b) The therapeutic interventions involved in changing lifestyle, including metformin, are available and they remain safe in conception and pregnancy in most instances. The promise of

such interventions remains unrewarded, but requires more detailed research in the future, which will determine how effective they are over the long run, particularly in the area of ensuring that the transmission of the metabolic vulnerability has been prevented to descend the children of PCOS mothers. More studies in the area are required to inform the clinical practice and community health responses.

(c) According to the DOHaD (developments origins of health and disease) framework, a maladapted uterine environment during maternal PCOS (aged at conception) is potentially the causal factor in later, non-communicable disease outcomes. Children of mothers who have PCOs have a higher likelihood of getting metabolic disorders in early adulthood and this may jeopardise the health of their own children. The importance of preventing the spread of PCOS to protect future generations can be demonstrated by the level of this intergenerational burden.

CONCLUSION

Nanoparticles' therapeutic potential for PCOS is a largely untouched area of research, which calls for dedicated studies to determine their toxicity, clearance, and effectiveness. One way that nanotechnology can solve the problem is through, as it were, drug absorption and circulation that is prolonged and targeted organs getting the exact delivery of the drugs which thus, improves efficacy and minimizes side effects. Several types of nanocarriers, which include liposomes, micelles, carbon nanotubes, quantum dots, and the use of bioactive or metallic nanoparticles, in combination with targeting ligands, have all shown the capability of optimizing drug efficacy and patient adherence. The use of novel systems such as nanocrystals and nano-emulsions significantly enhances both solubility and stability, the case of liposomal doxorubicin and albumin-bound paclitaxel, revealing the potential of nanomedicine to increase the safety and effectiveness of therapies. On the other hand, clinical translation involves thorough assessment of the long-term effects, toxicity and excretion pathways in PCOS patients.

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REFERENCES

A machine learning approach for non-invasive PCOS diagnosis from ultrasound and clinical features | Scientific Reports. (n.d.). Retrieved October 9, 2025, from https://www.nature.com/articles/s41598-025-10453-9

Abdallah, A. B. E., El-Ghannam, M. A., Hasan, A. A., Mohammad, L. G., Mesalam, N. M., & Alsayed, R. M. (2023). Selenium Nanoparticles Modulate Steroidogenesis-Related Genes and Improve Ovarian Functions via Regulating Androgen Receptors Expression in Polycystic Ovary Syndrome Rat Model. *Biological Trace Element Research*, *201*(12), 5721–5733. https://doi.org/10.1007/s12011-023-03616-0

Advancements in lead therapeutic phytochemicals polycystic ovary syndrome: A review—PMC. (n.d.). Retrieved October 9, 2025, from https://pmc.ncbi.nlm.nih.gov/articles/PMC9868606/

Ahmad, S., Jaiswal, R., Yadav, R., & Verma, S. (2024). Recent advances in green chemistry approaches for pharmaceutical synthesis. *Sustainable Chemistry One World*, *4*, 100029. https://doi.org/10.1016/j.scowo.2024.100029

Ali, F., Neha, K., & Parveen, S. (2023). Current regulatory landscape of nanomaterials and nanomedicines: A global perspective. *Journal of Drug Delivery Science and Technology*, *80*, 104118. https://doi.org/10.1016/j.jddst.2022.104118

Altammar, K. A. (2023). A review on nanoparticles: Characteristics, synthesis, applications, and challenges. *Frontiers in Microbiology*, *14*, 1155622. https://doi.org/10.3389/fmicb.2023.1155622

Alwan, S. H., & Al-Saeed, M. H. (2023). Silver Nanoparticles Biofabricated from Cinnamomum zeylanicum Reduce IL-6, IL-18, and TNF-α in Female Rats with Polycystic Ovarian Syndrome. *International Journal of Fertility and Sterility*, *17*(1), 80–84. https://doi.org/10.22074/IJFS.2022.539396.1189

Available Treatments and Adjunctive Therapies for Polycystic Ovarian Syndrome (PCOS) Patients of Reproductive Age: A Scoping Review—PMC. (n.d.). Retrieved September 27, 2025, from https://pmc.ncbi.nlm.nih.gov/articles/PMC11524647/

Bae, G., Berezhnoy, G., Koch, A., Cannet, C., Schäfer, H., Kommoss, S., Brucker, S., Beziere, N., & Trautwein, C. (2023). Stratification of ovarian cancer borderline from high-grade serous carcinoma patients by quantitative serum NMR spectroscopy of metabolites, lipoproteins, and inflammatory markers. *Frontiers in Molecular Biosciences*, *10*, 1158330. https://doi.org/10.3389/fmolb.2023.1158330

Balash, M., Boucetta, H., & He, W. (2025). Factors affecting drug delivery system translation: A focus on advanced technologies, biological barriers, and regulatory challenges. *Journal of Controlled Release*, *387*, 114167. https://doi.org/10.1016/j.jconrel.2025.114167

Balasubramanian, A., Veluswami, K., Rao, S., Aggarwal, S., & Mani, S. (2024). Exploring Clustered Regularly Interspaced Short Palindromic Repeats-CRISPR-Associated Protein 9 (CRISPR-Cas9) as a Therapeutic Modality for Cancer: A Scoping Review. *Cureus*. https://doi.org/10.7759/cureus.64324

Barber, T. M., & Franks, S. (2021). Obesity and polycystic ovary syndrome. *Clinical Endocrinology*, *95*(4), 531–541. https://doi.org/10.1111/cen.14421

