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Nanoengineered Drug Carriers as an Emerging Therapeutic Strategy for Effective Polycystic Ovary Syndrome Treatment

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Abstract
The endocrine disorder of polycystic ovary syndrome (PCOS) is the most common in reproductive-age women and is a leading cause of anovulatory infertility and consequent health and financial cost. At the moment, the drugs administered in PCOS treatment may cause some adverse effects, including fertility decrease and higher chances of developing venous thrombosis. In PCOS, the older and newer approaches of drug delivery systems such as long half-life, highly targeted-delivery, high-bioavailability and low-toxicity, defined, using nanomaterials, are already in use. Such a new method is becoming a popular solution in the enhancement of the therapeutic effect of drugs. Thus, the current paper will address the contributions of nanoparticles, nanocarriers, and targeted ligands in nanomaterial-based drug delivery schemes whatsoever to find out the ideal protocols of PCOS treatment employing nanomaterials. Further, emerging directions of research in orgnanomaterial based delivery systems in PCOS, and the relevance of the current knowledge to development of new treatment for PCOS is also pointed out.

Keywords: ***Polycystic ovary syndrome, nanoparticles, novel drug delivery systems, therapeutic efficacy.***

1.Introduction
Polycystic Ovary Syndrome (PCOS) is a multifactorial endocrine and metabolic syndrome that concerns a significant number of women of reproductive age. It is one of the most frequently identified hormonal disorders whose prevalence is estimated at 8-13% worldwide depending on used criteria of diagnosis. Being mainly marked by chronic anovulation, hyperandrogenism, and the appearance of PCO morphology, PCOS forms a complex clinical issue. In addition to reproductive dysfunction, the syndrome is closely connected to metabolic misalignments (insulin resistance, obesity, dyslipidemia), and may be associated with psychological comorbidity (anxiety and depression). Most importantly, PCOS has systemic implications on the health of women whereby it results to higher risk of type 2 diabetes, cardiovascular diseases as well as endometrial cancer and fertility.

Although subhofficially frequent and with an immense health burden, the pharmacological treatment of PCOS is mostly symptomatic with the aim to address a specific symptom (menstrual irregularities, hirsutism, or insulin resistance, etc)(1). They are mostly prescribed oral contraceptives, insulin sensitizer (including metformin), ovulation induction drugs (including clomiphene citrate) and anti-androgens (including spironolactone). Although they are effective in alleviating these symptoms, these therapies are often linked with unpleasant side-effects, inconsistency of action, and lastly low-long term compliance. Additionally, majority of therapy drugs have systemic effects, and non-targeted tissues might develop undesirable side effects. These shortcomings indicate the great need to find more useful, specific, and less harmful modes of treatment.

The new frontier of nanotechnology has also highlighted great opportunities in drug delivery especially on complex and chronic diseases such as PCOS. The use of engineered nanomaterials has many potential advantages over conventional administration of drugs because the therapeutic agent can be delivered through nanomedicine. These are like increased solubility of drugs, better bioavailability, longer circulation periods, controlled and sustained delivery of drugs and also the ability to target a particular location. Using these properties nanocarrier-based systems can lower dosage, lower side effects and improve therapeutic capability. Precision and efficiency in drug delivery may be especially useful in the case of PCOS wherein the disease process commonly requires long-term management of endocrine and metabolic disturbances, thus leading to enhancement of clinical outcomes and a higher quality of life(2).

Among the most interesting elements of nanotechnology as applied to the treatment of PCOS is the fact that it can disrupt the pathophysiological mechanism of the disease at many levels. The leading factors that cause PCOS and contribute to their development and progression are hyperandrogenism, insulin resistance, chronic inflammation, and oxidative stress. It has been shown that nanoparticles can control these biological processes. To use an

example, curcumin-loaded chitosan nanoparticles appeared to alleviate hyperandrogenic and insulin-resistant condition in preclinical types. In the same line, selenium and silver nanoparticle have been reported to have anti-inflammatory and antioxidant effects which can ameliorate follicular tissue and can normalize the ovarian dysfunction. There is also evidence that natural-derived nanoparticles could work, as nanoparticles with origin in ginger, cinnamon, or aloe vera successfully relieved metabolic imbalances and hormonal imbalance both in experimental PCOS models.

