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Review article

The utilization of nanotechnology in the female reproductive system and related disorders

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ABSTRACT

The health of the reproductive system is intricately linked to female fertility and quality of life. There has been a growing prevalence of reproductive system disorders among women, particularly in younger age groups, resulting in significant adverse effects on their reproductive health. Consequently, there is an urgent need for effective treatment modalities. Nanotechnology, as an advanced discipline, provides innovative avenues for managing and treating diseases of the female reproductive system by enabling precise manipulation and regulation of biological molecules and cells. By utilizing nanodelivery systems, drugs can be administered with pinpoint accuracy, leading to reduced side effects and improved therapeutic efficacy. Moreover, nanomaterial imaging techniques enhance diagnostic precision and sensitivity, aiding in the assessment of disease severity and progression. Furthermore, the implementation of nanobiosensors facilitates early detection and prevention of ailments. This comprehensive review aims to summarize recent applications of nanotechnology in the treatment of female reproductive system diseases. The latest advancements in drug delivery, diagnosis, and treatment approaches will be discussed, with an emphasis on the potential of nanotechnology to improve treatment outcomes and overall quality of life.

1. Introduction

The female reproductive system, comprised of the ovaries, fallopian tubes, uterus, vagina, and external genitalia, plays a pivotal role in women's quality of life and population equilibrium [1]. Its primary purpose lies in the creation of new life. Nevertheless, women's reproductive health is burdened by diverse ailments, presenting a global predicament. Common afflictions encompass uterine-related predicaments like pregnancy disorders, endometriosis, uterine fibroids, and cervical cancer; ovarian-related issues such as polycystic ovary syndrome (PCOS) and ovarian cancer; along with infections like HIV-related diseases, vaginitis, pelvic inflammatory disease, and pelvic inflammatory disease (Fig. 1.). These maladies exert a significant impact on women's well-being and quality of life. Epidemiological statistics reveal that the incidence of female reproductive system diseases has been on the rise in recent years,

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displaying a trend toward younger age groups. Female reproductive system diseases can result in organ damage, functional impairments, affecting reproductive capacity, and even infertility [2]. This presents substantial challenges to reproductive medicine and imparts adverse effects on patients' physical and mental health, as well as their family life.

Nanotechnology represents a realm that scrutinizes the characteristics and applications of materials at the nanometer scale (0.1–100 nm) [3,4]. It draws from classical and quantum mechanics principles while incorporating modern technologies like microelectronics, scanning tunneling microscopy, and nuclear analysis techniques [4]. Major branches of nanotechnology encompass nanosystem physics, nanoscale chemistry, nanomaterials science, nanobiology, nanoelectronics, nanofabrication, and nanomechanics [5]. By harnessing nanotechnology, more precise and efficient treatment modalities can be devised, such as targeted drug delivery and tissue engineering [4]. Furthermore, nanotechnology can be applied in biosensing and diagnostics, refining early detection capabilities and diagnostic accuracy for diseases [6–8].

Traditionally, treatment methods for female reproductive system diseases have faced limitations in terms of suboptimal drug efficacy and severe side effects [9]. Consequently, the pursuit of more effective and precise treatment strategies assumes paramount significance. Nanotechnology has exhibited tremendous potential in this domain, empowering targeted drug delivery through nanocarriers, thereby improving treatment efficacy while alleviating side effects [10]. Additionally, the utilization of nanoparticles as molecular labels in diagnostics can amplify the sensitivity and accuracy of detection techniques, facilitating early detection and precise lesion diagnosis [11].

This manuscript endeavors to explore recent advancements in nanotechnology concerning drug delivery, diagnostics, and treatment of female reproductive system diseases, underscoring its potential to ameliorate treatment outcomes and enhance quality of life. Through a comprehensive analysis of existing research and clinical practices, we aspire to gain an in-depth comprehension of the applications of nanotechnology in female reproductive system diseases and provide guidance and insights to steer future research and applications.

2. Application of nanotechnology in the diagnosis of female reproductive system and related disorders

2.1. Application of nanoparticle-labeled biomolecules for early cancer diagnosis

Female reproductive system cancers encompass various types such as ovarian, cervical, endometrial, and vaginal cancers [12]. Early diagnosis is crucial for improving treatment success rates and survival rates, as early-stage cancers often lack obvious symptoms. Therefore, exploring early diagnostic methods holds significant importance in enhancing patient prognosis (Fig. 2.).

2.1.1. Cervical cancer

Cervical cancer is one of the most common malignant tumors in women, primarily occurring in the cervical region of the female reproductive system. In recent years, there has been a global trend of increasing incidence of this cancer among younger populations [13,14]. Fluorescence imaging (FI) represents a potent technique for the visualization of biological specimens, finding extensive utility in both cellular and molecular investigations, as well as within the realm of medicine [15]. Nanoparticles adorned with ligand-modified fluorescent dyes effectively zero in on lesions, thereby facilitating initial diagnosis and subsequent treatment. Notably,

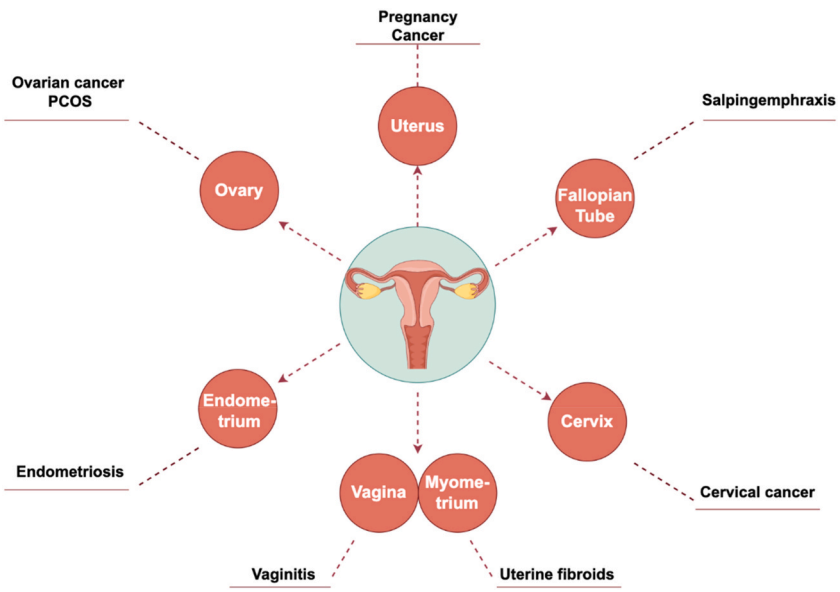

Fig. 1. Common diseases of the female reproductive system. According to their anatomical structures, the female reproductive system can be divided into several components, including the ovary, uterus, endometrium, vagina, fallopian tubes, and cervix.

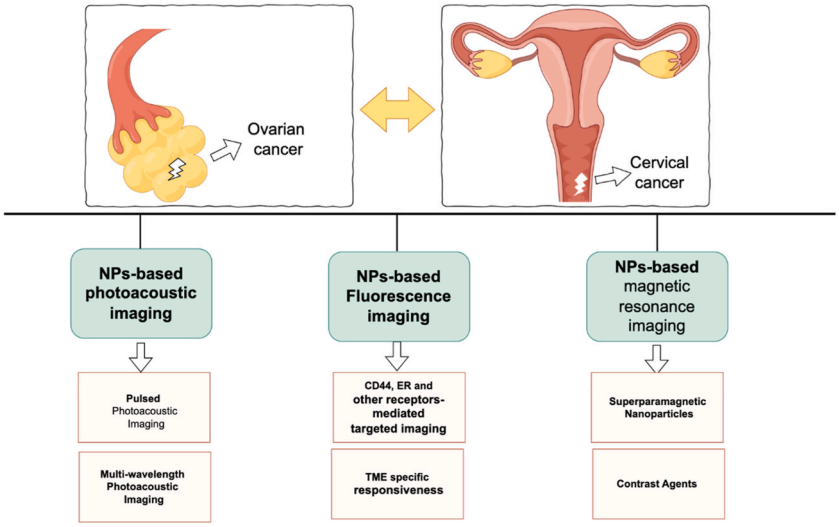

Fig. 2. The utilization of nanotechnology in the early detection of ovarian cancer and cervical cancer.

