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Review

Biomaterials for women's health: Recent progress in nanomaterials and innovative therapies for endometriosis treatment

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ABSTRACT

Endometriosis is a chronic inflammatory condition characterized by the presence of endometrial-like tissue outside the uterine cavity. Despite significant advances in understanding its pathophysiology, the clinical management of endometriosis remains a profound challenge. The disease is a leading cause of pelvic pain and infertility, significantly impairing the quality of life of affected individuals. Although endometriosis is histologically benign, its progressive, invasive nature and high recurrence rate pose serious morbidity risks, necessitating long-term therapeutic intervention. Current pharmacological treatments, primarily based on hormonal suppression, are often limited by systemic adverse effects, low patient adherence, and a lack of efficacy in preventing disease progression in refractory cases. Consequently, there is an urgent need to develop novel, targeted therapeutic strategies that overcome the limitations of systemic administration. This article provides a

List of abbreviations: ADMSCs, adipose-derived mesenchymal stem cells; AI, Artificial Intelligence; AFM, Atomic Force Microscopy; AMNPs, aminopropyl modified silica nanoparticles; ART, artesunate; BSA, bovine serum albumin; CA19–9, carbohydrate antigen 19–9; CHR, chrysin; CRGD, Cycloarginyl-glycyl-aspartic acid; CRP, C-reactive protein; CS, chitosan; CTLA-4, cytotoxic T-lymphocyte antigen 4; CUPNSs, Cuprorivaite nanosheets; DE, deep infiltrating endometriosis.; DECM, decellularized extracellular matrix; DIE, deep infiltrating endometriosis; DNA, Deoxyribonucleic acid; DDS, drug delivery system; EAPP, endometriosis-associated pelvic pain; EC, endometrial cancer; ECM, Extracellular matrix; ECSCs, endometriotic cyst stromal cells; ESHRE, European Society of Human Reproduction and Embryology; ESR1, estrogen receptor alpha; ESR2, estrogen receptor beta; EUT, ectopic uterine tissue; EV, extracellular vesicles; FBR, Foreign Body Response; FDA, Food and Drug Administration; Fg, fibrinogen; FI, fluorescent imaging; FITC, fluorescein isothiocyanate; FTIR, Fourier Transform Infrared Spectroscopy; FUT4, fucosyltransferase 4; GnRH, gonadotropin-releasing hormone; HA, hyaluronic acid; HAuNS, Au-based hollow nanoshells; HEC, hydroxyethyl cellulose; HEEC, human endometrial endothelial cells; HESCs, human primary endometrial stromal cells; HIF1A, Hypoxia-Inducible Factor 1; HMG-CoA, 3-hydroxy-3-methylglutaryl coenzyme A; HuECSCs, human endometrial carcinoma stem cells; HUVECs, human umbilical vein endothelial cells; IDEA, International Deep Endometriosis Analysis; IFN, Interferon; IL, interleukin; IONPs, Iron oxide nanoparticles; LDE, lipid emulsion; LDL, low-density lipoprotein; LIF, leukemia inhibitory factor; LNG, levonorgestrel; LNPs, lipid nanoparticles; MH, magnetic hyperthermia; Mif, mifepristone; MiRNA, Micro ribonucleic acid; MM-NS, nanosheets decorated with macrophage membrane; MMP9, Matrix metalloproteinase 9; MPA, Medroxyprogesterone acetate; MRI, magnetic resonance imaging; MRNA, messenger RNA; MTX, methotrexate; MWCNT, multiwalled carbon nanotubes; NHA, nano-hydroxyapatite; NIR, near infrared; NLC, nanostructured lipid carriers; OMA, ovarian endometriomas; PAI, photoacoustic imaging; PAMAM, Polyamidoamine; PCL, polycaprolactone; PECAM1, Platelet Endothelial Cell Adhesion Molecule 1; PEG, polyethylene glycol; PLA, polylactide; PLGA, polylactic-co-glycolic acid; PR-B, Progesterone receptor B; PT, polyD, L-lactide-co-trimethylene carbonate; PTT, photothermal therapy; PVA, polyvinyl alcohol; PVP, polyvinylpyrrolidone; RGD, arginyl-glycyl-aspartic acid; ROA, routes of administration; ROS, reactive oxygen species; SC, sildenafil citrate; SERM, Selective Estrogen Modulator; SF, silk fibroin; SiRNA, small interfering RNA; SLE-CuPPc, Cu-polyphthalocyanine network-based spike-linked enzyme; SLN, solid lipid nanoparticles; SLN, sentinel lymph nodes; SMP, shape memory polymer; SPIONs, superparamagnetic iron oxide nanoparticles; SPRM, Selective Progesterone Modulator; SUP, superficial peritoneal lesions; SVF, simulated vaginal fluid; TIMPs, Tissue inhibitors of metalloproteinases; TNF- α, Tumor necrosis factor; TV, tenofovir; TVUS, transvaginal ultrasound; UNPs, unmodified mesoporous silica nanoparticles; USPIO, ultrasmall superparamagnetic iron oxides; VAS, visual analog scale pelvic pain scores; VEGF, vascular endothelial growth factor; VEGFR-2, vascular endothelial growth factor receptor 2.

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comprehensive overview of the current state of preclinical research on advanced drug delivery systems for endometriosis therapy. We focus on nanomedicine and fibrous scaffold-based technologies, highlighting their potential to enable site-specific drug release, enhance therapeutic efficacy, and minimize off-target toxicity. Furthermore, we discuss the application of these systems in therapies utilizing external stimuli for precise drug release and the targeted elimination of ectopic lesions.

1. Introduction

Despite significant biological distinctions that necessitate specialized medical attention, gynecology accounts for only ca. 3.7% of clinical trials [1–5]. Against this backdrop, the investigation of innovative therapeutic strategies for endometriosis—particularly those involving advanced drug delivery systems or photothermal therapies—remains a notably rare and under-represented area of clinical research [5].