FIGURE 1 PCOS Treatments: Conventional vs. Nanotechnology

Besides therapeutic payload choice of the nanocarrier system as well as design is a pivotal determinant of the treatment success. Several nanocarriers including liposomes, micelles, carbon nanotubes, dendrimers and quantum dots have been utilized as a drug delivery vehicle in PCOS(3). The systems have different, distinctive structural and functional benefits. Biocompatible drug carriers such as liposomes have the ability to engulf both hydrophilic and hydrophobic medicines. Polymeric micelles: they are stable and applicable in poorly soluble drugs. Carbon nanotubes have a large available area and can enter the cell membrane but have a dangerous toxicity aspect. Surface modifications such as ligand association to modify the granulosa cell or oocyte targeting increases the specificity of these carriers enabling localized distribution of drugs to the ovarian niche.

Additionally, some recent studies point out to specific ligands as essential components adding precision to nanomedicine. Nanoparticles can be functionalized with ligands like chitosan, mannose and antibodies to identify and target particular receptors in ovarian cells. This targeting through receptors increases the concentration of drugs at the site of the disease but more importantly it does not expose the healthy tissues to the drug hence minimal systemic toxicity is experienced. As an instance, the nanoparticles coated with chitosan have the capability of targeting oocytes preferentially, so they will be able to restore follicular development and ovulatory activity. Likewise, nanoparticles which would penetrate granulosa cells could help restore hormonal imbalance and enhance fertility rates.

Although this is improved, the use of nanotechnology in clinical practice of PCOS has not yet advanced. The majority of work has been carried out so far in vitro or animal models and few have made the step to human studies. These are some of the challenges that include toxicity of nanoparticles, biodegradation, stability over long duration, and regulatory factors. In addition, there is disparity between individuals in their PCOS phenotypes, and this complicates the standardization of treatments(4). The scientific purpose should not only focus on the further improvement of nanocarrier designs but also on learning the most about the patient-specific responses and designing sound safety profiles in the future studies. Two aspects that could have significant potential to increase

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the clinical success of using nanomedicines in PCOS include development of biodegradable non-immunogenic nanoparticles and use of real time imaging to track the drug.

Conclusively, PCOS is a complex disorder requesting complex treatment. The new field of nanotechnology is also a promising field that can be used in the management of PCOS to make drug delivery systems leaner and smarter. Nanomaterial-based therapeutics may be able to rewrite the treatment paradigm and make the life quality of PCOS-afflicted women much better due to precise interventions, enhanced pharmacokinetic performance, and decreased systemic toxication. Further research funding into nanomedicine, as well as enhanced interdisciplinary interaction involving endocrinology, pharmacology and material sciences will be important towards realising these innovations to take them off the bench to bedside.

2.Pathophysiological Mechanisms

PCOS is basically an endocrine and metabolic dysfunction disorder of complex, multifactor origins where there is a combination of genetic, hormonal, metabolic and environmental components. The clinical manifestation of the condition is no longer a secret but the precise pathophysiological processes leading to the syndrome remain unclear which is also of major significance as far as the development of specific and curative therapies is concerned. Hypertriglyceridemic-hypertension syndrome, hyperandrogenism, and insulin resistance (IR) are chief in the pathology of PCOS and reflect off each other in circuitry to derail normal reproductive and metabolic operations. PCOS is an anomaly of dysbalance of hypothalamicthepituitaryovarian (HPO) axis, which is the central regulatory unit of female reproduction. An abnormal pulsatility of gonadotropin-releasing hormone (GnRH) in PCOS patients causes relative production of the luteinizing hormone (LH) relative to follicle-stimulating hormone (FSH). This excessive secretion has the effect of activating ovarian theca cells to secrete too many androgens including testosterone and androstenedione. In the meantime, the decreased concentration of FSH distorts the work of granulosa cells, which do not aromatize androgens into estrogens, and the process of maturation of primary follicles stops(5). Consequently, many of the small antral follicles build up on the ovary that are never subjected to ovulation, and hence the typical polycystic look emerges.