Choi et al. accomplished the successful development of nanoparticles that target CD44-overexpressing cervical cancer cells, employing near-infrared FI to scrutinize tumors in vivo and trace metastatic cancer cells [16]. Additionally, Alomari et al. harnessed tamoxifen (TAM) and poly(methyl methacrylate) nanoparticles loaded with Nile red to facilitate the delivery of TAM to ER-negative cervical cancer cells, thereby elucidating drug internalization [17]. Budhathoki et al. in turn, engineered subcellular-targeting nanoprobes for efficacious nuclear targeting, a property which was corroborated by their display of optical responses [18]. Moreover, FI nanoparticles exhibiting reactivity to the tumor microenvironment have also been tailored for diagnostic imaging purposes.

Photoacoustic imaging (PAI) manifests as an imaging modality that seamlessly merges optical and acoustic principles, having found widespread application in the diagnosis and monitoring of cervical cancer [19]. To illustrate, Zhang et al. have triumphantly devised a PAI platform utilizing nanocomposites boasting high near-infrared absorption, thereby enabling the capture of robust signals and facilitating the observation of drug accumulation within tumors [20]. Likewise, Rad et al. established a stable structure predicated upon BSA-Bi2S3–MnO2 nanodisks, which serve to capture high near-infrared absorption images [21]. In contrast to conventional ultrasound imaging, photoacoustic imaging touts superior spatial resolution, consequently affording heightened accuracy in the identification of morphological tissue characteristics, thereby aiding in the detection and localization of early lesions. Moreover, by synergistically blending photoacoustic imaging with other imaging modalities such as ultrasound imaging and fluorescence imaging, one can attain multimodal imaging capabilities, thereby facilitating the acquisition of comprehensive information from various vantage points [22]. The merits of this multimodal imaging approach enable physicians to holistically assess the morphological, functional, and molecular-level attributes of tissues concurrently, thus enhancing the precision of cervical cancer diagnosis.

Nanoparticle-enhanced magnetic resonance imaging (MRI) leverages nanoparticles as contrast agents to realize high-resolution imaging at lesion sites, concurrently acquiescing functional information [23]. In the context of cervical cancer, MRI techniques based on nanomaterials confer substantial advantages, proffering lucid anatomical structures of tissues along with demarcation of lesions, while also furnishing crucial insights into early diagnosis and localization. For instance, Liu et al. have employed biocompatible iron oxide copper nanoparticles boasting heightened relaxivity as contrast agents for both in vitro and in vivo MRI imaging, with commendable imaging outcomes [24]. Moreover, Luong et al. have devised superparamagnetic iron oxide nanoparticle cores adorned with folate-poly(amidoamine) dendrimers, simultaneously encapsulating 3,4-difluorobenzylurea-curcumin nanoparticles, which not only exhibit elevated contrast for magnetic resonance imaging but also facilitate drug accumulation and engender anti-cancer activity [25].

2.1.2. Ovarian cancer

FI is a safe and effective method for early screening, intraoperative surgical guidance, and postoperative prognosis monitoring of ovarian cancer [26,27]. Currently, commonly used fluorescent agents in biological visualization include small molecule fluorophores, inorganic nanoparticles, quantum dots, and carbon nanotubes [28,29]. Near-infrared fluorescence dyes have weak tissue absorption and good tissue penetration, providing excellent tissue imaging capabilities [30]. The FDA has approved indocyanine green as a near-infrared fluorescence probe for ovarian cancer imaging [31]. However, the OTL-38 fluorescent probe designed by Hoogstins et al. offers higher signal-to-noise ratio and deeper tumor detection ability [32]. Despite the type of near-infrared fluorescence dye used, the detection depth is limited to a few millimeters due to light excitation and emission scattering [33]. Hence, surgeons still rely on preoperative CT/MRI scans or other intraoperative imaging methods to locate tumors and determine the surgical approach [34]. Fluorescent nanoparticles possess high brightness and signal efficiency, can accumulate in ovarian tumor areas, and are easily modified. They can be combined with specific targeted drugs, significantly improving the specificity of ovarian tumor imaging detection. Hence, fluorescent nanoparticles show great potential in early screening, intraoperative assistance, and postoperative

prognosis of ovarian cancer.

PAI is also employed in the diagnosis of ovarian cancer [35]. Gold nanorods (AuNRs) possess strong near-infrared light absorption characteristics and serve as excellent photoacoustic imaging contrast agents [36,37]. Jokerst et al. developed a multimodal imaging agent that combines photoacoustic imaging and surface-enhanced Raman scattering imaging, achieving rapid imaging of three common ovarian cancer cell lines [36]. In recent years, copper sulfide nanomaterials have also demonstrated good performance in near-infrared absorption and photoacoustic signals [38,39]. Compared to traditional gold contrast agents, copper sulfide nanomaterials exhibit better biodegradability and compatibility [40]. Wang et al. prepared surface-modified copper sulfide nanosheets that exhibit strong bidirectional solid surface plasmon resonance in the near-infrared region, capable of detecting concentrations as low as 26 p.m. [40]. These nanosheets, with their size and photoacoustic effect, offer a powerful choice for ovarian tumor photoacoustic imaging. In addition, copper sulfide nanodisks and triangular nanosheets were reported as photoacoustic contrast agents for ovarian cancer [41].

Nano-multimodal imaging technology has garnered significant attention in the diagnosis and treatment of ovarian cancer due to its integration of various optical imaging techniques. For instance, PAI can enhance the resolution and sensitivity of FI. Research findings indicate that HER-2/targeted superparamagnetic iron oxide nanoparticles selectively accumulate in ovarian cancer tumors, resulting in a fivefold enhancement of photoacoustic imaging agent contrast [26]. Dual-mode near-infrared II region photoacoustic/fluorescence imaging exhibits high sensitivity and deep penetration, holding great potential for the early diagnosis and surgical guidance of ovarian cancer. Du et al. synthesized a novel organic near-infrared II dye (H10) using selenophene-dithienylbenzo [c] [1,2,5]thiadiazole (ST), which exhibited excellent aggregation-induced emission properties ($I/I0>1.6$) [42].

2.2. Utilization of nano-imaging technology for the diagnosis of additional female reproductive system disorders

2.2.1. Endometriosis

Endometriosis is characterized by the ectopic settlement of active endometrial cells beyond the confines of the uterine cavity [43,44]. Clinical detection typically employs imaging modalities like ultrasound and magnetic MRI. However, the absence of precise non-invasive detection techniques may lead to delays in symptom onset to diagnosis interval, consequently impacting treatment efficacy. Harnessing the potential of nanoparticle-based drug delivery, imaging reagents can be efficiently encapsulated while enhancing drug stability and targeting efficiency via ligand modifications. Taratula et al. devised nanoparticles comprising silicon naphthalocyanine dye, which exhibit high contrast between lesion areas and normal tissue along with fluorescence induction upon internalization by endometriotic cells [45,46]. By harnessing the photothermal effect, comprehensive diagnosis and treatment are facilitated through near-infrared light induced cell ablation. Importantly, iron oxide nanoparticles (Fe_3O_4) possess remarkable characteristics such as high relaxivity, superior contrast enhancement capabilities, and low toxicity, making them widely applicable not only in magnetic separation, catalysis, and drug/gene delivery but also as T2-weighted MRI negative contrast agents. Several studies have reported the correlation between MRI and endometriosis [47]. For instance, Lee et al. utilized ultra-small superparamagnetic iron oxide as an MRI contrast agent to diagnose deep infiltrating endometriosis [48]. Zhang et al. on the other hand, employed hyaluronic acid (HA)-modified Fe_3O_4 nanoparticles as an MRI contrast agent to observe morphological changes induced by CD44 receptor overexpression in rats presenting with pregnancy-like structures or ovarian cysts [49].

2.2.2. PCOS

PCOS is one of the most prevalent endocrine and metabolic disorders in premenopausal women [50,51]. It is characterized by hyperandrogenism, which manifests as clinical features such as hirsutism, acne, alopecia, and seborrheic skin, as well as reduced ovulation resulting in menstrual dysfunction, decreased fertility, and endometrial hyperplasia [50,52]. Additionally, PCOS is closely linked to insulin resistance and metabolic complications [52]. The utilization of nanoparticles as imaging agents can offer more precise and non-invasive diagnostic methods, augmenting the comprehension and diagnostic levels of PCOS.