Endometriosis is a chronic inflammatory condition affecting approximately 10% (190 million) of reproductive-age women globally [1]. It is characterized by the presence of endometrial-like tissue outside the uterine cavity, e.g., in the pelvic peritoneum, on the ovaries, in the recto-vaginal septum, in the bladder, and in the bowel. The condition in which endometrial tissue grows into the muscular wall of the uterus is called adenomyosis [6,8]. In the most severe cases, the outbreaks of endometriosis may be found outside of the pelvis, e.g., in the lungs, on the skin [6,7,9,10] (Fig. 1). Endometriosis is also the reason for infertility in up to 50% of women from this group, as well as chronic pelvic pain (50–80%) [10,11]. Despite its prevalence, patients often face substantial diagnostic delays, with an average of 6.7 years [12,13]. This diagnostic gap, coupled with limited public awareness and fragmented research, imposes a considerable burden on public health and the global economy [10]. It is worth noting that the figures given regarding the epidemiology of endometriosis may be subject to significant error and underestimation because of such factors as access to professional medical care or cultural reasons, and there is no public database for population-level statistics, like for cancer or diabetes [14–17]. Endometriosis represents a complex, chronic systemic disorder associated with a profound socio-economic burden, significantly affecting labor productivity and quality of life. Current epidemiological data indicate that while standardized incidence rates have shown a gradual decline, the absolute global burden—measured by disability-adjusted life years (DALYs)—continues to rise due to population growth and demographic changes shifts [18] (Fig. 2).

Nnoaham *et al.* published the results of a multicenter cross-sectional clinical study conducted on a group of 1418 premenopausal women concerning the impact of endometriosis on quality of life and work productivity [19]. Results show that overall work productivity loss due to endometriosis was significantly increased to 10.8 h/week compared with the asymptomatic control [19]. The economic consequences of the disease are substantial, primarily driven by indirect costs related to absenteeism and presenteeism. Recent nationwide surveys underscore

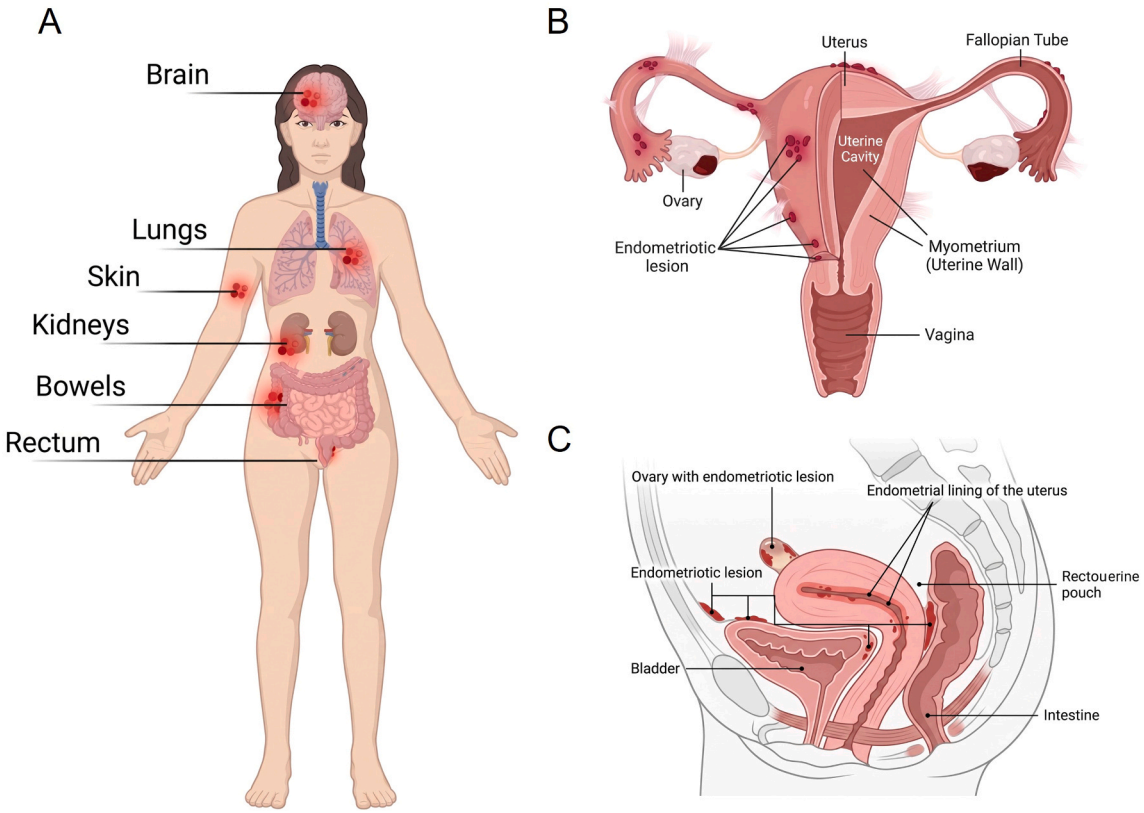

Fig. 1. Anatomical Distribution of Endometriotic Lesions. (A) Systemic Endometriosis Foci. Whole-body diagram illustrating possible extragenital body sites for endometriotic involvement beyond the reproductive organs, with labeled foci in the brain, lungs, skin, kidneys, bowels, and rectum, demonstrating multi-organ system involvement. (B) Endometriotic Lesions in the Uterus and Female Reproductive Organs. Foci of endometriotic lesions are highlighted, with specific emphasis on involvement of the uterus, fallopian tubes, and ovaries. (C) Sagittal View of Pelvis and Douglas Pouch Foci. Detailed sagittal pelvic cross-section illustrating relative organ positions and focused location of endometriotic lesion sites within the rectouterine pouch (also known as the pouch of Douglas), along with involvement of the bladder, ovaries, and intestine, detailing the endometrial lining and muscle wall. [6–8]. The figure was created with BioRender.

this impact, with annual per capita costs estimated at approximately Int $9864 in specific regional cohorts. In high-resource settings, macroeconomic analysis suggests that productivity loss accounts for up to 65% of the total economic burden associated with the condition [19,20]. The increasing recognition of endometriosis as a critical public health issue has catalyzed the establishment of numerous global and national organizations [21–27]. These entities, including major bodies such as the World Endometriosis Society [21], play a fundamental role in driving research initiatives, facilitating clinical guidelines, and providing necessary patient advocacy.