Basu, S., Biswas, P., Anto, M., Singh, N., & Mukherjee, K. (2024). Nanomaterial-enabled drug transport systems: A comprehensive exploration of current developments and future avenues in therapeutic delivery. *3 Biotech*, *14*(12), 289. https://doi.org/10.1007/s13205-024-04135-y

Beca, J. M., Chan, K. K. W., Naimark, D. M. J., & Pechlivanoglou, P. (2021). Impact of limited sample size and follow-up on single event survival extrapolation for health technology assessment: A simulation study. *BMC Medical Research Methodology*, *21*, 282. https://doi.org/10.1186/s12874-021-01468-7

Butt, M. A., Tabassum, S., Hardy, R. S., & Kiyani, M. M. (2025). Mechanistic insight into nanomedicine for polycystic ovary syndrome. *Molecular Biology Reports*, *52*(1), 618. https://doi.org/10.1007/s11033-025-10709-7

Cancer Nanomedicine: Emerging Strategies and Therapeutic Potentials. (n.d.). Retrieved October 9, 2025, from https://www.mdpi.com/1420-3049/28/13/5145

Cao, H., Duan, L., Zhang, Y., Cao, J., & Zhang, K. (2021). Current hydrogel advances in physicochemical and biological response-driven biomedical application diversity. *Signal Transduction and Targeted Therapy*, *6*(1), 426. https://doi.org/10.1038/s41392-021-00830-x

Che, Y., Yu, J., Li, Y.-S., Zhu, Y.-C., & Tao, T. (2023). Polycystic Ovary Syndrome: Challenges and Possible Solutions. *Journal of Clinical Medicine*, *12*(4), 1500. https://doi.org/10.3390/jcm12041500

Chen, W., & Pang, Y. (2021). Metabolic Syndrome and PCOS: Pathogenesis and the Role of Metabolites. *Metabolites*, *11*(12), 869. https://doi.org/10.3390/metabo11120869

Christ, J. P., & Cedars, M. I. (2023). Current Guidelines for Diagnosing PCOS. *Diagnostics*, *13*(6), 1113. https://doi.org/10.3390/diagnostics13061113

Cinti, C., Trivella, M. G., Joulie, M., Ayoub, H., & Frenzel, M. (2024). The Roadmap toward Personalized Medicine: Challenges and Opportunities. *Journal of Personalized Medicine*, *14*(6), 546. https://doi.org/10.3390/jpm14060546

CRISPR Technology Information | Thermo Fisher Scientific—IN. (n.d.). Retrieved October 9, 2025, from https://www.thermofisher.com/in/en/home/life-science/genome-editing/genome-editing-learning-center/crispr-cas9-technology-information.html?ef_id=745af40fabfc1f21c9c49ce815d23757:G:s&s_kwcid=AL!3652!10!76759856878772!!!76760083577185!!471266840!1228155570022931&cid=bid_clb_gme_r01_co_cp0000_pjt0000_bid00000_0se_bng_nt_pur_con

Dave, R., Pandey, K., Patel, R., Gour, N., & Bhatia, D. (2025). Leveraging 3D cell culture and AI technologies for next-generation drug discovery. *Cell Biomaterials*, *1*(3), 100050. https://doi.org/10.1016/j.celbio.2025.100050

Dewani, D., Karwade, P., & Mahajan, K. S. (2023). The Invisible Struggle: The Psychosocial Aspects of Polycystic Ovary Syndrome. *Cureus*. https://doi.org/10.7759/cureus.51321

Dixit, P. V., & Mishra, D. K. (2025). Nanotechnology advances in treatment of reproductive diseases: From bench to bedside. *Journal of Reproductive Healthcare and Medicine*, *6*, 1. https://doi.org/10.25259/JRHM_28_2024

Endometrial Organoids and Their Role in Modeling Human Infertility—PubMed. (n.d.). Retrieved October 9, 2025, from https://pubmed.ncbi.nlm.nih.gov/40498005/

Erten, O., & Yılmaz, B. N. (2018). Three-Dimensional Imaging in Orthodontics. *Turkish Journal of Orthodontics*, *31*(3), 86–94. https://doi.org/10.5152/TurkJOrthod.2018.17041

Ezeh, U., Chen, Y. I., Pall, M., Buyalos, R. P., Chan, J. L., Pisarska, M. D., & Azziz, R. (2024). Alterations in nonesterified free fatty acid trafficking rather than hyperandrogenism contribute to metabolic health in obese women with polycystic ovary syndrome. *Fertility and Sterility*, *121*(6), 1040–1052. https://doi.org/10.1016/j.fertnstert.2024.01.030

Fatemi Abhari, S. M., Khanbabaei, R., Hayati Roodbari, N., Parivar, K., & Yaghmaei, P. (2020). Curcumin-loaded super-paramagnetic iron oxide nanoparticle affects on apoptotic factors expression and histological changes in a prepubertal mouse model of polycystic ovary syndrome-induced by dehydroepiandrosterone—A molecular and stereological study. *Life Sciences*, *249*(March), 117515. https://doi.org/10.1016/j.lfs.2020.117515

Female Reproductive System Organ-On-A-Chip Model Development Services—Creative Biolabs. (n.d.). Retrieved October 9, 2025, from https://microfluidics.creative-biolabs.com/female-reproductive-system-organ-on-a-chip-model.htm

Friederich, J., & Lazarova-Molnar, S. (2024). Reliability assessment of manufacturing systems: A comprehensive overview, challenges and opportunities. *Journal of Manufacturing Systems*, *72*, 38–58. https://doi.org/10.1016/j.jmsy.2023.11.001