Nanoparticle imaging techniques have several applications in the diagnosis of PCOS, including ultrasound imaging, MRI, optical imaging, and magnetic resonance elastography (MRE) [53]. For instance, using nanoparticles as contrast agents during ultrasound imaging enhances image contrast and improves the accuracy of PCOS diagnosis [54]. Nanoparticles can also be directed towards ovarian tissue to observe and evaluate cysts or other anomalous changes. Furthermore, nanoparticles can serve as contrast agents, providing clearer imaging information in MRI. By combining nanoparticles with specific markers, localization, and detection of PCOS-related biomarkers can be achieved, enabling a more accurate diagnosis [55]. In addition, fluorescently labeled nanoparticles facilitate the observation and assessment of cellular activity and metabolic changes in ovarian tissue, revealing the pathological processes of PCOS [56]. Finally, by using nanoparticles as contrast agents and combining them with MRE, the elasticity of ovarian tissue can be measured, thereby further assessing its functional status and degree of pathology.

3. Application of nanotechnology in the treatment of female reproductive system and related disorders

3.1. Refinement of nanomedicine delivery systems

The development of nanomedicine delivery systems entails the design and fabrication of drug delivery platforms utilizing nanotechnology [57]. These platforms serve to deliver drugs precisely to designated treatment regions. They employ carrier materials like nanoparticles, nanomicelles, nanofibers, and nanotubes to encapsulate and shield the drugs, facilitating their release at optimal times and locations [58]. Due to their distinctive advantages, extensive research and application of nanomedicine delivery systems have

been observed across diverse domains, encompassing cancer treatment, drug therapy, gene therapy, and vaccine administration (Fig. 3.).

3.1.1. Nanoparticle

Nanoparticles are widely used as drug delivery systems, including metal nanoparticles, polymer nanoparticles, and lipid nanoparticles [59,60]. These particles have a small size and large surface area, which enables the encapsulation and protection of drugs [61]. Controlled release and stability of drugs can be achieved through concentration effects and surface modifications [61]. For instance, Zhang et al. proposed multifunctional magnetic nanoparticles that synergistically combine magnetic targeting, photothermal therapy, and chemical drug release for cancer treatment [62]. Park et al. introduced pH-responsive gold nanoparticles that release drugs in the acidic tumor environment, thereby enhancing the efficacy of photothermal therapy [63]. Li et al. utilized mesoporous silica nanoparticles combined with fluorescence imaging and MRI for tumor diagnosis and treatment monitoring [64]. Zhang et al. achieved targeted delivery of cisplatin using hormone peptide-releasing polymer nanoparticles that bind to receptors on cancer cell surfaces, thereby increasing the effectiveness of anticancer drugs [65]. Moreover, Zhang et al. developed a redox-responsive co-delivery system based on mesoporous silica nanoparticles that target brain tumors with dual-targeting, enabling precise drug delivery and release within the tumor microenvironment, resulting in improved treatment outcomes [66]. Shen et al. discovered that cross-linking PD-L1 inhibitors with a polymer hydrogel can produce nanoparticles with controlled release capabilities, enhancing the efficacy of tumor radioimmunotherapy [67]. These studies demonstrate the enormous potential of nanoparticle delivery systems in drug therapy [68]. The nanoparticles not only possess multiple functionalities but also provide targeted delivery strategies for specific cancer types. Through the integration of different functionalities such as magnetic targeting, photothermal therapy, and chemical drug release, these nanoparticles can enhance treatment efficacy and play a vital role in disease diagnosis and treatment monitoring [69].

3.1.2. Nanomicelle

Nanomicelles are nanostructures composed of one or more layers of surfactant molecules arranged in a spherical shape, where drugs can be encapsulated within the core [70]. Due to their hydrophilic and hydrophobic regions, micelles effectively enhance drug solubility, stability, and prolong the in vivo circulation time [71]. Zhang et al. employed polymer micelles to deliver cationic steroidal antibiotics into cells, thereby improving their stability and cellular uptake, leading to a potent therapeutic efficacy against infections [72]. Gautam et al. designed a responsive redox environment polymer micelle that releases drugs within tumor cells, resulting in improved treatment outcomes [73]. Zhou et al. demonstrated a dual-stimuli-responsive hybrid liposome-polymer micelle complex that attained precise drug delivery through temperature and pH changes, offering controlled drug release [74]. Yuan et al. developed self-assembled polymer micelle nanocarriers with efficient drug encapsulation capacity and stability, enabling targeted therapy for

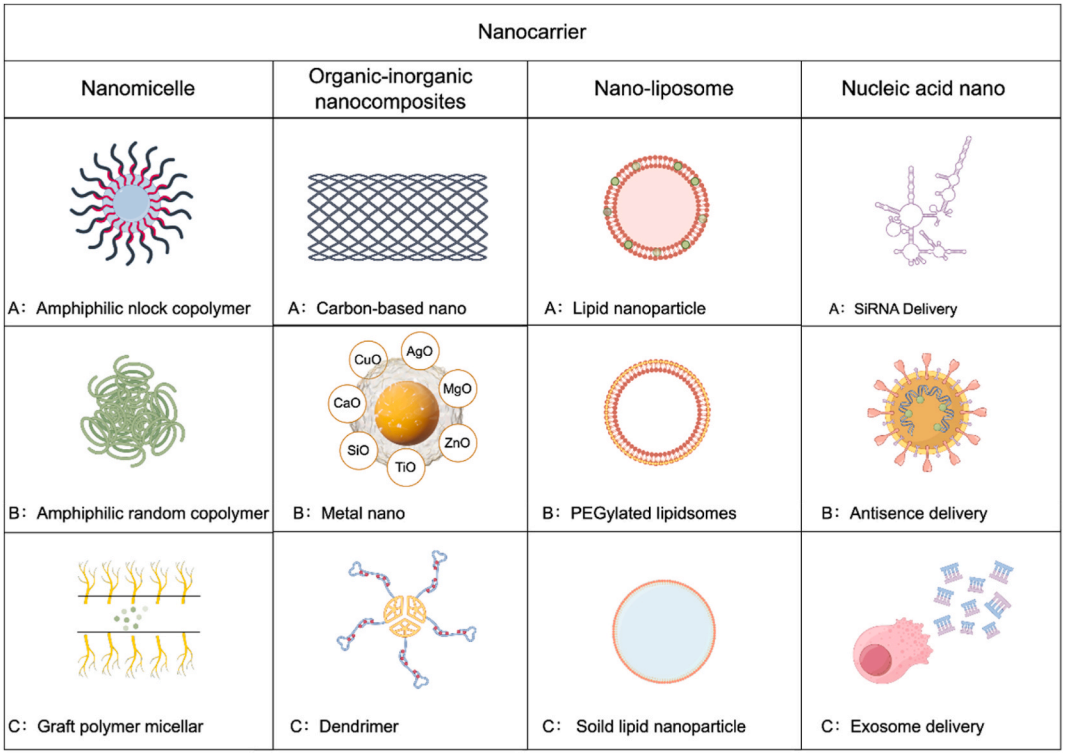

Fig. 3. Classification of nanomedicine delivery systems. Nanomedicine delivery systems utilize carrier materials such as nanoparticles, nanomicelles, nanofibers, and nanotubes to encapsulate and shield drugs, facilitating optimal timing and location for drug release.

specific cells or tissues [75]. Incorporating drugs into the core of nanomicelles utilizing their hydrophilic and hydrophobic regions can enhance drug solubility and stability and prolong the in vivo circulation time, providing new opportunities for future clinical treatment and personalized medicine.