Abnormally high circulating androgens often in the form of hyperandrogenism are essentially characteristics and a cause of PCOS pathogenesis. These androgens do not only interfere with the functioning of ovaries but also with the peripheral metabolic tissues. They impair insulin signaling pathways, facilitate abdominal adiposity and worsen insulin resistance, which is a prime metabolic characteristic seen in 70 -80 percent of PCOS. Moreover, the hyperandrogenization harms the endometrium and leads to irregular menstruation and a threat of endometrial hyperplasia and cancer.

Insulin resistance is also one of the primary pathogenic factors in PCOS, causing reproductive as well as metabolic disorders. Many women with PCOS are characterized by a reduced sensitivity of insulin independent of body weight especially skeletal muscle and adipose tissues. The pancreas increases the release of insulin in order to balance this and causes hyperinsulinemia. The high insulin influence synergistically with LH in providing the androgens to theca cells to increase its production and also decrease the production of the sex hormone-binding globulin (SHBG) in the liver and thereby enhance the availability of free androgens. In addition to reproductive effects, insulin resistance in patients of PCOS tends to exposing them to diabetes mellitus type 2, cardiovascular diseases, and metabolic syndrome.

Inflammation is becoming regarded as a major pathophysiological contributor to PCOS. Chronic low-grade inflammation manifested by an increase in C- reactive protein (CRP), tumor necrosis factor-alpha (TNF- 1), and interleukins- IL -6 and IL -18 exists in PCOS patients. It is believed that this inflammatory condition has its origin in visceral adiposity and perpetuated by both hormonal and metabolic dysregulations. The use of inflammatory cytokines aggravates insulin sensitivity, which can also harm the ovaries and oocytes that they pass directly through regulators follicular cells and quality oocyte. Oxidative stress is also involved since it was discovered that a large concentration of reactive oxygen species (ROS) damaged granulosa cells, abrogated the functioning of mitochondria, and decreased the competence of oocyte.

Supplementary adrenal androgens are also to add towards hyperandrogenemia in some of the patients with PCOS. The consequence of androgen excess, which is contributed both by the ovaries and due to increased adrenal activity, can occur as a result of hypothalamic-pituitary-adrenal (HPA) axis dysregulation. There are studies that indicate that PCOS might have led to cortisol metabolic dysregulation that inhibits the negative feedback loop of

the HPA axis to secrete more adrenocorticotropic hormone (ACTH) more resulting in an increase in adrenal androgens.

Obesity is also another condition that contributes towards PCOS though it is not a precondition to PCOS. Nevertheless, it affects the increase in the intensity of symptoms. Adipose tissue, especially visceral fat, is an endocrine organ, and produces adipokines and cytokines that interrupt insulin functions and androgen carbohydrate metabolism. Compared with the lean patients with PCOS, obese patients with PCOS have been found to have greater hyperinsulinemia, increased androgen levels, and increased menstrual irregularity. Remarkably, metabolic dysfunction can be found even in lean subjects with PCOS, meaning that intracellular insulin resistance and hormonal disorders are independent of obesity in a significant number of cases.

The net impact of all these interrelated pathologies is an anti-ovulatory and anti-fertility reproductive environment. Combination of follicular arrest, oocyte poor quality, impaired endometrial receptivity and hormonal disturbances all play roles towards subfertility or infertility in women with PCOS. Further, there are the metabolic and cardiovascular implications that preclude a short-term approach to managing PCOS and include an approach outside of fertility issues(6).

Recent research has been indicating that there are possible epigenetic changes and genetic predispositions toward the development of PCOS too. Insulin signaling, androgen receptor, and Gonadotropin secretion genes polymorphisms are identified. The presence of these genetic predispositions alongside environmental conditions triggers environmental factors; poor diet, sedentary lifestyle, and endocrine disrupting chemicals, may precipitate or aggravate the phenotypic expression of PCOS. But genetic investigations are unresolved and point to polygenic and multifactorial pattern of inheritance instead of a single gene defect.