Frontiers | Application of machine learning and artificial intelligence in the diagnosis and classification of polycystic ovarian syndrome: A systematic review. (n.d.). Retrieved October 9, 2025, from https://www.frontiersin.org/journals/endocrinology/articles/10.3389/fendo.2023.1106625/full

Fukutomi, R., Ohishi, T., Koyama, Y., Pervin, M., Nakamura, Y., & Isemura, M. (2021). Beneficial Effects of Epigallocatechin-3-O-Gallate, Chlorogenic Acid, Resveratrol, and Curcumin on Neurodegenerative Diseases. *Molecules*, *26*(2), 415. https://doi.org/10.3390/molecules26020415

Ghafari, A., Maftoohi, M., Samarin, M. E., Barani, S., Banimohammad, M., & Samie, R. (2025a). The last update on polycystic ovary syndrome(PCOS), diagnosis criteria, and novel treatment. *Endocrine and Metabolic Science*, *17*, 100228. https://doi.org/10.1016/j.endmts.2025.100228

Ghafari, A., Maftoohi, M., Samarin, M. E., Barani, S., Banimohammad, M., & Samie, R. (2025b). The last update on polycystic ovary syndrome(PCOS), diagnosis criteria, and novel treatment. *Endocrine and Metabolic Science*, *17*, 100228. https://doi.org/10.1016/j.endmts.2025.100228

Gonzalez, J. C., Park, K. W., Evans, D. B., Sharma, R., Sahaym, O., Gopalakrishnan, S., Dar, A. I., Valdez, T. A., & Sharma, A. (2025). Nano Approaches to Nucleic Acid Delivery: Barriers, Solutions, and Current Landscape. *WIREs Nanomedicine and Nanobiotechnology*, *17*(2), e70010. https://doi.org/10.1002/wnan.70010

Gorgey, A. S., Ennasr, A. N., Farkas, G. J., & Gater, D. R. (2021). Anthropometric Prediction of Visceral Adiposity in Persons With Spinal Cord Injury. *Topics in Spinal Cord Injury Rehabilitation*, *27*(1), 23–35. https://doi.org/10.46292/sci20-00055

Grant, P. (2010). Spearmint herbal tea has significant anti-androgen effects in polycystic ovarian syndrome. A randomized controlled trial. *Phytotherapy Research*, *24*(2), 186–188. https://doi.org/10.1002/ptr.2900

Guo, W., Xu, Y., Tian, T., Yang, S., Li, R., Qiao, J., & Zheng, X. (2023). Outcomes of the Next In Vitro Fertilization Cycle in Women with Polycystic Ovary Syndrome after a Failed In Vitro Maturation Attempt. *Journal of Clinical Medicine*, *12*(17), 5761. https://doi.org/10.3390/jcm12175761

Gupta, U., Kosey, S., & Pal, R. (2025). Advancements in nanotechnology-based targeted drug delivery systems for glioblastoma chemotherapy: A comprehensive review. *Journal of Drug Delivery Science and Technology*, *111*, 107181. https://doi.org/10.1016/j.jddst.2025.107181

Hanssen, N. M. J., Kraakman, M. J., Flynn, M. C., Nagareddy, P. R., Schalkwijk, C. G., & Murphy, A. J. (2020). Postprandial Glucose Spikes, an Important Contributor to Cardiovascular Disease in Diabetes? *Frontiers in Cardiovascular Medicine*, *7*, 570553. https://doi.org/10.3389/fcvm.2020.570553

Heery, Aprn, Aocns, Cbcn, M., Farley, PharmD, Bcop, S., Sparkman, PharmD, R., Healy, Bs, PharmD, J., Eighmy, PharmD, W., Zahrah, Md, G., & Zelkowitz, Md, R. (2020). Precautions for Patients Taking Aromatase Inhibitors. *Journal of the Advanced Practitioner in Oncology*, *11*(2). https://doi.org/10.6004/jadpro.2020.11.2.6

Holland-Letz, T., & Kopp-Schneider, A. (2015). Optimal experimental designs for dose–response studies with continuous endpoints. *Archives of Toxicology*, *89*(11), 2059–2068. https://doi.org/10.1007/s00204-014-1335-2

Höller, M., Steindl, H., Abramov-Sommariva, D., Kleemann, J., Loleit, A., Abels, C., & Stute, P. (2024). Use of Vitex agnus-castus in patients with menstrual cycle disorders: A single-center retrospective longitudinal cohort study. *Archives of Gynecology and Obstetrics*, *309*(5), 2089–2098. https://doi.org/10.1007/s00404-023-07363-4

Human organoid systems in modeling reproductive tissue development, function, and disease | Human Reproduction | Oxford Academic. (n.d.). Retrieved October 9, 2025, from https://academic.oup.com/humrep/article/38/8/1449/7147082?login=false

Intharuksa, A., Kuljarusnont, S., Sasaki, Y., & Tungmunnithum, D. (2024). Flavonoids and Other Polyphenols: Bioactive Molecules from Traditional Medicine Recipes/Medicinal Plants and Their Potential for Phytopharmaceutical and Medical Application. *Molecules*, *29*(23), 5760. https://doi.org/10.3390/molecules29235760

Jamshidi, N., & Cohen, M. M. (2017). The Clinical Efficacy and Safety of Tulsi in Humans: A Systematic Review of the Literature. *Evidence-Based Complementary and Alternative Medicine*, *2017*(1), 9217567. https://doi.org/10.1155/2017/9217567