3.1.3. Lipid nanoparticle

Lipid nanoparticles are minute droplets or vesicles enclosed by layers of phospholipids, typically exhibiting a bilayer structure [76]. Serving as a crucial drug delivery system, lipid nanoparticles have showcased extensive practicality within the domain of nanomedicine. Mo et al. have conducted a comprehensive review encompassing the preparation methods, structural regulation, and functional realization of lipid nanoparticles across diverse fields [77]. Through modulation of phospholipid composition and structure, lipid nanoparticles can achieve precise control over drug release rate and specificity, thereby enhancing the efficacy of ovarian cancer treatment. In a separate study, Palanee-Phillips et al. explored the vaginal mucosal delivery of the anti-HIV drug tenofovir disoproxil fumarate [78]. Their innovative approach entailed designing and preparing polymer nanoparticles that form a film. Experimental results have confirmed that this lipid nanoparticle formulation enhances drug concentration and bioavailability at the vaginal site, thereby bolstering the prevention and treatment of HIV/AIDS. Additionally, Ayatollahi et al. undertook the encapsulation of ketoconazole in lipid nanoparticles through formulation optimization [79]. They assessed the drug release and bioactivity at the target site via in vitro and in vivo experiments. The outcomes demonstrated the effective delivery of the drug to the vaginal mucosa, facilitated by the lipid nanoparticle formulation, which exhibited favorable drug release and antifungal activity. As an exceptional drug delivery system, lipid nanoparticles offer advantages in precisely controlling drug release, improving efficacy, and reducing side effects.

3.1.4. Organic-inorganic nanocomposite

Organic-inorganic nanocomposites are composite systems at the nanoscale that amalgamate organic materials with inorganic materials [80]. These composites capitalize on the unique properties of inorganic materials, such as magnetism and optical properties, to achieve targeted drug delivery and controlled release [81]. Lee et al. develop a pH-responsive folic acid-grafted organic/inorganic hybrid nanocomposite system for site-selective oral delivery of therapeutic antibodies [82]. Furthermore, Aloisi et al. provide a comprehensive summary of recent advances in organic-inorganic hybrid nanomaterials within the realm of women's reproductive health [83]. This review offers an intricate introduction to the applications of organic-inorganic nanocomposites in treating gynecological diseases, thereby proposing novel solutions for gynecological tumors, female infertility, and infectious diseases.

3.1.5. Nucleic acid nanocarrier

Nucleic acid nanomaterials are exceptionally minute particles primarily composed of DNA or RNA, typically exhibiting diameters ranging from 1 to 100 nm [84]. A variety of nucleic acid nanomaterials, including nucleic acid nanoparticles, nucleic acid nanostructures, and nucleic acid nanochips, can be fabricated using chemical methods [85]. Within the domain of female reproductive system diseases, nucleic acid nanomaterials find applications in gene therapy, drug delivery, diagnostics, and antimicrobial research. Baxi et al. report a lipid-based nucleic acid nanocarrier designed for localized treatment of reproductive system diseases [86]. Encapsulation of small interfering RNA within the lipid nanoparticles enables targeted delivery and gene silencing within the reproductive system. Garzon et al. conduct a comprehensive review of nanoparticle applications in treating endometriosis. Various types of nanoparticles are introduced, and their potential in drug delivery, anti-inflammatory effects, and tissue regeneration are discussed [87]. Additionally, Yang et al. present research on nanomedicines for enhanced local drug delivery against vaginal infections [88]. The researchers employ nucleic acid nanomaterials to fabricate nanocarriers with high permeability and stability, aiming to improve drug accumulation and therapeutic efficacy in vaginal tissues. These studies offer evidence of the potential application of nucleic acid nanomaterials within the realm of reproductive system research. They can be employed for localized treatment of reproductive organ-related diseases, such as endometriosis and vaginal infections.

3.2. Magnetic nanoparticles

Magnetic nanoparticles, which are nano-sized particles composed of magnetic materials such as iron, nickel, and cobalt, possess magnetic properties [89]. In the context of female reproductive system diseases, magnetic nanoparticles have demonstrated promising applications and achieved encouraging progress. Shalaby et al. developed a programmable drug delivery system utilizing magnetic nanoparticles for the selective dissolution of uterine fibroid cells [90]. Shalaby et al. developed a localized nonsurgical adenovirus-based alternative for the treatment of uterine fibroids that combines viral-based gene delivery with nanotechnology for more efficient targeting [90]. Furthermore, Yi et al.'s study highlighted the therapeutic effect of micelle-encapsulated zinc-doped copper oxide nano-composites on PARP inhibitor-resistant ovarian cancer, offering potential insights for clinical diagnosis and treatment [91].

3.3. Biologically active nanomaterials

Biologically active nanomaterials refer to a class of nanoscale materials with unique structures and functions that interact with biological systems and exhibit biological activities [92]. In the field of female reproductive system diseases, biologically active nanomaterials hold significant potential. The applications of these materials primarily involve diagnostics and therapeutics. In diagnostics, biologically active nanomaterials find extensive utilization in the domains of bioimaging and biosensors. By attaching probes such as fluorescent tags to nanomaterials, highly sensitive detection of disease biomarkers, including those associated with

breast cancer and endometriosis, can be achieved [93]. Furthermore, biologically active nanomaterials can serve as contrast agents, facilitating improved contrast in MRI and ultrasound imaging, thereby contributing to more accurate disease diagnosis [94]. In terms of therapeutics, biologically active nanomaterials can act as efficient drug carriers, enabling targeted therapy. Through adjustments in the nanomaterials' size, surface modifications, and release mechanisms, their accumulation and drug delivery efficiency at the lesion site can be enhanced while minimizing adverse effects on healthy tissues. For example, in the treatment of uterine fibroids, drugs encapsulated within biologically active nanomaterials can be released at the specific lesion site through precise targeting mechanisms, enabling localized treatment [95,96]. Additionally, biologically active nanomaterials can be employed in thermotherapy utilizing magnetic hyperthermia, where an externally applied magnetic field generates heat, leading to thermal ablation of the lesions [97]. The application of nanomaterials in uterine fibroid treatment is still in the research stage, necessitating further validation and clinical practices. However, these nanotechnologies offer a potential new avenue for treating uterine fibroids, with anticipated benefits including improvements in drug delivery efficiency, treatment effectiveness, and reduced adverse reactions.

3.4. Utilization of nanotechnology for the regulation of ovarian hormones

Ovarian hormones, including estrogen and progesterone, play a crucial role in the female reproductive system [98]. Nanotechnology offers potential applications for modulating the synthesis, release, and response of these hormones (Fig. 4.).

3.4.1. Estrogen

Nanotechnology offers a means to regulate estrogen levels by modulating ovarian feedback mechanisms. Nucleic acid nanomaterials can be harnessed to selectively inhibit the regulatory factors involved in estrogen synthesis, effectively reducing its production and release. Multiple studies have substantiated the utility of nanocarriers for delivering anti-estrogen drugs [99–101]. Nanoparticles and nanocapsules, among other carriers, have found extensive application in anti-estrogen drug delivery. These carriers play a pivotal role in enhancing drug stability, bioavailability, and enabling targeted delivery, thus contributing to dose reduction and mitigating adverse effects. Furthermore, nucleic acid nanomaterials like liposomes and polymer nanoparticles have been employed to deliver gene therapy drugs, including siRNA, to intervene in estrogen synthesis or response processes [102]. This gene therapy