From a clinical engineering perspective, the pathology is characterized by extrapelvic manifestations and a high prevalence of infertility, occurring in 30–50% of affected populations [11,28]. Despite these severe outcomes, clinical management remains hampered by diagnostic delays and a reliance on symptom-focused palliative interventions rather than curative technologies. Surgical management, while a standard of care, is associated with recurrence rates exceeding 40% within five years, highlighting a critical unmet need for innovation in both diagnostic modalities and therapeutic biomaterials [28]. Currently, pharmacotherapy plays a crucial role in the treatment of endometriosis. Progestins and estroprogestines, used as contraception, are one of the most often used for endometriosis treatment. Their primary purpose is symptom relief. This therapy aims to induce, artificial menopause'' to achieve a hormonal state in which the activity of the endometrium is limited. Unfortunately, such standard therapy in most patients gives limited benefit, and pain is still present in almost 5–59% of treated women [28]. The above-mentioned products were created for the treatment of medical conditions other than endometriosis, and the active substances used in them, the method of drug delivery, or their actions are not targeted to the specific etiology of endometriosis.

This review focuses on the current state of preclinical research regarding novel biomaterials for local drug delivery in endometriosis. The primary objectives of this work are to synthesize current knowledge on the limitations of conventional systemic pharmacotherapy for endometriosis and justify the clinical need for localized drug delivery systems. Moreover, critical evaluation of recent preclinical advancements in biomaterial-based therapeutic vectors will be presented. Ultimately, the critical research gaps and future directions will be identified for the clinical translation of smart biomaterials in endometriosis management.

2. Endometriosis: ethiology and characteristics

The endometrium is a unique tissue in the human body. First, it constantly changes during the monthly cycle under hormonal stimulation, and second, it can accept foreign genetic material. The primary function of the endometrium is to create optimal conditions for the healthy growth and development of the embryo when fertilization occurs. A serious medical problem begins when endometrial tissue implants in a place other than the uterus. Nowadays, three phenotypes of endometriosis are distinguished: superficial peritoneal lesions (SUP), ovarian endometriomas (OMA), and deep infiltrating endometriosis (DIE or DE). Endometriosis with the SUP phenotype is described as the mildest form of this condition, characterized by the development of endometriotic lesions in the peritoneum. The OMA phenotype, on the other hand, is characterized by cystic masses arising from ectopic endometrial tissue that grow in the ovary. The DIE phenotype is considered the most difficult to treat, defined as subperitoneal lesions that penetrate the tissue deeper than 5 mm below the peritoneal surface (e.g., the uterosacral ligaments) or as lesions that infiltrate the muscular layer of organs surrounding the uterus, such as the bladder or intestine. A specific condition is adenomyosis, characterized by the infiltration of endometrial tissue into the uterine muscle [29,30]. The following symptoms are characteristic of endometriosis: severe, life-impacting pain, dysmenorrhea, dyspareunia, and infertility. Because endometrial tissue responds to hormonal stimuli regardless of its location, women particularly experience symptoms of endometriosis during menstruation. In the most severe clinical cases of this condition, pain is not

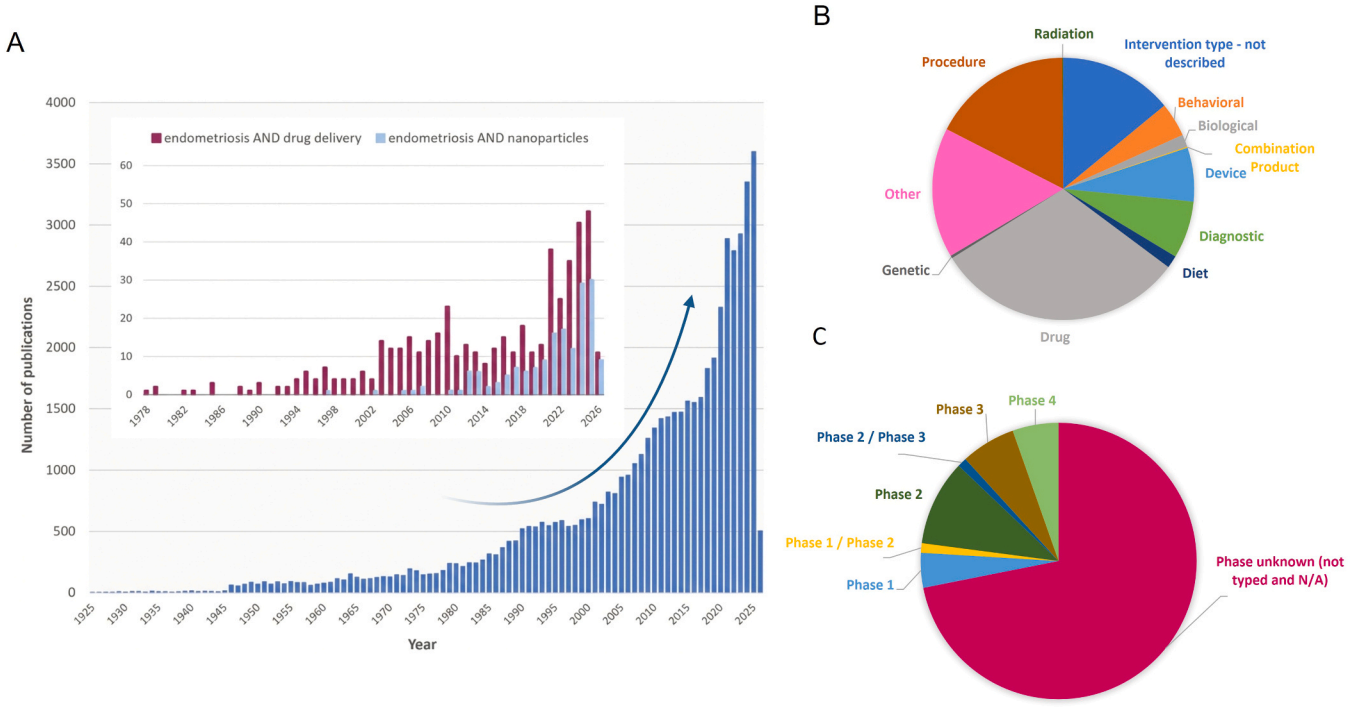

Fig. 2. Bibliometric trends and clinical trial characteristics in endometriosis research. (A) Annual progression of endometriosis-related publications retrieved from the Scopus database, with an inset highlighting the specific evolution of research focused on drug delivery systems and nanoparticle-based therapies. (B) Distribution of intervention types among 914 clinical trials identified via ClinicalTrials.gov. (C) Classification of clinical trials by phase status, highlighting that 712 trials are marked as "completed" as of June 2026.