The topics in the pathophysiology of PCOS are critical in designing specific treatments. The conventional approaches have been to manage symptoms without dealing with the causes. Nevertheless, as our understanding of the molecular and cellular basis of PCOS increases, novel treatment modalities, including drug delivery systems based on nanomaterials, appear. The advantage of these advanced systems is that they have a potential ability to be tailored to attack a specific pathological process, e.g. oxidative stress, inflammation or hormonal imbalances with high specificity and little or no systemic side effects.

Altogether, we can summarize that PCOS is a multifactorial condition characterized by a chain of various interdependent impairments. Intersecting hypergenito, veneration, alarities, and hyperinsulinism with chronic inflammation form a feed-forward cycle of the reproductive, metabolic, and psychological impact of the disease is the basis. There lies not only the significance of working out the intricacy of these pathophysiology processes with regard to the enhancement of the diagnostic criteria but also the breaking into the realm of the next-generation therapeutics that would go beyond palliative care and actually resolve the basis of the causes of the syndrome.

3.Conventional Diagnosis and Treatment Approaches

Polycystic Ovary Syndrome (PCOS) in its clinical complexity demands sensitive diagnostic systems and individually developed management strategies. Conventionally known as a reproductive disorder, PCOS is known to have a wider systemic effect. Proper diagnosis is very important, not just in the start of correct treatment but also in reducing the long term metabolic and cardiovascular effects related to the condition. Though recent treatments have brought us closer to PCOS, there is still a lack of clarity in diagnosing PCOS coupled with treatment inability. The given section discusses the existing diagnostic criteria, and describes the traditional and conventional pharmacological, and non-pharmacological treatment, strengths, and limitations.

There has been debate in the diagnosis of PCOS due to which numerous criteria were developed. The most common among these are the Rotterdam Criteria, which got a unison of experts endorsement in 2003. Based on this classification, PCOS is diagnosed in the presence of any two of the following three criteria: (1) oligo- or anovulation; (2) clinical and/or biochemical hyperandrogenism; (3) suspicious ovarian morphology (PCOM), which is polycystic as assessed by ultrasound involving 20 or more follicles (2 to 9 mm) per ovary or expanded ovarian volume (more than 10 mL). Noteworthy, the diagnosis requires ruling out of other possible, endocrinopathies namely, thyroid dysfunction, hyperprolactinemia, adrenal hyperplasia, which can present similar to PCOS-like symptoms(7).

Although Rotterdam Criteria have achieved popularity, its large-scale phenotype expression has created clinical heterogeneity with various symptoms combinations resulting in various PCOS phenotypes. This variability influences the interpretation of research and decisions in the course of administration of treatment. Consequently,

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other classification systems include the NIH Criteria, and the Androgen Excess-PCOS Society (AE-PCOS) criteria, which are less concerned with hyperandrogenism and ovulatory dysfunction. Nevertheless, even such definitions do not wholly cover the range of metabolic reproductive and psychological issues that occur in PCOS. With such insights, more contemporary practice guidelines are promoting a holistic diagnostics model that will consider the detection of insulin sensitivity, inflammatory, and psychological wellness, as well as the cardiometabolic risk factors.

After a diagnosis, the treatment of PCOS usually follows the priority of the patient and might be based on infertility, metabolic side, hirsutism, or menstrual abnormality. Traditional methods of treatment are focused on improvement of the signs of the disorder but not on eliminating the disease, and this is why the management of long-term control is so crucial. The initial treatment of the majority of women involves a change of lifestyle, namely, optimization of nutrition, reduction of extra weight, and enhancement of physical activity. Results of current studies indicate that insulin sensitivity, ovulatory cycle, and androgen levels can be enhanced with a smaller percentage change in weight (5%-10%) with major effects.