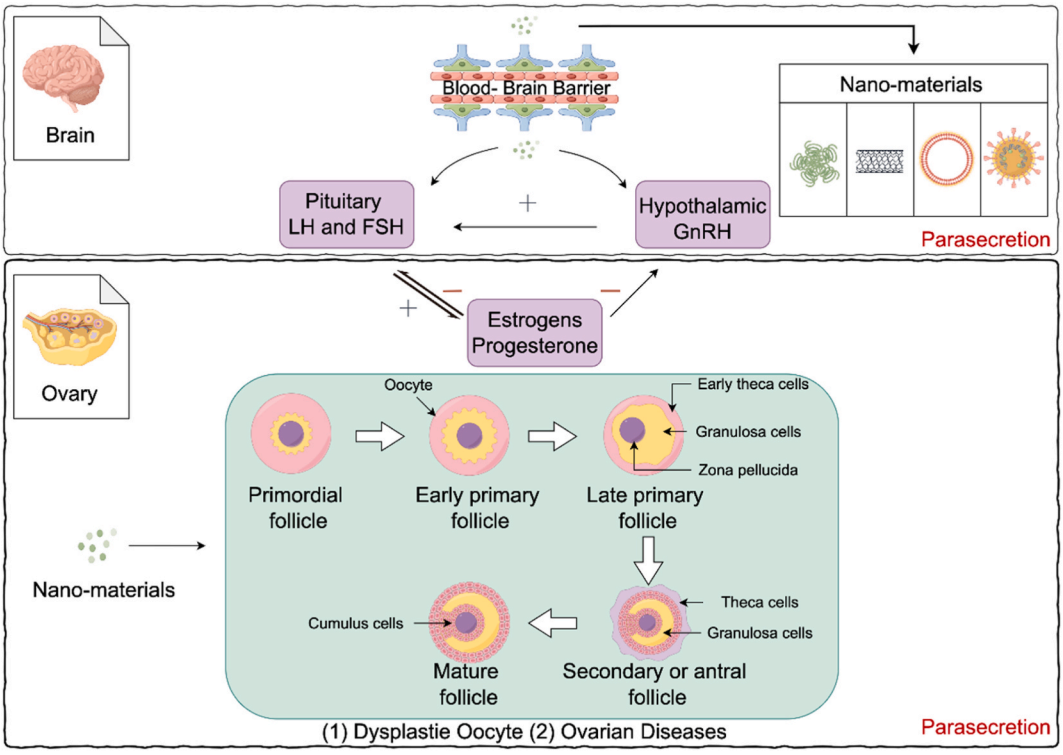

Fig. 4. The Application of nanotechnology in the ovarian and hypothalamic-pituitary-gonadal axis hormone secretion system. Nanoparticles have the potential to influence hormone secretion through two distinct mechanisms: 1) their ability to traverse the blood-brain barrier and target the hypothalamus and pituitary secretory cells, thereby modulating the release of GnRH, LH, and FSH hormones. Consequently, this disruption interferes with the intricate positive and negative feedback loop of the hypothalamic-pituitary-gonadal axis, ultimately impacting the regular secretion of ovarian estrogen and progesterone; 2) their circulation towards the ovaries, where they accumulate within membrane cells and granulosa cells, leading to perturbed steroidogenesis. Ultimately, these dysregulated hormonal secretions contribute to impaired oocyte development and the onset of various ovarian diseases.

approach utilizing nanomaterial carriers facilitates efficient drug delivery and brings forth novel prospects for treatment.

3.4.2. Progesterone

Nanotechnology also holds promise for progesterone regulation. Progesterone assumes a critical hormone status, exerting pivotal influences on physiological and pathological processes, notably implicated in diseases such as breast cancer and osteoporosis [103]. By investigating progesterone receptor signaling pathways, researchers strive to develop more efficacious treatment modalities. Nanotechnology plays a momentous role by enabling the design and fabrication of targeted drugs for progesterone receptors, thereby bolstering treatment efficacy while minimizing side effects. Secondly, in the realm of nanotechnology-mediated delivery of progesterone drugs, nanoparticles, nanocapsules, and nanofibers have been extensively utilized [104–106]. These carriers exhibit exceptional drug stability, bioavailability, and enable targeted delivery. Encapsulation of progesterone drugs within nanocarriers facilitates enhancements in drug solubility, controlled release kinetics, and targeting capabilities, thereby amplifying therapeutic effectiveness and diminishing dosage and adverse effects.

3.4.3. Luteinizing hormone (LH) and follicle-stimulating hormone (FSH)

LH and FSH, secreted by the pituitary gland, play a crucial role in regulating synthesis and release of ovarian hormones [107]. Nanotechnology holds the potential to modulate LH and FSH synthesis or release, thus influencing ovarian hormone levels. Experimental findings have illustrated successful entrapment and controlled release of FSH using nanoparticle carriers, resulting in enhanced bioactivity and stability [108]. To enhance ovarian reserve function, temperature-sensitive hydrogel-based nanocapsules have been devised for controlled FSH delivery [109]. These nanocapsules have exhibited effective release of FSH both in vitro and in vivo, indicating promising prospects for optimizing ovarian reserve function. Furthermore, conceptual investigations have explored the utilization of targeted nanoparticle carriers for controlled FSH release in order to ameliorate fertility outcomes in polycystic ovary syndrome [110]. Encouraging results highlight the potential viability of these nanoparticle carriers as a therapeutic strategy for polycystic ovary syndrome. Harnessing nanocarriers for the delivery of ovulation-inducing drugs represents a potent therapeutic approach with the capacity to augment local drug concentrations and escalate treatment efficacy [111]. These studies assume significant importance in comprehending the application of nanotechnology within the realm of reproductive health.

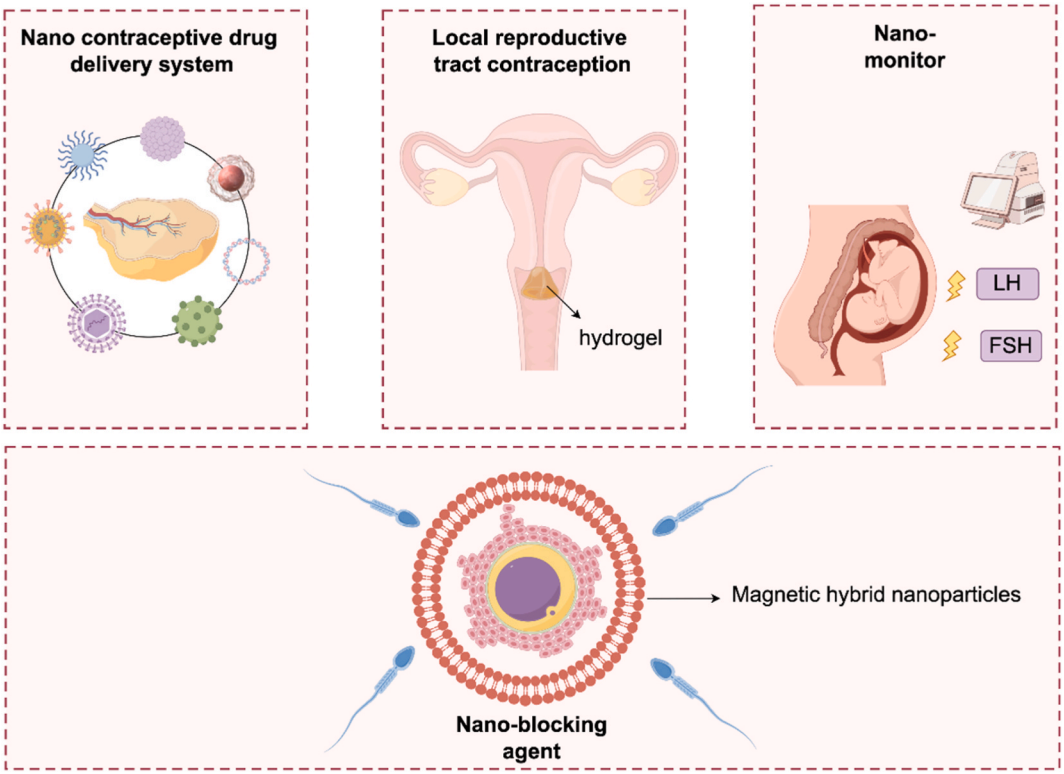

Fig. 5. The application of nanomaterials in contraception and fertility control entails: 1) Delivery of contraceptive drugs; 2) Modulation of sperm motility and functionality; 3) Implementation of localized contraception methods; 4) Monitoring of reproductive status.

4. The role of nanotechnology in the prevention and management of disorders in the female reproductive system

4.1. Utilization of nanomaterials in the field of contraception and fertility control

Nanomaterials exhibit promising potential in the domains of contraception and fertility control (Fig. 5.).

4.1.1. Contraceptive drug delivery system

Nanoparticles can serve as carriers for contraceptive drugs, facilitating more efficacious birth control. By encapsulating or modifying the drugs with nanoparticles, controlled release mechanisms can be achieved, enhancing drug stability and bioavailability. Subcutaneous contraceptive implants, utilizing biodegradable materials, entail the integration of hormones with diverse biomaterial structures like capsules or rods, which are subsequently implanted beneath the skin to accomplish continuous and stable drug release. This method presents an enduring contraceptive effect coupled with notable reversibility. A solitary implant can provide contraception for a duration of 5 years, boasting a superb Pearl Index of 0.1, while fertility is wholly reinstated upon removal of the implant [112]. The implantable contraceptive extended-release delivery system, Implanon with ethyl acetate (EVA) as the carrier matrix, represents another variant in this category. EVA exhibits exceptional elasticity, flexibility, water resistance, and corrosion resistance while also demonstrating superior tolerance towards fillers compared to silicone rubber [113]. Conville et al. demonstrated the efficacy of a hydrogel delivery system composed of a blend of polyethylene vinyl acetate (PEVA) and polylactic acid (PLA) with hydrophilic tenofovir [114]. Through careful optimization of the PLA to PEVA ratio, the researchers achieved a favorable performance in achieving long-acting slow-release for contraception, pregnancy prevention, and HIV transmission inhibition.