Józkowiak, M., Kobylarek, D., Bryja, A., Gogola-Mruk, J., Czajkowski, M., Skupin-Mrugalska, P., Kempisty, B., Spaczyński, R. Z., & Piotrowska-Kempisty, H. (2023). Steroidogenic activity of liposomal methylated resveratrol analog 3,4,5,4′-tetramethoxystilbene (DMU-212) in human luteinized granulosa cells in a primary three-dimensional in vitro model. *Endocrine*, *82*(3), 681–694. https://doi.org/10.1007/s12020-023-03458-9

Juguilon, C., Khosravi, R., Radisic, M., & Wu, J. C. (2025). In Vitro Modeling of Interorgan Crosstalk: Multi-Organ-on-a-Chip for Studying Cardiovascular-Kidney-Metabolic Syndrome. *Circulation Research*, *136*(11), 1476–1493. https://doi.org/10.1161/CIRCRESAHA.125.325497

Jyoti *, Sonia, Chennu M. M. Prasada Rao, T. R. and R. K. S. (2025). Unveiling the Anti-Diabetic Potential of Quercetin As a Natural Bioactive Compound—A Review. *International Journal of Pharmacognosy*, *12*(1), 1–23. https://doi.org/10.13040/IJPSR.0975-8232.IJP.12(1).1-12

Kaushal, A., Musafir, A., Sharma, G., Rani, S., Singh, R. K., Kumar, A., Bhadada, S. K., Barnwal, R. P., & Singh, G. (2025). Revolutionizing Diabetes Management Through Nanotechnology-Driven Smart Systems. *Pharmaceutics*, *17*(6), 777. https://doi.org/10.3390/pharmaceutics17060777

Kim, K.-W. (2021). Unravelling Polycystic Ovary Syndrome and Its Comorbidities. *Journal of Obesity & Metabolic Syndrome*, *30*(3), 209–221. https://doi.org/10.7570/jomes21043

Kouame, K., Peter, A. I., Akang, E. N., Moodley, R., Naidu, E. C., & Azu, O. O. (2019). Histological and biochemical effects of Cinnamomum cassia nanoparticles in kidneys of diabetic Sprague-Dawley rats. *Bosnian Journal of Basic Medical Sciences*, *19*(2), 138–145. https://doi.org/10.17305/bjbms.2019.3481

Kumar, A., Sundaram, K., Teng, Y., Mu, J., Sriwastva, M. K., Zhang, L., Hood, J. L., Yan, J., Zhang, X., Park, J. W., Merchant, M. L., & Zhang, H. G. (2022). Ginger nanoparticles mediated induction of Foxa2 prevents high-fat diet-induced insulin resistance. *Theranostics*, *12*(3), 1388–1403. https://doi.org/10.7150/thno.62514

Kumar, R. (2023). Nanotechnology in herbal medicine: Challenges and future perspectives. In *Nanotechnology in Herbal Medicine* (pp. 515–548). Elsevier. https://doi.org/10.1016/B978-0-323-99527-6.00008-2

Liang, J., Gao, Y., Feng, Z., Zhang, B., Na, Z., & Li, D. (2023). Reactive oxygen species and ovarian diseases: Antioxidant strategies. *Redox Biology*, *62*, 102659. https://doi.org/10.1016/j.redox.2023.102659

Lino, C., Barrias, S., Chaves, R., Adega, F., Martins-Lopes, P., & Fernandes, J. R. (2022). Biosensors as diagnostic tools in clinical applications. *Biochimica et Biophysica Acta (BBA) - Reviews on Cancer*, *1877*(3), 188726. https://doi.org/10.1016/j.bbcan.2022.188726

Liu, Y., Liang, Y., Yuhong, J., Xin, P., Han, J. L., Du, Y., Yu, X., Zhu, R., Zhang, M., Chen, W., & Ma, Y. (2024). Advances in Nanotechnology for Enhancing the Solubility and Bioavailability of Poorly Soluble Drugs. *Drug Design, Development and Therapy*, *Volume 18*, 1469–1495. https://doi.org/10.2147/DDDT.S447496

Livadas, S., Anagnostis, P., Bosdou, J. K., Bantouna, D., & Paparodis, R. (2022). Polycystic ovary syndrome and type 2 diabetes mellitus: A state-of-the-art review. *World Journal of Diabetes*, *13*(1), 5–26. https://doi.org/10.4239/wjd.v13.i1.5

Luo, E. D., Jiang, H. M., Chen, W., Wang, Y., Tang, M., Guo, W. M., Diao, H. Y., Cai, N. Y., Yang, X., Bian, Y., & Xing, S. S. (2023). Advancements in lead therapeutic phytochemicals polycystic ovary syndrome: A review. *Frontiers in Pharmacology*, *13*(January), 1–21. https://doi.org/10.3389/fphar.2022.1065243

Luo, X., Jia, K., Xing, J., & Yi, J. (2024). The utilization of nanotechnology in the female reproductive system and related disorders. *Heliyon*, *10*(3), e25477. https://doi.org/10.1016/j.heliyon.2024.e25477

Maan, P., Gautam, R., Vasudevan, S., Menon, G. R., Arora, A., Nair, A., Jabbar, P. K., & Arora, T. (2025). Pharmacological and Non-Pharmacological Interventions for Polycystic Ovary Syndrome (PCOS) in Indian Women: A Systematic Review and Meta-Analysis. *Pharmaceuticals*, *18*(5), 680. https://doi.org/10.3390/ph18050680

Mahalmani, V., Sinha, S., Prakash, A., & Medhi, B. (2022a). Translational research: Bridging the gap between preclinical and clinical research. *Indian Journal of Pharmacology*, *54*(6), 393–396. https://doi.org/10.4103/ijp.ijp_860_22