Oral contraceptive pills (OCPs) are the mainstay of treatment of patients wanting to control their menstrual cycles or improve the symptoms of hyperandrogenism (including hirsutism and acne). Such drugs usually include the combination of estrogen and progestin, which collaboratively inhibit the androgen production in ovaries and raise SHBG in turn decreasing free testosterone. Nevertheless, there are a number of risks against the benefits of OCPs that include venous thromboembolism, high blood pressure and the possibility of future fertility interference.

Where insulin resistance has been dominant, insulin-sensitizing agents are usually used, in particular metformin. Metformin enhances peripheral glucose disposal, restrains gluconeogenesis in the liver and has an indirect effect on the lowering of androgen levels by causing the reduction in the insulin-stimulated insulin stimulation of theca cells in the ovary(8). It is very efficient in PCOS women owing to impaired glucose tolerance or type 2 diabetes mellitus. Its tolerability by some patients is however restricted by gastrointestinal side effects like nausea and diarrhea.

Ovulation induction agents such as clomiphene citrate and letrozole are commonly used in treating infertility among people with anovulation. The use of aromatase intrusion such as letrozole has been favoured over the past years as it has larger ovulations and live birth rates than clomiphene. Assisted reproductive technologies (ART) can be used in refractory cases e.g. in vitro fertilization (IVF). Nonetheless, ART is associated with another risk, ovarian hyperstimulation syndrome, and economic burden.

Dermatological manifestations including hirsutism and acne are treated with the help of anti-androgen drugs such as spironolactone, flutamide and finasteride. Although they are effective, these medicines are dangerous to unborn children should it happen and they have to be taken with quality birth control. As well, during long-term use there should be consistent monitoring of hepatotoxicity and electrolyte imbalances.

Other treatments involve use of statins in the case of lipid abnormalities, glucocorticoids in adrenal hyperandrogenism, and psychological interventions in mood disturbance, commonly associated with PCOS patients. Mindfulness training, stress management interventions, and cognitive behavior therapy (CBT) potential has been demonstrated to enhance psychological aspects as well as alter metabolic measures.

And yet with this pharmacologic and supportive therapy arsenal, there are bountiful limitations. Majority of the conventional therapies are known to effectively relieve the symptoms without necessarily tackling the etiology of PCOS. Moreover, problems such as side effects, non-compliance by patients and not having treatment protocols tailored to an individual patient are still limiting best care. Patients with PCOS report feelings of dissatisfaction over the care and information they are given, and hence there is room to improve on this in a more integrated and patient-oriented manner.

Here lies the opportunity of nanotechnology-based drug delivery systems that is quite attractive. This is opposed to regular forms of therapy which not only have effects with the whole body but lacks the possibility of selective delivery of medications to only the area of the problem without causing unneeded exposure to other body organs. The downsides of this particular specificity would be the minimization of side effects, the increased bioavailability of drugs, and the increased compliance of patients. As an example, clomiphene nanoformulated drug could be administered directly to the follicles of the ovary to lessen the anti-estrogenic characteristics of the drug to the endometrium and increase implantation(9).

With an ever-increasing level of knowledge about PCOS and technological prowess, the realization emerges that the existing model of how PCOS is treated is long overdue when it comes to changing. Incorporating emerging

technology like nanotechnology into the traditional forms of treatment may lead to better, patient-specific, and longer-term ways of controlling PCOS in the days to come.

4.Nanotechnology in the Therapeutic Management

Nanotechnology, the new promising player in biomedical science, has brought new possibilities to improve the drug delivery system and in a number of chronic and complicated maladies, such as Polycystic Ovary Syndrome (PCOS). The traditional pharmacological approaches to the management of PCOS are usually plagued with general side effects, low bioavailability and non-specific targeting. By contrast, delivery systems based on nanomaterials are precise, effective, and flexible, which is why they can be used to shape the multifaceted pathophysiology of PCOS. Nanocarriers can increase solubility of a drug, prolong its system circulation, enable site-specific drug absorption and controlled release, hence, preventing inevitable undesired toxicity and improving therapeutic efficacy.