limited to the menstrual period but is experienced by patients practically constantly [17]. This is due to numerous endometriotic lesions and adhesions, which impair the function of the affected tissues. A constant feeling of pain combined with infertility is often a reason for patients' depression [31,32]. Infertility is also one of the most characteristic symptoms of this disease. It is estimated that the peak incidence of endometriosis falls in the age group of 25–45 years [33], and the correct diagnosis of this disease is made only after 8–10 years on average [34].

There are currently several groups of theories about the origin of endometriosis, the most common are: transplantation theory- metastases of endometrial tissues to an ectopic location; metaplastic theory- metaplastic development of endometrial tissue on the ectopic site, and Müllerian remnants theory - changes of the embryonic duct remnant epithelium into endometrial epithelium. The most common theory of endometriosis origin, described in 1927, is Sampson's implantation theory, in which retrograde menstruation is responsible for the formation of ectopic endometrial lesions [35–37]. The transplantation theory assumes that endometrial tissue is transferred from the uterus to another location in the body. There are many potential routes for endometrial cell transfer, including retrograde menstruation, iatrogenic, lymphogenic, and hematogenous dissemination, which is responsible for the rare, extraperitoneal lesions of endometriosis. Retrograde menstruation is the most frequently cited route of cell migration, scientifically confirmed, and is a widely accepted mechanism of endometriosis histogenesis. In this mechanism, some of the secretion flows retrogradely through the fallopian tubes into the peritoneal cavity. Retrograde menstruation is characterized by a high incidence in the female population. Studies conducted by Halme *et al.* confirm that up to 90% of women with patent fallopian tubes undergoing laparoscopy during the perimenstrual period have traces of menstrual blood in the peritoneal fluid [38]. In other metaplastic theories of endometriosis development, it is assumed that the peritoneal mesothelium and ovarian surface epithelium may undergo metaplasia into the endometrial epithelium and stroma, thereby inducing endometriosis [39]. The Müllerian Remnants Theory concerns the differentiation and migration of the Müllerian ducts, which develop from the coelomic epithelium and give rise to the fallopian tubes, uterus, and upper vagina. This theory posits that during fetal organogenesis, some primordial cells may spread into the posterior pelvic floor [40].

The development of the disease is influenced by many factors, widely described in the professional literature. The most important groups of factors influencing the development of the disease are: genetics (NFE2L3 and HOXA10) [41], hormonal balance (mainly estradiol) [42], oxidative stress [43], and inflammation (macrophage activity influences important differences in the cytokine/chemokine profile) [44]. Additionally, other factors such as angiogenesis [45–47], environmental factors (e.g., exposure to dioxane, bisphenol A, polychlorinated biphenyls, and phthalates) [48–50], or vaginal microbiota (*S. agalactiae, F. nucleatum*) [51,52] may promote endometriosis development.

3. Diagnostics and clinical treatment strategies of endometriosis

The initial diagnostic approach for endometriosis relies on a comprehensive medical interview and clinical assessment [53]. While pelvic and abdominal examination is fundamental, its sensitivity is limited; a normal physical examination, even during menstruation, does not exclude the presence of the disease. Consequently, advanced imaging modalities, including transvaginal ultrasound (TVUS) and magnetic resonance imaging (MRI), have become the cornerstone of non-invasive diagnostics [54]. These techniques facilitate the identification of specific disease phenotypes, such as superficial peritoneal implants, ovarian endometriomas, and deep infiltrating endometriosis, as well as the concurrent presence of adenomyosis. Given that imaging accuracy is highly operator-dependent, examinations should be performed by specialists with expertise in endometriosis protocols to maximize diagnostic yield [54].

Several inflammatory serum biomarkers are elevated in women with endometriosis compared with controls, including C-reactive protein (CRP), interleukin (IL)−6, IL-8, and TNF-alpha [55]. Research conducted in numerous centers is constantly trying to define reliable indicators of this disease. As it is known, endometriosis is an estrogen-dependent disease, which was confirmed in human and animal studies. Endometriosis is regulated through the ESRs alpha and beta (ESR1 and ESR2). This dysregulated receptor profile, characterized by an abnormally low ESR1:ESR2 ratio, fosters an estrogen-driven inflammatory milieu and contributes to progesterone resistance, thereby impairing normal cellular differentiation. These molecular aberrations, largely sustained by aberrant epigenetic programming such as differential DNA methylation, ultimately promote the survival, proliferation, and persistence of endometriotic cells in ectopic environments [56]. Challenging the prevailing paradigm of universal hyperestrogenism, Nie *et al.* demonstrated that estrogen signaling in ectopic endometrial lesions progressively diminishes in concordance with increasing lesional fibrosis, with deep endometriosis lesions exhibiting biosynthetic and receptor activity profiles comparable to those of eutopic control tissue [57]. Studies are also attempting to determine the relationship between VEGF (vascular endothelial growth factor) levels and the development of endometriosis. Current evidence suggests that VEGF promotes angiogenesis within endometriotic lesions. However, data comparing VEGF levels in women with endometriosis versus healthy women are inconsistent [45,58–60]. Other angiogenic factors associated with adhesion and maintenance of endometriosis lesions, including hypoxia factors (ie, HIF1A), MMPs (ie, MMP9), PECAM1, and microRNAs (miRNAs) [46].