Mahalmani, V., Sinha, S., Prakash, A., & Medhi, B. (2022b). Translational research: Bridging the gap between preclinical and clinical research. *Indian Journal of Pharmacology*, *54*(6), 393–396. https://doi.org/10.4103/ijp.ijp_860_22

Malik, S., Singh, J., Goyat, R., Saharan, Y., Chaudhry, V., Umar, A., Ibrahim, A. A., Akbar, S., Ameen, S., & Baskoutas, S. (2023). Nanomaterials-based biosensor and their applications: A review. *Heliyon*, *9*(9), e19929. https://doi.org/10.1016/j.heliyon.2023.e19929

Mangla, B., Kumar, P., Javed, S., Pathan, T., Ahsan, W., & Aggarwal, G. (2025). Regulating nanomedicines: Challenges, opportunities, and the path forward. *Nanomedicine (London, England)*, *20*(15), 1911–1927. https://doi.org/10.1080/17435889.2025.2533107

Mechanistic Review on the Role of Gut Microbiota in the Pathology of Cardiovascular Diseases. (2024). *Cardiovascular & Hematological Disorders-Drug Targets*, *24*(1), 13–39. https://doi.org/10.2174/011871529X310857240607103028

Mehta, M., Bui, T. A., Yang, X., Aksoy, Y., Goldys, E. M., & Deng, W. (2023). Lipid-Based Nanoparticles for Drug/Gene Delivery: An Overview of the Production Techniques and Difficulties Encountered in Their Industrial Development. *ACS Materials Au*, *3*(6), 600–619. https://doi.org/10.1021/acsmaterialsau.3c00032

Meissner, H. O., Mscisz, A., Reich-Bilinska, H., Mrozikiewicz, P., Bobkiewicz-Kozlowska, T., Kedzia, B., Lowicka, A., & Barchia, I. (2006). Hormone-Balancing Effect of Pre-Gelatinized Organic Maca (Lepidium peruvianum Chacon): (III) Clinical responses of early-postmenopausal women to Maca in double blind, randomized, Placebo-controlled, crossover configuration, outpatient study. *International Journal of Biomedical Science: IJBS*, *2*(4), 375–394.

Merza, W. M., Yaseen, A. K., & Mahmood, M. A. (2025). FSH, LH, lipid and adipokines in Polycystic Ovary Syndrome: Clinical biochemistry insights for diagnosis and management. *The Journal of Steroid Biochemistry and Molecular Biology*, *251*, 106773. https://doi.org/10.1016/j.jsbmb.2025.106773

Miller, L. B., Feuz, M. B., Meyer, R. G., & Meyer-Ficca, M. L. (2024). Reproductive toxicology: Keeping up with our changing world. *Frontiers in Toxicology*, *6*, 1456687. https://doi.org/10.3389/ftox.2024.1456687

Mohammed, S., Cockburn, B. N., & Sundaram, V. (2024). Exploring the Novel Alternative and Modern Treatment Options for Polycystic Ovary Syndrome-A Review. *Integrative Medicine Reports*, *3*(1), 33–42. https://doi.org/10.1089/imr.2023.0045

Moka, M. K., Sriram, D. K., & George, M. (2025). Recent Advances in Individualized Clinical Strategies for Polycystic Ovary Syndrome: Evidence From Clinical Trials and Emerging Pharmacotherapies. *Clinical Therapeutics*, *47*(2), 158–167. https://doi.org/10.1016/j.clinthera.2024.11.015

Montanino Oliva, M., Gambioli, R., Forte, G., Porcaro, G., Aragona, C., & Unfer, V. (2022). Unopposed estrogens: Current and future perspectives. *European Review for Medical and Pharmacological Sciences*, *26*(8), 2975–2989. https://doi.org/10.26355/eurrev_202204_28629

Mukherjee, S., Chopra, H., Goyal, R., Jin, S., Dong, Z., Das, T., & Bhattacharya, T. (2024). Therapeutic effect of targeted antioxidant natural products. *Discover Nano*, *19*(1), 144. https://doi.org/10.1186/s11671-024-04100-x

Muskan, Gupta, D., & Negi, N. P. (2022). 3D bioprinting: Printing the future and recent advances. *Bioprinting*, *27*, e00211. https://doi.org/10.1016/j.bprint.2022.e00211

Muthukumaran, D., & Shanmugam, R. (2024a). Nanoparticle-based interventions for polycystic ovary syndrome: A review of mechanisms and therapeutic potential. *Journal of Drug Delivery Science and Technology*, *102*, 106348. https://doi.org/10.1016/j.jddst.2024.106348

Muthukumaran, D., & Shanmugam, R. (2024b). Nanoparticle-based interventions for polycystic ovary syndrome: A review of mechanisms and therapeutic potential. *Journal of Drug Delivery Science and Technology*, *102*, 106348. https://doi.org/10.1016/j.jddst.2024.106348

Muthukumaran, D., & Shanmugam, R. (2024c). Nanoparticle-based interventions for polycystic ovary syndrome: A review of mechanisms and therapeutic potential. *Journal of Drug Delivery Science and Technology*, *102*, 106348. https://doi.org/10.1016/j.jddst.2024.106348

Nanoparticle-based interventions for polycystic ovary syndrome: A review of mechanisms and therapeutic potential—ScienceDirect. (n.d.). Retrieved October 9, 2025, from https://www.sciencedirect.com/science/article/abs/pii/S1773224724010177