PCOS is fuelled by cascade of intersectional processes which involve hyperandrogenism, insulin resistance, inflammation cardiac in addition to oxidative stress. Numerous combinations of the systemic malfunctions need to be addressed with multifaceted therapeutic strategies. Nanomedicine offers the opportunity of concomitant addressing of these constituent pathophysiological aspects by encapsulation of bioactive molecules in designed nanostructures. In preclinical experiments, an extensive range of nanocarriers, such as polymeric nanoparticles, liposomes, micelles, carbon nanotubes, and quantum dots, has also shown a good outcome in targeting the hormonal and metabolic derangements of PCOS(10).

Curcumin, polyphenolic molecule with antioxidant, anti-inflammatory and anti-androgenic properties is one of the most studied natural ingredients in PCOS therapy. But, the clinical usage of curcumin is limited due to low water solubility and easy metabolism. When encapsulated in chitosan nanoparticle, controllable biodegradable and non-toxic polymer, curcumin has been found to be much more stable and enhances its bioavailability. These chitosan-curcumin nanoparticles were efficient in animal models to bring down serum testosterone, insulin, and the luteinizing hormone and positively improved the metabolic and reproductive symptoms. The nanoparticles had also a positive effect on the ovarian morphology which indicates a restorative effect on folliculogenesis.

On the same note, nanoparticles retrieved out of plants have been very promising in manipulation of insulin resistance, inflammatory pathways in PCOS. Examples are ginger derived nanoparticles, which have bioactive constituents with regulation of glucose metabolism and insulin resistance. These nanoparticles have shown to enhance insulin signaling (inducing the expression of transcription factors such as Foxa2 and regulating exosomal communication in intestinal epithelial cells) which is one of the new mechanisms that has been identified with PCOS-related insulin resistance.

Other natural healing compounds like cinnamon, aloe vera and camellia sinensis have also been repackaged in a nano-sized delivery vehicles. The cinnamon extracts have been used to form silver nanoparticles that show anti-inflammatory effect of reducing the levels of pro-inflammatory cytokines, such as TNF-alpha, IL-6, and IL-18 decrease in PCOS animal models. These results are especially significant against the background of the known fact that chronic low-grade inflammation plays a role in worsening the symptoms of PCOS and its subsequent metabolic risks.

Along with the natural ones, the metal-based nanoparticles (silver, selenium, iron oxide, and copper) are under investigation as therapeutic agents in cases of PCOS. These nanoparticles also have innate biochemical functions such as antioxidant, anti-inflammatory properties, which could be used towards restoring the ovarian tissue disease caused by PCOS. As an example, selenium nanoparticle has been found to down-regulate androgen receptor expression thus leading to interruption of the vicious cycle of overproduction of the androgen. Moreover, selenium nanoparticles have the ability to regulate signaling signal as PI3K/Akt in order to enhance insulin response; thus, minimizing oxidative stress.

When loaded with curcumin or any other agent, the iron oxide nanoparticle can block apoptosis of cells of the ovary and regenerate normal hormone levels. Such dual-function systems act both as carriers of therapeutic agents and themselves produce biological effect leading to synergistic effect. Nevertheless, metal nanoparticles have not yet acquired the profile of their toxicity and long-term safety which is also an ongoing study. They are studied to make them less immunogenic and limiting in non-target organs and are studied with surface modifications and biodegradable coatings.

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Liposomes are versatile and well-developed nanocarriers suitable for synthetic agents. Liposomes are phospholipid bilayers that can carry hydrophilic drugs, lipophilic drugs and be modified to deliver to a target. As an example, liposomal derivatives of resveratrol (e.g. DMU-212) have been shown to have potential to enhance estradiol and progesterone secretion by granulosa cells in vitro. This might be helpful in ameliorating the ovulatory cycles and hormonal imbalance in the PCOS women, especially with those who have estrogen deficiency.

Semitrans parentheses astronomically large surface acreage carbon nanotubes (CNTs) parenthes\%09unplugged and simple to functionalize conch the subject of contemplation as well. Despite the still ongoing concerns about cytotoxicity CNTs may be engineered in a manner that lessens the safety profiles. N-doped carbon nanorods have proved to be effective in lowering blood glucose and alleviating the oxidative stress in the PCOS-induced animal models. Additionally, CNTs are also diagnostic candidates since they can be customized to identify any PCOS-related biomarkers such as fetuin-A at a greater sensitivity than normal assays.