Regarding histopathological diagnosis, the gold standard requires the concurrent presence of both endometrial glands and stroma in tissue samples collected from outside the uterine cavity. Moreover, also endometrial epithelium and hemosiderin-filled macrophages may be detected [61].

According to the 2022 ESHRE guidelines, laparoscopy is no longer the gold standard for diagnosing endometriosis [54]. According to the diagnostic scheme proposed by the International Deep Endometriosis Analysis (IDEA), the basis for diagnosing endometriosis is the result of an expert TV ultrasound examination performed by an experienced physician. Magnetic resonance imaging (MRI) serves as an established secondary diagnostic modality. However, its diagnostic accuracy remains limited in detecting superficial peritoneal endometriosis or atypical disease localizations [54]. Consequently, laparoscopy remains the clinical reference standard for definitive diagnosis. This surgical approach is indicated for patients with high clinical suspicion of endometriosis who present with negative or inconclusive imaging findings, allowing for direct visualization and histopathological confirmation. [54]. In this area, the medical community is making significant ongoing efforts to improve current endometriosis diagnostic protocols [62].

Currently, there are no universally reimbursed, non-invasive outpatient diagnostic tests for endometriosis with high sensitivity and specificity. Consequently, clinical research is increasingly focused on developing specific diagnostic tools to bridge the gap between patient symptoms and surgical confirmation. Recent advancements include the introduction of commercially available tests, such as EndoRNA (Poland), HerResolve (USA) Ziwig Endotest® (EU). The EndoRNA test measures the expression of fucosyltransferase 4 (FUT4). Higher FUT4 expression is characteristic of endometrial cells in patients with endometriosis. The Medical Research Agency (Poland) is currently conducting a clinical trial to assess the specificity and sensitivity of the EndoRNA test and demonstrate its clinical utility [63,64]. The Ziwig Endotest® is a test that analyzes microRNAs from saliva [65]. This test utilizes Next-Generation Sequencing of microRNAs with AI and has been validated for use in patients between 18 and 43 years old. The sensitivity of this test was validated in clinical trials and was calculated as $> 97\%$, and the specificity was 93% [66]. Although biomarkers hold potential for earlier diagnosis and longitudinal monitoring of disease progression,

current evidence is insufficient for their adoption as a gold standard [54,63]. Despite promising results from validation studies, these tests are not yet widely recommended by international scientific societies for routine clinical practice and do not replace US/MRI imaging as a first-line diagnostic approach.

In milder cases of endometriosis, treatment only involves reducing pain, monitoring the possible progression of the disease, and protecting the patient's fertility. A holistic approach to endometriosis treatment is particularly important to improve treatment outcomes and reduce symptoms [54]. For example, patients are encouraged to maintain a special diet that eliminates pro-inflammatory ingredients [54].

Surgical management of DIE requires extensive expertise [54]. The modern surgical paradigm prioritizes the radical resection of endometriotic lesions while striving to preserve the anatomical structures (nerve-sparing surgery). Contrary to outdated approaches, hysterectomy or oophorectomy is not considered a routine treatment for DIE and is reserved for specific, complex clinical scenarios. Given the high variability and anatomical complexity of DIE, the objective remains the complete eradication of all visible lesions to maximize symptom relief and improve long-term patient outcomes [54].

4. Commercially available pharmaceuticals for endometriosis treatment

Contemporary pharmacological strategies for endometriosis are primarily directed toward symptom management and the suppression of disease progression, rather than the regression of established endometriotic lesions. For this purpose, well-known hormonal contraception medical devices and pharmaceuticals containing estrogens and progestogens have been used for many years, e.g., intravaginal rings, pills, transdermal patches, intrauterine systems, long-acting implants, and injectable products [67] (Table 1). So far, most new studies concerning drug delivery in endometriosis have focused on the use of combined oral contraceptives. This approach is justified due to the disease characteristics, e.g., the formation of numerous endometrial foci, often throughout the body [67]. In this paragraph, commercially available products will be discussed briefly, with an indication of their main advantages and disadvantages in the treatment of endometriosis. The therapeutic effects in the case of endometriosis, especially in the case of OMA and DIE, are not satisfactory. In connection with the need to improve the effectiveness and convenience of the endometriosis treatment, various drug delivery systems have been developed recently and are described later in the article [68] (Table 2).

4.1. Progestins and Estroprogestins

In endometriosis treatment, the progestins and estroprogestins are the first-line therapy (e.g., Progering®) [69,70]. These synthetic compounds mimic the action of progesterone or estrogen. The progestins inhibit the secretion of the gonadotropin-releasing hormone (GnRH) and other gonadotropins, in consequence suppressing the ovarian function, which generates a hypoestrogenic state, allowing the control of the symptoms and regression of endometriotic implants. The various routes of administration (ROA) of synthetic progesterone are in use; the most common is oral, but intranasal or dermal have also been proposed [71]. However, this approach for endometriosis treatment is not fully effective. As it was demonstrated, no improvement after hormonal-based therapy was noted in one-third of patients with endometriosis [72,73]. This problem was first noticed in the 1980s by Vierikko *et al.* [74], leading to the hypothesis of endometriosis resistance to progesterone, which was later proved by Attia *et al.* [75]. As it was analysed, it is caused by a significant reduction in progesterone receptors, particularly the active PR-B isoform [76]. In consequence, progesterone functions, transitioning the endometrial cells from the proliferative to the secretory stage, are inhibited and contribute to the development of endometriosis. Progesterone resistance regulated by cell signalling has been studied so far in the context of the Hippo signalling pathway, microRNA and ERK pathway, PI3K/AKT pathway, the Notch pathway, and others [76]. For these reasons, there was a need to search for substances that better match the specificity of this disease and provide better therapeutic effects, e.g., selective progesterone modulators described later or aromatase inhibitors, described later.

Estroprogestins are a combination of estrogens and progestogens. They act by inhibiting ovulation and stabilizing hormone levels, which leads to a reduction in the production of estrogens, the main factor stimulating the growth and maintenance of endometrial lesions. Consequently, this reduces pain symptoms, such as chronic pelvic pain. The most commonly used preparations are combined oral contraceptives containing ethinylestradiol in combination with various progestogens [77].