4.1.2. Nano-spermicides

Nanomaterials possess utility in impeding sperm motility, thus promoting contraception. By tailoring specific surface structures or chemical compositions of nanoparticles, it is conceivable to thwart sperm-egg binding and penetration, thereby achieving contraceptive effects [115]. The mechanism of Cu-IUD is considered that the release of $Cu2+$ causes the inactivation of sperm and the suppression of myometrial contractions [116]. Hu et al. reported on the use of Nano-Cu/LDPE as a copper carrier in intrauterine devices for contraception [117]. Copper nanoparticles were combined with LDPE through physical and chemical methods to form a composite material, resulting in an even distribution of nanoparticles within the composite. By separating the copper nanoparticles from LDPE, their proximity to the corrosive medium ($Cu2+$ ions) was controlled to effectively regulate the corrosion rate, which allowed for a rapid and constant release rate within 5 h [118].

4.1.3. Utilization of nanomaterials for local contraception

Nanomaterials have immense potential for local contraception, including regulation of the vaginal environment and localized contraceptive acidification. Conville et al. elucidated the efficacy of a hydrogel delivery system based on a composite blend of PEVA and PLA incorporated with hydrophilic tenofovir [114]. By carefully manipulating the PLA to PEVA ratio, the researchers achieved a desirable performance in terms of long-acting slow-release, thereby showcasing its potential for contraception, pregnancy prevention, and HIV transmission inhibition applications. Malik et al. fabricated biodegradable nanoparticles composed of poly (lactic acid, PLA) using a single emulsion technique [119]. These Nanoparticles had an average size of 75 nm. When administered into the vaginal cavity of mice in estrus, the Nanoparticles exhibited retrograde transport, crossing the cervix and accumulating in the uterus. Analysis of uterine lavage samples taken after NP instillation revealed the activation of proinflammatory signals, such as RANTES and TNF, within the uterine microenvironment. This inflammation created an adverse milieu that hindered the successful establishment of pregnancy.

4.1.4. Nanosensors for contraceptive monitoring

The application of nanomaterials in contraceptive monitoring represents a promising area of research. By utilizing nanoparticle labeling of specific physiological molecules or indicators, real-time monitoring of fertility status can be achieved, providing more accurate information for contraception. For instance, in monitoring women's ovulation cycles, nanomaterials can be used to label relevant biomarkers such as FSH and LH [120,121]. Changes in these markers can determine whether a woman is ovulating or in different stages of fertility, aiding in the determination of appropriate contraceptive methods or fertility planning. Additionally, nanomaterials can be employed to monitor levels of hormones within a woman's body. For example, estrogen and progesterone levels can be monitored using nanoparticle sensors to assess fertility, menstrual cycles, and hormone imbalances [101,103]. The application of nanomaterials can also extend to other areas of contraceptive control, such as male contraception. Nanoparticles can serve as drug carriers to deliver contraceptive drugs or spermicidal agents into the male reproductive system, achieving controlled contraceptive effects.

4.2. Application of nanotechnology in the treatment of infertility

4.2.1. Reproductive cell preservation

The utilization of nanotechnology can enhance the quality of cryopreserved sperm and oocytes through the use of various nanomaterials, which provide protective barriers to prevent crystallization and cellular damage during the freezing process [122]. Bisla et al. explore the application of nanoparticles in male fertility, specifically the ways in which metals, polymers, and carbon-based materials protect sperm, improve their quality, and reduce cell damage during the freezing-thawing process [123]. Additionally, Isaac et al. investigate further the application of nanoparticles in human sperm cryopreservation and find that these particles can

stabilize sperm cell membranes, reduce oxidative stress, and freezing-induced cell damage, thus improving sperm viability and motility [124]. Furthermore, Fraser et al.'s study examines the potential benefits of nanoparticles in the treatment of infertility [125].

4.2.2. Drug delivery systems

Nanoparticles can function as efficient drug delivery systems, providing direct delivery of drugs or bioactive molecules to reproductive organs, ovaries, testes, and other targeted tissues. This targeted delivery approach enhances local drug concentration, reduces side effects, and improves treatment effectiveness. Cai et al. provided a comprehensive overview of the recent advancements in uterine endometrial repair methods, with a particular focus on the application status of biomaterial-based hydrogel delivery systems in intrauterine injury repair [126]. The review delved into the principles of preparation, therapeutic efficacy, repair mechanisms, as well as current limitations and future prospects of this approach. Jahanbani et al. elucidated the recent progress in the development of functionalized biomaterials aimed at enhancing the preservation of exosome bioactivity and enabling controlled release. The study emphasized the diagnostic and therapeutic role of exosomes in reproductive system disorders pertaining to both males and females [127].

4.2.3. Support for assisted reproductive technology (ART)

Nanotechnology is increasingly recognized as an effective approach for enhancing success rates in assisted reproductive technology. Magdanz et al. describes the potential of sperm-driven micro-bio-robots in the biomedical field such as drug delivery or single cell manipulation [128]. Roshanfekr et al. emphasize the use of nanomaterials in embryo culture media, which can optimize environmental conditions and improve embryo development [129]. Additionally, nanoparticles employed in embryo imaging contribute to selecting the most promising embryos. Additionally, Lu et al. developed the silk fibroin (SF)-based microneedles for transdermal delivery of triptorelin-loaded Nanoparticles to improve bioavailability and achieve safe and efficacious self-administration of triptorelin [130].

4.2.4. Gene editing and repair

Nanotechnology is capable of gene editing and repair, offering an avenue to address specific genetic defects that cause infertility. By adjusting the surface properties of nanoparticles, therapeutic agents or genes can be transported into reproductive cells, enabling proper gene function. Zhen et al. developed a novel lipid nanoparticle formulation containing CRISPR/Cas2019 gene editing tools,

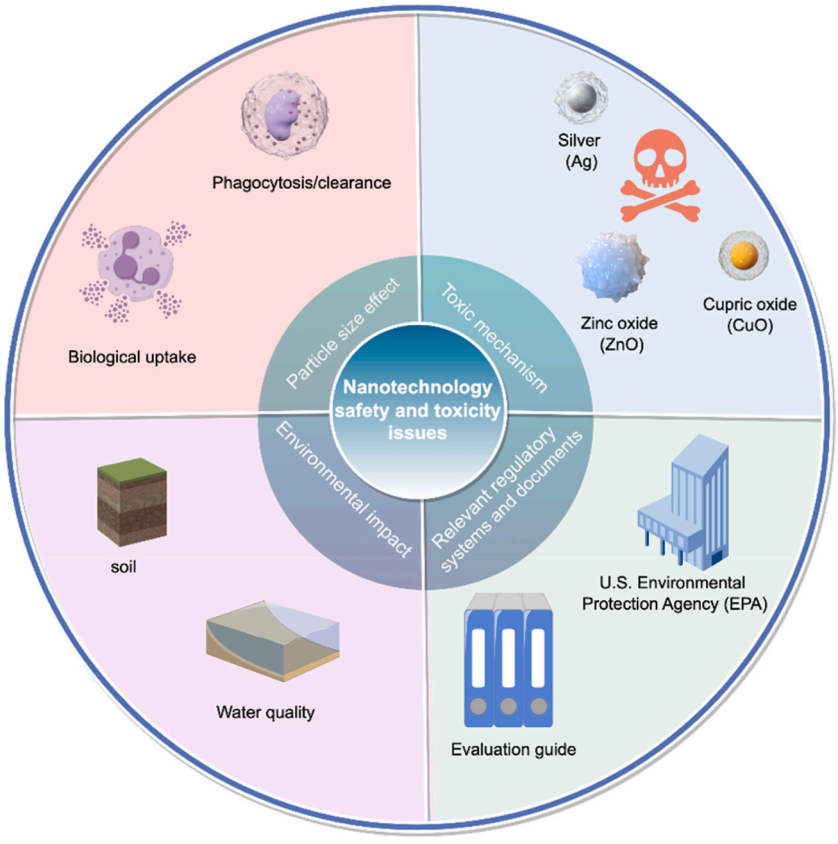

Fig. 6. Limitations of nanotechnology in biomedicine encompass several factors: 1) The particle size disparities leading to the particle size effect; 2) Biological toxicity considerations; 3) The ecological implications of release and accumulation; 4) Industry regulation and risk assessment measures.

which effectively suppressed proliferation and induced apoptosis in hr-HPV9E/E16-positive cervical cancer SiHa cells by targeting the inactivation of the HPV16 oncogene [131]. Rosenblum et al. published a study describing the development of lipid nanoparticles encapsulating PLK1-targeting Cas9 mRNA and sgRNA gene editing tools. They successfully established a mouse model of peritoneal disseminated ovarian cancer (OV8-Mcherry) and administered the nanoparticles via intraperitoneal injectio [132]. Meanwhile, Wiweko and colleagues investigate the diverse applications of nanotechnology for reproduction, including gene editing and repair, as well as imaging and diagnostics [133].