The other emergent nanotechnology with uses in drug delivery and diagnostics is the quantum dots. They have special optical characteristics that enable them to be imaged and their distribution tracked in real-time. An example is the recently developed pegylated graphene oxide quantum dots (GOQDs) that can potentially target and pass metformin-one of the first line agents used in insulin resistance in PCOS. Such systems support a prolonged release and increase the uptake of glucose in the model of insulin-resistant cells, understating the therapeutic effects of metformin.

Micellesous Acyl amphiphilic molecules self-assemble in water into nanoparticles that stabilize an entrapment of hydrophobic drugs. Micelle-encapsulated curcumin has also exhibited an outstanding activity in PCOS models than free curcumin significantly decreasing oxidative damage and inflammation of the ovarian tissues. New developments, such co-delivery micelles with the capacity to ferry more than one agent, have been made to hit more than one pathway implicated in PCOS pathogenesis.

Although the preclinical results of nanomedicine in PCOS have been positive, converting the results to clinical 련 cyl2613 core area is important to consider the aspect of biocompatibility, toxicity and pharmacokinetics. Drugs have to be developed to breakdown safely in the body, not causing any immune reactions and have retained therapeutic effect in circulation. Surface PEGylation, ligand conjugation, and controlled polymer degradation are potential methods used to overcome the issues.

To conclude, nanotechnology is a revolutionary milestone in the management of PCOS. Nanocarriers have the potential to surpass the inefficacies of traditional drug therapies by allowing specific, multifaceted, and less invasive therapies. As this field advances, nanomedicine combined with other genomic, hormonal, and metabolic profiling has the potential of leading to a well-personalised and successful management of PCOS approaches.

5.Conclusion and Future work

Polycystic Ovary Syndrome (PCOS) is still one of the least curable endocrine-metabolic diseases of young women, as it is heterogeneous in etiology, affects many systems, and does not have many possible solutions. Despite the fact that conventional treatment provides symptomatic treatment, the long term efficacy is often limited by low specificity, side effects, and patient non-optimality. As research demonstrating the interaction between hyperandrogenism, insulin resistance, oxidative stress and chronic inflammation in the pathophysiology of PCOS mounts, so does the requirement of a more precise therapeutic strategy capable of targeting specific pathophysiological processes.

In this regard, nanotechnology has come out as a very potential tool which introduces a new level in drug delivery as it enhances bioavailability, offers control over release patterns and facilitates targeting of specific tissues within ovaries and metabolism. There is a myriad of nanomaterials such as biopolymer-based nanoparticles, liposomes, carbon nanotubes, and metal-based nanostructures with a strong preclinical potential to improve both metabolic and reproductive manifestations of PCOS. Such progressive carriers are able to enclose phytochemical, hormones, or synthetic drugs that can burgeon their pharmacological stability lesser numerical toxicity.

Moreover, by incorporation of targeting ligands into the nanocarriers we can have a selective interaction with the oocytes or the granulosa cells, which is a major step towards personalized reproductive medicine. This selectivity enhances efficacy of the therapy, not to mention its reduced risk of damaging healthy tissues since this is a significant side effect of existing PCOS medications. Nevertheless, with this positive development, major issues

on nanoparticle safety, bio-degradability and regulatory acceptance have to be fixed, so that such technologies be regularly fielded in clinical practices.

The need of further investigation is aimed at the creation of long-term safety evaluations, extensive clinical studies, and the invention of multifunctional nanocarrier platforms able to co-deliver compounds to regulate multiple disease pathways. As long as the interdisciplinary work regarding nanotechnology, endocrinology, and reproductive medicine continues, there is a transformative potential of using nano materials in the treatment of PCOS not only to treat symptoms more efficiently, but within the disorder itself, on the molecular level.

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Conflicts of interest

The authors have no conflicts of interest to declare

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