Nanoparticles for Polycystic Ovary Syndrome (PCOS) Therapy: Exosomes and Synthetic Nanoparticles, Challenges and Opportunities—PubMed. (n.d.). Retrieved October 9, 2025, from https://pubmed.ncbi.nlm.nih.gov/40892199/

Next-Generation Drug Delivery for Neurotherapeutics: The Promise of Stimuli-Triggered Nanocarriers—PMC. (n.d.). Retrieved October 9, 2025, from https://pmc.ncbi.nlm.nih.gov/articles/PMC12191273/

Oguz, S. H., & Yildiz, B. O. (2021). An Update on Contraception in Polycystic Ovary Syndrome. *Endocrinology and Metabolism*, *36*(2), 296–311. https://doi.org/10.3803/EnM.2021.958

Overcoming the barriers of two-dimensional cell culture systems with three-dimensional cell culture systems: Techniques, drug discovery, and biomedical applications—ScienceDirect. (n.d.). Retrieved October 9, 2025, from https://www.sciencedirect.com/science/article/abs/pii/B9780128239667000037

Overview of clinical study designs—PMC. (n.d.). Retrieved October 9, 2025, from https://pmc.ncbi.nlm.nih.gov/articles/PMC11009715/

Pandey, V., Sharma, S., & Pokharel, Y. R. (2025). Exploring CRISPR-Cas: The transformative impact of gene editing in molecular biology. *Molecular Therapy Nucleic Acids*, *36*(4), 102717. https://doi.org/10.1016/j.omtn.2025.102717

Parashar, A. K., Hardenia, A., Dwivedi, S. K., Saraogi, G. K., & Hardenia, S. (2025). Next-Generation Nucleic Acid Delivery: A Review of Nanobiosystem Design and Applications. *Current Gene Therapy*, *25*. https://doi.org/10.2174/0115665232367377250519114910

Parihar, A., Parihar, D. S., Gaur, K., Arya, N., Choubey, V. K., & Khan, R. (2024). 3D bioprinting for drug development and screening: Recent trends towards personalized medicine. *Hybrid Advances*, *7*, 100320. https://doi.org/10.1016/j.hybadv.2024.100320

Park, C. H., Park, J. H., & Suh, Y. J. (2024). Perspective of 3D culture in medicine: Transforming disease research and therapeutic applications. *Frontiers in Bioengineering and Biotechnology*, *12*. https://doi.org/10.3389/fbioe.2024.1491669

Pal, Rahul & Pandey, Prachi & Chawra, Himmat & Khan, Zuber. (2025). Nano Drug Delivery Carriers (Nanocarriers): A Promising Targeted Strategy in Tuberculosis and Pain Treatment. Pharmaceutical Nanotechnology. 13. 10.2174/0122117385367493250224103839.

Polycystic Ovarian Syndrome: A Review of Multi-omics Analyses | Reproductive Sciences. (n.d.). Retrieved October 9, 2025, from https://link.springer.com/article/10.1007/s43032-025-01789-8

Prakash, S. (2023). Nano-based drug delivery system for therapeutics: A comprehensive review. *Biomedical Physics & Engineering Express*, *9*(5), 052002. https://doi.org/10.1088/2057-1976/acedb2

Mishra, R., Pal, R., Khan, Z., Sahoo, S., Chawra, H. S., & Kumar, D. (2025). Solid Lipid Nanoparticles (SLNPs): A State-of-the-Art Formulation Strategy and their Applications against Tuberculosis (TB) and Analgesic Effects. Nanoscience & Nanotechnology-Asia, 15(3), E22106812379362.

Principles of nanoparticle design for overcoming biological barriers to drug delivery | Nature Biotechnology. (n.d.). Retrieved October 9, 2025, from https://www.nature.com/articles/nbt.3330

Purwar, A., & Nagpure, S. (2022). Insulin Resistance in Polycystic Ovarian Syndrome. *Cureus*. https://doi.org/10.7759/cureus.30351

Rabah, H. M., Mohamed, D. A., Mariah, R. A., Abd El-Khalik, S. R., Khattab, H. A., AbuoHashish, N. A., Abdelsattar, A. M., Raslan, M. A., Farghal, E. E., & Eltokhy, A. K. (2023). Novel insights into the synergistic effects of selenium nanoparticles and metformin treatment of letrozole—Induced polycystic ovarian syndrome: Targeting PI3K/Akt signalling pathway, redox status and mitochondrial dysfunction in ovarian tissue. *Redox Report*, *28*(1). https://doi.org/10.1080/13510002.2022.2160569

Pal, R., Pandey, P., Chawra, H. S., & Singh, R. P. (2025). Niosomal as Potential Vesicular Drug Nano-carriers for the Treatment of Tuberculosis (TB). Nanoscience & Nanotechnology-Asia, 15(1), E22106812323829.