4.2. Gonadotropin-Releasing Hormone (GnRH) Agonists

An alternative to the above substances is GnRH agonists, which are a second-line treatment [78]. However, their evaluation parameters have been inconsistent. GnRH agonists represent a reasonable choice for second-line treatment. The effect of these agents on fertility has been previously discussed [79]. In addition to the benefits, there are side effects such as hot flashes, sweating, and loss of bone minerals, especially with long-term use [80]. An example of GnRH agonists is dienogest, leuprorelin (Eligard®) suppress ovarian function and block the release of gonadotropins [81]. As a result, the body enters a hypoestrogenic state, which reduces pain and endometrial inflammation. Lately, a case report from 2025 showed that leuprorelin can be an effective treatment for reducing endometriosis symptoms [82]. In the case of dienogest, the results published in 2022 revealed that a 2 mg dose of dienogest administered per 24 months did not improve the EAPP in 16.3% of the patients, and 5.1% reported deterioration [83].

4.3. Aromatase Inhibitors

Aromatase inhibitors are drugs that inhibit the enzyme responsible for converting androgens into estrogens. Because estrogens promote the growth and maintenance of endometriosis lesions, reducing their synthesis leads to a reduction in the activity and size of endometrial lesions. Drugs such as letrozole and anastrozole are particularly effective in patients with endometriosis refractory to standard treatment, especially when used in combination with progestogens or GnRH analogues, thereby simultaneously reducing the symptoms associated with estrogen deficiency [84]. A clinical trial from 2021 shows that aromatase inhibitor (Anastrozole) used with Mirena® (intrauterine device levonorgestrel-releasing system) can reduce the pain and delay endometriosis relapses [85]. However, there are no significant changes compared to using the Mirena® system alone. This issue requires further detailed research.

4.4. Selective Progesterone (SPRMs) and Estrogen Modulators (SERMs)

SPRMs are medications that work by inhibiting endometrial proliferation to minimize endometrial lesions. They work by partially blocking or activating progestin receptors and have minimal side effects similar to GnRH agonist therapy. The most well-known examples of these medications are ulipristal acetate [86] and mifepristone (RU486) [87], but also asoprisnil, telapristone acetate, and vilaprisan [88]. The former acts through partial agonist-antagonist modulation of progesterone receptors, while the latter exhibits a strong antagonistic effect on the progesterone receptor and, at higher doses, also on the glucocorticoid receptor. Both medications alleviate pain but also inhibit ovulation, may occur as an intrauterine implant [89,90].

Selective estrogen modulators (SERMs) exhibit tissue-selective estrogenic or antiestrogenic effects and are considered potential therapies for endometriosis. Their mechanism involves inhibiting the effects of

estrogen on endometrial lesions while maintaining their beneficial effects in other tissues [91]. Raloxifene has been evaluated in clinical trials, but has not demonstrated efficacy in reducing endometriosis pain. Recent studies indicate that fluorination may reduce its toxicity [92]. TAS−108 (bazedoxifene) is a newer SERM with potent antiestrogenic effects in the endometrium, which remains in experimental development [93]. Currently, SERMs are not standard treatment for endometriosis and require further clinical evaluation.

4.5. Danazol

Danazol is a synthetic androgen that inhibits the secretion of luteinizing hormone (LH), acting as a gonadotropin inhibitor. It is used in the treatment of endometriosis and for the symptomatic relief of severe pain and tenderness associated with benign cystic mastopathy [94]. A study demonstrated that the use of danazol co-crystals with malonic acid significantly increased the drug's solubility, potentially improving its therapeutic efficacy in endometriosis. The optimized tablet formulation (e.g., Danazol®/Danol®/Danocrine®) demonstrated rapid disintegration and a high degree of active ingredient release, exceeding commercially available formulations, confirming the potential of cocrystallization to improve danazol bioavailability. These results indicate that cocrystallization and formulation optimization may be an effective strategy for improving the bioavailability of danazol in the treatment of endometriosis [95].

4.6. Recent Innovations In Therapeutics For Endometriosis Treatment

Recent innovations in the treatment of endometriosis have focused on developing therapies that are both effective and better tolerated by patients. An interesting path of research may be the use of statins, specifically simvastatin. Simvastatin, a 3-hydroxy−3-methylglutaryl coenzyme A (HMG-CoA) reductase inhibitor, has been widely used in cardiovascular diseases and can lower LDL cholesterol levels. It may also have applications in cancer therapy, including ovaries, colon, leukemia, prostate, breast, endometrium, and lately the endometriosis treatment [96–99]. *In vitro* studies have shown that simvastatin inhibits the proliferation of endometrial cancer cells (HEC−1A and RL95–2) and mesenchymal stem cells associated with endometrial cancer (EmCaMSC) [97]. In subsequent pilot studies, liposomal nanoparticles with simvastatin were tested on xenografted tissues from patients in an *in vivo* mouse model and showed a reduction in inflammatory foci; however, more detailed studies are necessary [100]. Scientists also assessed the effect of simvastatin on the Wnt/β-catenin pathway, the disruption of which leads to benign tumors of the female reproductive system. Simvastatin has been shown to have a beneficial effect on uterine leiomyomas by inhibiting Wnt/β-catenin [101].

Also, oxidative stress plays an important role in the pathogenesis of endometriosis, which is why, in recent years, numerous studies have been conducted on drugs with antioxidant and antiangiogenic effects, which may limit its impact on the development of the disease. Firstly, matrix metalloproteinases (MMPs) and their natural inhibitors (TIMPs), which participate in tissue remodeling and influence the invasiveness of endometrial lesions, have been shown to inhibit the activity of MMPs or increase the expression of TIMPs. These inhibitors can inhibit matrix degradation processes and thus hinder the development of endometrial lesions [102–104]. Concurrently, research is underway on immunomodulators aimed at restoring the proper balance in the immune system of patients with endometriosis. Examples of such compounds include muramyl dipeptide and N-acetylglucosaminyl-N-acetylmuramyl-L-alanyl-D-isoglutamine, which may influence macrophage activity and modulate the inflammatory response in ectopic endometrial tissue [105]. Immune checkpoint inhibitors, such as anti-CTLA−4 antibodies, are also being investigated in the context of immune therapies. They may influence T-cell activation and modulate the immune response in the endometrial environment [106]. Another promising research direction is the use of interfering RNA (siRNA), which enables the selective silencing of genes involved in inflammation, angiogenesis, and endometrial cell proliferation. SiRNA therapy allows for targeted interventions on specific molecular pathways, minimizing the risk of side effects typical of traditional hormonal therapies [107].