5. Challenges and prospects of nanotechnology

5.1. Safety and toxicity

The safety and toxicity concerns associated with nanotechnology have consistently garnered significant research attention. Despite the vast potential applications of nanomaterials in scientific, medical, and engineering domains, it is imperative to conduct comprehensive evaluations regarding their safety and potential toxicological effects (Fig. 6.).

5.1.1. Effects of particle size

The particle size of nanomaterials has a significant impact on their properties and behaviors, commonly known as the particle size effect [134,135]. Materials at the nanoscale exhibit distinct variations in their physical, chemical, and biological characteristics compared to macroscopic materials [136]. Understanding the particle size effect is paramount for ensuring the safety of nanomaterials. In general, smaller nanoparticles possess a relatively large surface area, which enhances their chemical reactivity and biological activity. The increased contact area between nanoparticles and the surrounding environment or biological systems facilitates interactions with cells, proteins, and other biomolecules [137,138]. Furthermore, the small size of nanoparticles can influence their pharmacokinetics, cellular uptake, tissue penetration, and excretion pathways. These factors play a crucial role in the biodistribution, transport, and clearance processes of nanomaterials, thereby affecting their potential toxicity within an organism. Numerous studies have demonstrated smaller nanoparticles are more readily taken up by cells and may exert more pronounced toxic effects, whereas larger nanoparticles are more susceptible to engulfment and clearance by macrophages [139–141].

5.1.2. Mechanisms of toxicity

The mechanisms underlying the toxicity of nanomaterials are intricate and depend on specific materials and applications. Certain nanomaterials are capable of inducing adverse effects, including cell toxicity, inflammation, and oxidative stress [142,143]. These effects are thought to be influenced by various factors, such as the chemical composition, structural characteristics (e.g., shape and surface modifications), and dosage of the nanoparticles. Boyadzhiev et al. investigated DNA damaging effects in adherent murine lung epithelial cells exposed for 2–4 h to different doses of ZnO, CuO, and TiO2 Nanoparticles, MPs as well as zinc and copper chloride salts [144]. The findings revealed that nanoparticle size and dosage are critical determinants of cellular toxicity. Lekki-Porębski et al. demonstrated that the cellular toxicity mechanism of ZnO Nanoparticles is based on the induction of oxidative stress in CCRF-CEM cells, which is caused by the release of free zinc ions from ZnO Nanoparticles [145].

5.1.3. Environmental impacts

The release and accumulation of nanomaterials have the potential to exert environmental effects. When nanoparticles enter the environment, they can interact with organisms, soil, water, and other constituents, thereby posing adverse consequences for ecosystems [146–148]. Consequently, assessing the behavior and bioavailability of nanomaterials within the environment becomes pivotal. In a study conducted, the authors evaluated the biocompatibility and toxicity of silver nanoparticle-loaded polyester fabrics used as antimicrobial agents [149]. Their findings revealed that the material exhibited a certain degree of cytotoxicity toward human cells, which correlated with the concentration and exposure duration of the silver nanoparticles.

5.1.4. Relevant regulatory frameworks and documents

Numerous countries have formulated policies and regulations pertaining to nanotechnology to ensure its safe implementation. For instance, the U.S. Environmental Protection Agency (EPA) has issued guidelines and risk assessment methodologies for utilizing nanomaterials [150], while the European Commission has enacted regulations catered specifically to nanomaterials [151]. Moreover, international organizations actively advocate for global collaboration in nanotechnology safety. Notable examples include the World Health Organization (WHO), which has developed guidelines for assessing the health risks associated with nanomaterials [152], and the International Organization for Standardization (ISO), which has established a series of standards addressing nanotechnology safety [153]. Extensive research has been conducted by independent research institutions and academic scholars to evaluate the potential risks of nanomaterials and to devise guidelines for their secure application [154–157]. These research outcomes furnish scientific evidence regarding the safety of nanotechnology. Importantly, it should be highlighted that nanotechnology remains an evolving domain, and investigations into its safety and toxicity persist. Collaboration among the scientific community, government agencies, and industry is imperative to promote the sustainable development of nanotechnology while ensuring its safety and environmental compatibility in practical applications.

5.2. Obstacles to clinical translation

Promoting the application of nanomaterials in clinical translation plays a crucial role in the development of nanomedicine, but currently faces various challenges and obstacles.

5.2.1. Safety and toxicity assessment

Comprehensive evaluations of safety and toxicity are imperative for nanomaterials due to their distinctive physicochemical attributes. These assessments encompass several facets, including pharmacokinetics, toxicology, and immunology, in order to ascertain the safety of nanomaterials in clinical applications-a critical consideration. Firstly, the evaluation of pharmacokinetics involves scrutinizing how nanomaterials are absorbed, distributed, metabolized, and excreted within the body [158]. Given the unique size, shape, and surface properties of nanomaterials, their behavior and transformation in the body may deviate from that of conventional drugs. Consequently, comprehending the pharmacokinetic characteristics of nanomaterials is pivotal for evaluating their safety in clinical usage. Secondly, toxicology assessments are conducted to identify potential toxic effects of nanomaterials on human tissues, organs, and cells [159].

Existing research findings suggest that nanoparticles can penetrate the blood-testis barrier and accumulate in the interstitial cells, supporting cells, and sperm cells in the testes [160]. It is worth noting that nanoparticles have the ability to cross the placental barrier, thereby affecting the growth and development of offspring [161]. Additionally, immunological assessments investigate the impact of nanomaterials on the immune system [162]. Nanomaterials have the capacity to interact with immune cells or molecules, potentially leading to alterations or irregularities in immune responses. Understanding the influence of nanomaterials on the immune system aids in assessing their immunotoxicity potential and instilling confidence in their safe clinical usage.

5.2.2. Lack of standardization and regulations

The intricate and diverse nature of nanomaterials currently results in a lack of unified standardized methodologies and regulations for their characterization, quality control, and batch consistency assessment [163]. This absence of uniform standards presents a series of challenges for the clinical translation of nanomaterials, impeding comparability and reproducibility of outcomes. Primarily, the complexity and diversity of nanomaterials render their evaluation arduous. The properties of nanomaterials are influenced by various factors such as size, shape, and surface modifications. Nevertheless, prevailing techniques and parameters for assessing nanomaterials lack standardization, leading to disparate evaluation methods employed by diverse research institutions or laboratories. Consequently, making meaningful comparisons between findings becomes a formidable task. Secondly, the absence of unified quality control methods curtails the usage of nanomaterials in clinical translation. The preparation and synthesis processes of nanomaterials frequently involve intricate conditions and process parameters. However, due to the lack of standardized quality control methods, ensuring consistency and stability across different batches becomes challenging-an influential limiting factor for the clinical application of nanomaterials. Furthermore, the dearth of uniform evaluation standards also poses challenges to safety assessments during the clinical translation of nanomaterials. In the realm of toxicity evaluation for nanomaterials, the absence of standardized methods and indicators hinders direct comparison of toxicity results from distinct studies. This impedes our comprehensive understanding of potential risks associated with nanomaterials and obstructs reliable assessment of their secure applications.