Rai, A., Shukla, S., Gupta, R. K., & Mishra, A. (2025). ALS: A Silent Slayer of Motor Neurons. Traditional Chinese Herbal Medicine as an Effective Therapy. *Current Pharmaceutical Design*, *31*(17), 1328–1346. https://doi.org/10.2174/0113816128329141241205063352

Raja, M. A., Maldonado, M., Chen, J., Zhong, Y., & Gu, J. (2021). Development and evaluation of curcumin encapsulated self-assembled nanoparticles as potential remedial treatment for pcos in a female rat model. *International Journal of Nanomedicine*, *16*, 6231–6247. https://doi.org/10.2147/IJN.S302161

Rashid, R., Mir, S. A., Kareem, O., Ali, T., Ara, R., Malik, A., Amin, F., & Bader, G. N. (2022). Polycystic ovarian syndrome-current pharmacotherapy and clinical implications. *Taiwanese Journal of Obstetrics and Gynecology*, *61*(1), 40–50. https://doi.org/10.1016/j.tjog.2021.11.009

Rashidi, N., Davidson, M., Apostolopoulos, V., & Nurgali, K. (2024). Nanoparticles in cancer diagnosis and treatment: Progress, challenges, and opportunities. *Journal of Drug Delivery Science and Technology*, *95*, 105599. https://doi.org/10.1016/j.jddst.2024.105599

Recent advances and FDA approvals in nanoformulations for drug delivery | Journal of Nanoparticle Research. (n.d.). Retrieved October 9, 2025, from https://link.springer.com/article/10.1007/s11051-024-06199-6

Recent Advances in the Management of Polycystic Ovary Syndrome: A Review Article—PMC. (n.d.). Retrieved September 27, 2025, from https://pmc.ncbi.nlm.nih.gov/articles/PMC9440853/

Recent Review on Biological Barriers and Host–Material Interfaces in Precision Drug Delivery: Advancement in Biomaterial Engineering for Better Treatment Therapies—PMC. (n.d.). Retrieved October 9, 2025, from https://pmc.ncbi.nlm.nih.gov/articles/PMC11360117/

Rodríguez-Yoldi, M. J. (2021). Anti-Inflammatory and Antioxidant Properties of Plant Extracts. *Antioxidants*, *10*(6), 921. https://doi.org/10.3390/antiox10060921

Ryu, Y., Kim, S. W., Kim, Y. Y., & Ku, S.-Y. (2019). Animal Models for Human Polycystic Ovary Syndrome (PCOS) Focused on the Use of Indirect Hormonal Perturbations: A Review of the Literature. *International Journal of Molecular Sciences*, *20*(11), 2720. https://doi.org/10.3390/ijms20112720

Sabbadin, C., Andrisani, A., Zermiani, M., Donà, G., Bordin, L., Ragazzi, E., Boscaro, M., Ambrosini, G., & Armanini, D. (2016). Spironolactone and intermenstrual bleeding in polycystic ovary syndrome with normal BMI. *Journal of Endocrinological Investigation*, *39*(9), 1015–1021. https://doi.org/10.1007/s40618-016-0466-0

Sabir, S., Thani, A. S. B., & Abbas, Q. (2025). Nanotechnology in cancer treatment: Revolutionizing strategies against drug resistance. *Frontiers in Bioengineering and Biotechnology*, *13*, 1548588. https://doi.org/10.3389/fbioe.2025.1548588

Sahu, T., Ratre, Y. K., Chauhan, S., Bhaskar, L. V. K. S., Nair, M. P., & Verma, H. K. (2021). Nanotechnology based drug delivery system: Current strategies and emerging therapeutic potential for medical science. *Journal of Drug Delivery Science and Technology*, *63*, 102487. https://doi.org/10.1016/j.jddst.2021.102487

Salm, S., Rutz, J., Van Den Akker, M., Blaheta, R. A., & Bachmeier, B. E. (2023). Current state of research on the clinical benefits of herbal medicines for non-life-threatening ailments. *Frontiers in Pharmacology*, *14*, 1234701. https://doi.org/10.3389/fphar.2023.1234701

Sarkar, K., Chatterjee, A., Bankura, B., Bank, S., Paul, N., Chatterjee, S., Das, A., Dutta, K., Chakraborty, S., De, S., Al-Masud, A. A., Khan, G. A., Chattopadhyay, D., & Das, M. (2024). Efficacy of pegylated Graphene oxide quantum dots as a nanoconjugate sustained release metformin delivery system in in vitro insulin resistance model. *PLoS ONE*, *19*(8 August), 1–15. https://doi.org/10.1371/journal.pone.0307166

Serrano, D. R., Kara, A., Yuste, I., Luciano, F. C., Ongoren, B., Anaya, B. J., Molina, G., Diez, L., Ramirez, B. I., Ramirez, I. O., Sánchez-Guirales, S. A., Fernández-García, R., Bautista, L., Ruiz, H. K., & Lalatsa, A. (2023). 3D Printing Technologies in Personalized Medicine, Nanomedicines, and Biopharmaceuticals. *Pharmaceutics*, *15*(2), 313. https://doi.org/10.3390/pharmaceutics15020313

Shandilya, R., Pathak, N., Lohiya, N. K., Sharma, R. S., & Mishra, P. K. (2020). Nanotechnology in reproductive medicine: Opportunities for clinical translation. *Clinical and Experimental Reproductive Medicine*, *47*(4), 245–262. https://doi.org/10.5653/cerm.2020.03650

Shang, C., Lin, H., Fang, X., Wang, Y., Jiang, Z., Qu, Y., Xiang, M., Shen, Z., Xin, L., Lu, Y., Gao, J., & Cui, X. (2021). Beneficial effects of cinnamon and its extracts in the management of

cardiovascular diseases and diabetes. *Food & Function*, *12*(24), 12194–12220. https://doi.org/10.1039/D1FO01935J

Sheikh, I. M., Hassan, O. A., Adam, S. M., Ali, A. I., Ogedegbe, O. J., Tabowei, G., Barbarawi, A., Yussuf, F. M., & Nor, M. A. (2023). Association of Pioglitazone With Major Adverse Cardiovascular Events, All-Cause Mortality, and Heart Failure Hospitalizations: A Systematic Review. *Cureus*. https://doi.org/10.7759/cureus.46911