Verteporfin is being investigated experimentally as a potential therapy for endometriosis due to its ability to inhibit the YAP/TAZ pathway, which plays a crucial role in the proliferation and survival of endometrial cells. This drug exhibits antiproliferative and proapoptotic effects in endometriosis cells, independent of the classic estrogen pathway. YAP/TAZ has been shown to play a significant role in progestogen resistance by regulating the PI3K-Akt pathway in ECs, which may represent a new avenue for clinical development of targeted therapy for progestogen resistance. Additionally, verteporfin, as a YAP/TAZ inhibitor, can enhance the sensitivity of Ishikawa PR cells to progestogens both in vivo and in vitro [108]. Currently, verteporfin is not used clinically in endometriosis and remains an investigational drug.

5. Nanotechnology and novel drug delivery techniques for endometriosis treatment under pre-clinical studies

Achieving effective endometriosis remission via conventional therapeutic modalities remains a significant clinical challenge, largely attributable to the limited penetration of drugs into deep, fibrotic lesions and the lack of specificity inherent in systemic hormonal protocols [54, 146]. Addressing these obstacles, modern biomaterials engineering is pivoting toward systems with precisely designed functionalities. To date, studies have primarily focused on utilizing nanoparticles as a drug carrier in targeted therapy for endometriosis [144,145]. In this chapter, the advanced therapeutic platform will be discussed, which can be categorized into two primary functional classes. The first focuses on optimizing the physicochemical properties of carriers to circumvent biological barriers—specifically the rigid, pro-fibrotic extracellular matrix (ECM)—thereby facilitating efficient drug diffusion into the lesion core (Chapter 5.1) [146]. The second category encompasses intelligent nanostructures engineered for multifunctional synergy, integrating ablation techniques (e.g., photothermal therapy), the induction of controlled cell death (including ferroptosis), and precise modulation of the immune microenvironment within a single carrier (Chapters 5.2 and 6). This approach transcends classical pharmacokinetics, enabling a radical enhancement in therapeutic precision while simultaneously minimizing systemic toxicity and collateral damage to healthy surrounding tissues [147,148].

5.1. Nanoparticles

5.1.1. Lipid nanoparticles (LNPs)

Lipid nanoparticles (LNPs)—including liposomes, solid lipid nanoparticles (SLNs), and nanostructured lipid carriers (NLCs)—represent a versatile drug delivery platform for endometriosis [149]. These systems, composed of biocompatible lipids (e.g., phospholipids, glycerides), facilitate the encapsulation and controlled release of therapeutic agents, addressing bioavailability limitations [150–154] (Fig. 3). NLCs, characterized by a hybrid solid-liquid lipid matrix, offer superior transport capacity and drug loading stability compared to traditional systems [155]. These properties are critical for targeted endometriosis treatment. For instance, RGD-modified NLCs facilitate the delivery of sildenafil citrate to endometrial cells by binding to surface integrins, thereby modulating VEGF and LIF levels to improve endometrial receptivity [156].

What is more, *in vitro* implantation assay indicated that these NPs enhance the rate of endometrial attachment potential, demonstrating that NLC-RGD serves as an effective drug delivery system for sildenafil citrate to endometrial cells, thereby improving endometrial receptivity [156]. Similarly, encapsulating tamoxifen in SLNs has been shown to reduce oxidative stress and downregulate estrogen receptor- alfa and

Table 1
List of commercially available products (as well as products in clinical trials) used in the treatment of endometriosis.

ACTIVE SUBSTANCE	PRODUCT TRADE NAME	MAIN INDICATION	INDICATION IN ENDOMETRIOSIS	EFFECT	MARKET AVAILABILITY	REF.
VAGINAL RINGS						
Combination of steroids: etonogestrel and ethinylestradiol	NuvaRing®	Contraception	Symptoms limitation	The released hormones block the ovaries, preventing the release of an egg cell	Available	[109–111]
Progesterone	Fertiring®	Contraception	Symptoms limitation	Prevent the growth of ectopic endometrial tissue, thereby reducing pain and inflammation.	Available	[111]
	Progering®	Contraception	Symptoms limitation		Available	
Etonogestrel	Ornibel® MyRing™ SyreniRing® EluRyng™ Perlinring	Contraception	Symptoms limitation	Releases hormones directly into the bloodstream, avoiding the liver's first-pass effect	Available	[110,112, 113]
17β-estradiol	Estring®	Menopause treatment	Symptoms limitation	Estradiol ultimately replenishes estrogen deficiency after menopause. When used in the treatment of endometriosis, it alleviates symptoms such as vaginal dryness and irritation, improves the condition of the epithelium and mucosa, and supports normal urinary and reproductive system function.	Available	[114,115]
Segesterone acetate and ethinyl estradiol	Annovera™	Contraception	Symptoms limitation	The hormones contained in the disc prevent the release of the egg from the ovary	Rarely available	[116]
NON-COMMERCIAL VAGINAL RINGS						
Levonorgestrel	-	Contraception	Symptoms limitation	-	Clinical trials	[117]
Nestorone	-	Contraception	Symptoms limitation	-		[118]
Nestorone and ethinylestradiol	-	Contraception	Symptoms limitation	-	Clinical trials	[119]
TRANSDERMAL PATCHES						
Ethinyl estradiol	Ortho Evra®	Contraception	Symptoms limitation	Regulating menstruation, reducing the amount of bleeding and pain in endometriosis	Available	[120]
Estradiol + Norethisterone	CombiPatch®	Reduces menopausal symptoms	Symptoms limitation	Suppresses ovulation, reduces the proliferation of endometrial foci, and controls bleeding	Available	[121]
Estradiol	Estradot®	Reduces menopausal symptoms	Symptoms limitation	Stabilize hormone levels and can be used as part of combination therapy (with progestogen) to reduce symptoms and prevent recurrence of endometriosis	Available	[122]
Estradiol	FemSeven®	Reduces menopausal symptoms	Symptoms limitation	Reduce symptoms of endometriosis	Available	[123]
Estradiol	Evorel®	Reduces menopausal symptoms	Symptoms limitation	Reduce symptoms of endometriosis	Available	[124]
INTRAUTERINE SYSTEMS						
Levonorgestrel	Mirena®	Contraception	Symptoms limitation	Reducing the growth of the endometrium, which relieves menstrual pain, inflammation, and excessive bleeding	Available	[125]
Levonorgestrel	Kyleena®	Contraception	Symptoms limitation	It releases progestogen locally, inhibiting endometrial proliferation and reducing symptoms associated with endometriosis, such as bleeding and pain, with less systemic action.	Available	[126]
Levonorgestrel	Levosert®	Contraception	Symptoms limitation	Reduction of bleeding	Available	[127]
LONG-ACTING IMPLANTS						
Progestin etonogestrel	Implanon®	Contraception	Symptoms limitation	Effective in treating pain associated with menstrual bleeding in endometriosis sufferers.	Available	[128]