5.2.3. Targeting efficiency and drug delivery

In order to achieve optimal drug delivery in the field of nanomedicine, precise targeting to the disease site and controlled release of drugs are crucial. However, the delivery efficiency and stability of nanomaterials pose challenges in complex biological environments, necessitating further research and optimization. Researchers are currently exploring various strategies to enhance the delivery efficiency of nanomaterials. For example, modifying the surface of nanomaterials can improve their targeting specificity, enabling accurate recognition and binding to disease biomarkers or cell receptors [164–166]. Moreover, intelligent targeted delivery of nanomaterials can be achieved by utilizing biological molecules (such as antibodies and peptides) or stimuli-responsive mechanisms [167,168]. Another key concern is ensuring effective drug release at the target site. Some nanomaterials can initiate drug release in response to changes in biological conditions like pH, temperature, or enzymes, thereby enhancing delivery efficiency [169–171]. Furthermore, ongoing research is focused on achieving controlled delivery and drug release of nanomaterials through external stimuli such as light, magnetic fields, or sound waves [172,173].

5.2.4. Production costs and scalability

The preparation and production of nanomaterials are often intricate processes associated with high costs and technological challenges. To facilitate the clinical translation of nanomaterials, it is important to address issues related to large-scale preparation, production scalability, cost control, and affordability. Researchers are actively developing more efficient synthesis methods and advanced technologies to reduce the preparation costs of nanomaterials. Innovative techniques like microfluidic technology, nanoparticle assembly, and self-assembly enable rapid and controllable preparation of nanomaterials [174–176]. Additionally, the utilization of bio-synthesis and renewable resources can contribute to reducing preparation costs and minimizing environmental impact. Furthermore, scaling up production while maintaining consistent quality is a significant consideration. Meeting the demands of clinical applications requires conducting large-scale production of nanomaterials with stable preparation. Therefore, it is imperative to explore new processes and equipment to enhance the production efficiency and controllability of nanomaterials.

5.2.5. Regulatory and governance constraints

The clinical applications of nanomaterials are subject to regulatory requirements established by national and regional authorities [177]. Due to the unique properties of nanomaterials, many countries are formulating policies and regulations to ensure their safety and efficacy. This often results in complex and time-consuming approval processes. Regulatory requirements for nanomaterials encompass assessments of toxicity, biocompatibility, compliance testing, and supervision, aiming to guarantee their safety, efficacy, and reliability in clinical applications. To adhere to regulatory and governance constraints, researchers and manufacturers must conduct comprehensive safety assessments and preclinical studies to gather the necessary data and evidence. Active communication and collaboration with regulatory agencies are also essential to ensure compliance and facilitate smooth clinical translation of nanomaterials.

5.2.6. Ethical challenges

The primary ethical concern with nanotechnology is its safety, specifically whether the research and application of nanotechnology have any adverse effects on the health and lives of researchers and users. Currently, most of the research on nanotechnology in reproductive system diseases is preclinical, and there is a lack of practical clinical trials on nanoparticle treatments.

One question to consider regarding the clinical translation of nanoparticles in sensitive areas such as women's reproductive systems is the potential for transgenerational risks. Studies have shown that regulating the size and charge of nanoparticles can limit their ability to cross the placenta [178]. Currently, there are various in vitro, ex vivo, and in vivo models available to study the distribution of nanoparticles in tissues (including fetuses) [179]. Therefore, designing suitable nanoparticles and generating sufficient preclinical data to prove the ethical feasibility of conducting phase I trials in pregnant women is necessary. Another concern is the restrictions on assisted reproductive technologies. For example, the nanorobotics project has made revolutionary progress in assisted reproductive technology by efficiently and accurately picking up sperm and achieving targeted manipulation of sperm, but long-term safety and feasibility issues still require further research and validation [180].

5.3. The potential of nanotechnology application

Nanomaterials hold tremendous potential in the realm of female reproductive system diseases, with targeted therapy, early diagnosis, drug delivery systems, and tissue engineering and regenerative medicine among their future focus areas [9,83,181].

A few clinical trials have evaluated the potential of nanotechnology in gynecological diseases. A prospective clinical study analyzed the oncogenic viral tumor interaction forces and interaction dynamics based on nanomechanics and nanoelectromechanical sensors (NCT01387997). The efficacy of MILTA® therapy has been demonstrated in various pain management cases, but it has never been used for pain associated with perineal scars. An interventional clinical trial, NCT05345600, is planned to recruit 110 participants to evaluate the effectiveness of MILTA® compared to placebo in relieving postpartum pain associated with perineal scars. Feasibility of real-time dosimetry monitoring using a novel nanoscale scintillating fiber-optic dosimeter (nanoFOD) during external beam radiotherapy has been determined through two observational studies (NCT02407977, NCT02040155). SNB-101 is a novel nanoparticle formulation of the active metabolite SN-38 of irinotecan (CPT-11). NCT04640480 is a phase I clinical trial aiming to evaluate the safety, tolerability, and pharmacokinetics of intravenous infusion of SNB-101 in advanced solid tumor patients, including epithelial ovarian cancer.

Regarding targeted therapy, nanomaterials can achieve molecular-level precision for female reproductive system diseases through rational design and functionalization. Surface property modification enables selective recognition and binding to disease cells or tissues, allowing for precise release of therapeutic drugs at the site and reducing harmful side effects while enhancing efficacy. In the realm of early diagnosis, nanomaterials can improve the diagnostic capabilities of female reproductive system diseases. Optical, magnetic, or acoustic manipulation of nanomaterials can yield highly sensitive and specific nanoprobes for detecting and imaging disease biomarkers or abnormal physiological states, enabling earlier disease diagnosis. Nanomaterials can also serve as drug delivery systems to enhance the treatment effectiveness of female reproductive system diseases. Encapsulating therapeutic drugs like anticancer agents and anti-infective drugs and delivering them accurately to the disease site increases drug stability and bioavailability, while reducing toxic side effects. Moreover, nanomaterials have significant implications in the field of tissue engineering and regenerative medicine for the female reproductive system. They have the potential to construct functional tissues such as artificial uteri or ovaries, promoting tissue repair and regeneration of the reproductive system. Furthermore, nanomaterials play a constructive role in supporting cell growth, differentiation, and functional expression, offering novel strategies for the treatment of female reproductive system diseases.

6. Conclusion

Nanotechnology holds immense potential in the field of female reproductive system diseases. This review highlights the applications of nanomaterials in targeted therapy, early diagnosis, drug delivery systems, and tissue engineering and regenerative medicine. Nanomaterials can be tailored and functionalized to specifically target and treat female reproductive system diseases, minimizing side effects and enhancing efficacy. Additionally, nanotechnology plays a significant role in early disease detection by developing highly sensitive and specific nanoprobes capable of identifying disease biomarkers or abnormal physiological states. Furthermore, nanomaterials serve as effective drug delivery systems, improving the treatment outcomes of female reproductive system diseases. By encapsulating therapeutic drugs within nanomaterials and delivering them to disease sites, drug stability is increased while reducing toxic side effects. However, further research and clinical validation are necessary to ensure the safety, effectiveness, and feasibility of

these applications. Nanotechnology offers hope for addressing female reproductive health issues and has the potential to become a crucial clinical practice in the future.

CRediT authorship contribution statement

Xin Luo: Writing – review & editing, Writing – original draft, Methodology, Investigation, Formal analysis. **Keran Jia:** Writing – review & editing, Writing – original draft, Validation, Formal analysis. **Jinshan Xing:** Writing – original draft, Supervision, Investigation, Funding acquisition, Conceptualization. **Jingyan Yi:** Writing – review & editing, Writing – original draft, Visualization, Project administration, Funding acquisition.

Declaration of competing interest

The authors declare that they have no known competing financial interests or personal relationships that could have appeared to influence the work reported in this paper.

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Abbreviations

PCOS	Polycystic ovary syndrome
FI	Fluorescence imaging
TAM	Tamoxifen
PAI	Photoacoustic imaging
MRI	Magnetic resonance imaging
ST	Selenophene-dithienylbenzo[c][1,2,5]thiadiazole
HA	Hyaluronic acid
MRE	Magnetic resonance elastography
LH	Luteinizing hormone
FSH	Follicle-stimulating hormone
EVA	Ethyl acetate
PEVA	Polyethylene vinyl acetate
PLA	Polylactic acid
ART	Assisted reproductive technology
EPA	Environmental Protection Agency
WHO	World Health Organization
ISO	International Organization for Standardization

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