Shi, M., Li, X., Xing, L., Li, Z., Zhou, S., Wang, Z., Zou, X., She, Y., Zhao, R., & Qin, D. (2024). Polycystic Ovary Syndrome and the Potential for Nanomaterial-Based Drug Delivery in Therapy of This Disease. *Pharmaceutics*, *16*(12), 1556. https://doi.org/10.3390/pharmaceutics16121556

Singh, D. (2025). Nanotechnology-based Diagnostic Approaches for Early Detection and Monitoring of Polycystic Ovary Syndrome (PCOS). *Current Analytical Chemistry*, *21*(4), 263–275. https://doi.org/10.2174/0115734110311450240612051821

Singh, S., Arya, V., Mishra, R. K., Rajput, S. K., & Dhanasekaran, M. (2024). Nanotechnology in the diagnosis and management of polycystic ovary syndrome: A systematic scoping analysis to improve patient care. *Next Research*, *1*(1), 100004. https://doi.org/10.1016/j.nexres.2024.100004

Su, P., Chen, C., & Sun, Y. (2025). Physiopathology of polycystic ovary syndrome in endocrinology, metabolism and inflammation. *Journal of Ovarian Research*, *18*(1), 34. https://doi.org/10.1186/s13048-025-01621-6

Teja, P. K., Mithiya, J., Kate, A. S., Bairwa, K., & Chauthe, S. K. (2022). Herbal nanomedicines: Recent advancements, challenges, opportunities and regulatory overview. *Phytomedicine*, *96*, 153890. https://doi.org/10.1016/j.phymed.2021.153890

The interaction between nanoparticles and immune system: Application in the treatment of inflammatory diseases | Journal of Nanobiotechnology | Full Text. (n.d.). Retrieved October 9, 2025, from https://jnanobiotechnology.biomedcentral.com/articles/10.1186/s12951-022-01343-7

The Promise of Nanotechnology in Personalized Medicine—PMC. (n.d.). Retrieved October 9, 2025, from https://pmc.ncbi.nlm.nih.gov/articles/PMC9142986/

Therapeutic Nanoparticles and Their Targeted Delivery Applications—PMC. (n.d.). Retrieved October 9, 2025, from https://pmc.ncbi.nlm.nih.gov/articles/PMC7248934/

Tumour-on-Chip Models for the Study of Ovarian Cancer: Current Challenges and Future Prospects. (n.d.). Retrieved October 9, 2025, from https://www.mdpi.com/2072-6694/17/19/3239

Unluhizarci, K., Karaca, Z., & Kelestimur, F. (2021). Role of insulin and insulin resistance in androgen excess disorders. *World Journal of Diabetes*, *12*(5), 616–629. https://doi.org/10.4239/wjd.v12.i5.616

Vasudevan, S., Gautam, R., Maan, P., Arora, A., Ganie, A., Jabbar, P. K., & Arora, T. (2025). A sustainable public health framework for PCOS management in low- and middle-income countries: A narrative review. *Frontiers in Reproductive Health*, *7*. https://doi.org/10.3389/frph.2025.1627670

Veerasamy, R. (2024). Development of Nanoparticles: Recent Developments and Future Prospects. In S. Bose, A. C. Shukla, M. R. Baig, & S. Banerjee (Eds.), *Concepts in Pharmaceutical Biotechnology and Drug Development* (pp. 67–89). Springer Nature Singapore. https://doi.org/10.1007/978-981-97-1148-2_5

Wang, H., & Yang, L. (2025). Ovarian Mechanobiology: Understanding the Interplay Between Mechanics and Follicular Development. *Cells*, *14*(5), 355. https://doi.org/10.3390/cells14050355

Wang, K., Li, Y., & Chen, Y. (2023). Androgen excess: A hallmark of polycystic ovary syndrome. *Frontiers in Endocrinology*, *14*, 1273542. https://doi.org/10.3389/fendo.2023.1273542

Yang, C., & Merlin, D. (2023). Challenges to Safe Nanomedicine Treatment. *Nanomaterials*, *13*(7), 1171. https://doi.org/10.3390/nano13071171

Yilmaz, S., Yilmaz Sezer, N., Gönenç, İ. M., İlhan, S. E., & Yilmaz, E. (2018). Safety of clomiphene citrate: A literature review. *Cytotechnology*, *70*(2), 489–495. https://doi.org/10.1007/s10616-017-0169-1

Yoon, J. H., Ahn, S.-Y., Jung, S.-H., Lee, J.-J., Choi, W., Park, J. Y., Hong, A. R., Kim, H. K., & Kang, H.-C. (2021). Prevalence and Risk Factors for Adrenal Insufficiency in Patients with Multiple Myeloma Receiving Long-Term Chemotherapy including Corticosteroids: A Retrospective Cohort Study. *BioMed Research International*, *2021*(1), 2330417. https://doi.org/10.1155/2021/2330417

Zhao, H., Wang, D., Xing, C., Lv, B., Wang, X., & He, B. (2023). Pioglitazone can improve liver sex hormone-binding globulin levels and lipid metabolism in polycystic ovary syndrome by regulating hepatocyte nuclear factor-4α. *The Journal of Steroid Biochemistry and Molecular Biology*, *229*, 106265. https://doi.org/10.1016/j.jsbmb.2023.106265

Zhao, S., Tang, Y., Wang, R., & Najafi, M. (2022). Mechanisms of cancer cell death induction by paclitaxel: An updated review. *Apoptosis*, *27*(9–10), 647–667. https://doi.org/10.1007/s10495-022-01750-z