(*continued on next page*)

Table 1 (*continued*)

ACTIVE SUBSTANCE	PRODUCT TRADE NAME	MAIN INDICATION	INDICATION IN ENDOMETRIOSIS	EFFECT	MARKET AVAILABILITY	REF.
Levonorgestrel	Jadelle®	Contraception	Symptoms limitation	Inhibition of ovulation and prevention of endometrial changes may alleviate symptoms (pain, bleeding).	Available	[129]
Levonorgestrel	Sino-implant® / Levoplant®	Contraception	Symptoms limitation	May reduce the proliferation of the mucosa, inhibit ovulation, which translates into symptoms associated with endometriosis foci	Available	[130]
Levonorgestrel	LNG-IUSs	Contraceptive	Symptoms limitation	reduced pain and menstrual blood loss	Available	[131]
INJECTABLE PRODUCTS						
Medroxyprogesterone acetate	Depo-Provera®	Contraception	Symptoms limitation	Treatment for pelvic pain caused by endometriosis	Available	[132]
Medroxyprogesterone acetate	Lupron Depot®	Prostate cancer treatment	Symptoms limitation	Reducing endometrial inflammation	Available	[133]
Goserelin	Zoladex®	Prostate cancer treatment	Symptoms limitation	An anticancer drug that works by reducing the concentration of sex hormones; pain control	Available	[134]
Leuprorelin	Eligard®	Anti-cancer treatment	Symptoms limitation	Painkiller	Available	[135]
Norethisterone enanthate	Noristerat®	Contraception	Symptoms limitation	Inhibiting the progression of endometrial lesions, used in women who do not tolerate estrogens or prefer the injectable form.	Available	[136]
ORAL ADMINISTRATION						
Mifepristone	Mifepristone®	Misoprostol is used to prevent stomach and/or duodenal ulcers in people taking non-steroidal anti-inflammatory drugs.	Symptoms limitation	A synthetic drug used in medicine to terminate early pregnancy; a progesterone and glucocorticoid receptor antagonist	Available	[87]
Ulipristal acetate	EllaOne®	Contraception	Symptoms limitation	A selective progesterone receptor modulator that inhibits endometrial cell growth and reduces tumor size.	Available	[137]
Danazol	Danazol® / Danol® / Danocrine®	Pelvic pain	Symptoms limitation	Gonadotropin inhibitor leads to inactivation and atrophy of normal and ectopic endometrium, causing regression of lesions in most cases	Available	[95]
Dienogest	Visanne®	Endometriosis treatment	Symptoms limitation	Inhibits endometrial proliferation, causes atrophy of endometrial lesions, and reduces pain and bleeding. It works without estrogen, so it doesn't cause hormonal fluctuations.	Available	[138]
Dienogest	Visabelle®/ Dienogest/Teva /Dienorette	Endometriosis treatment	Symptoms limitation	Inhibit ovulation, reduce endometriosis foci, and relieve pain.	Withdrawn/ available/ Withdrawn/ Withdrawn	[139]
Desogestrel / Drospirenone / other progestogens	Visanova®, Nacrez®, Azalia®, Slinda®	Contraception	Symptoms limitation	Inhibit ovulation and cause endometrial atrophy.	Available	[140]
Ethinylestradiol + drospirenone/ dienogest/estradiol valerate	Yasmin®, Yasminelle®, Jeanine®, Qlaira®	Contraception	Symptoms limitation	Stop the menstrual cycle and reduce the symptoms of endometriosis (pain, bleeding).	Available	[141]
Elagolix / Relugolix / Linzagolix	Orilissa® (USA) / Relugolix®, Linzagolix	Endometriosis treatment	Symptoms limitation	They reduce estrogen production without the need for injections. They significantly reduce menstrual and chronic pain.	Available	[80]
Medroxyprogesterone acetate (MPA)	Provera®	Endometriosis treatment	Symptoms limitation	Inhibits ovulation and endometrial proliferation and reduces pain.	Available	[142]
PHARMACEUTICALS IN CLINICAL TRIALS						
Ulipristal acetate	-	Endometriosis treatment/oral administration	Symptoms limitation	Reduction of symptoms in women suffering from chronic	Clinical trials	[143]

(*continued on next page*)

Table 1 (*continued*)

ACTIVE SUBSTANCE	PRODUCT TRADE NAME	MAIN INDICATION	INDICATION IN ENDOMETRIOSIS	EFFECT	MARKET AVAILABILITY	REF.
				pelvic pain associated with endometriosis.		
Goserline Acetate / Dienogest	-	Endometriosis treatment/injection	Symptoms limitation	Reduction of pain and symptoms of endometriosis.	Clinical trials	[144]
Ulipristal acetate	-	Endometriosis treatment/oral administration	Symptoms limitation	Pain and bleeding control for women with adenomyosis.	Clinical trials	[145]

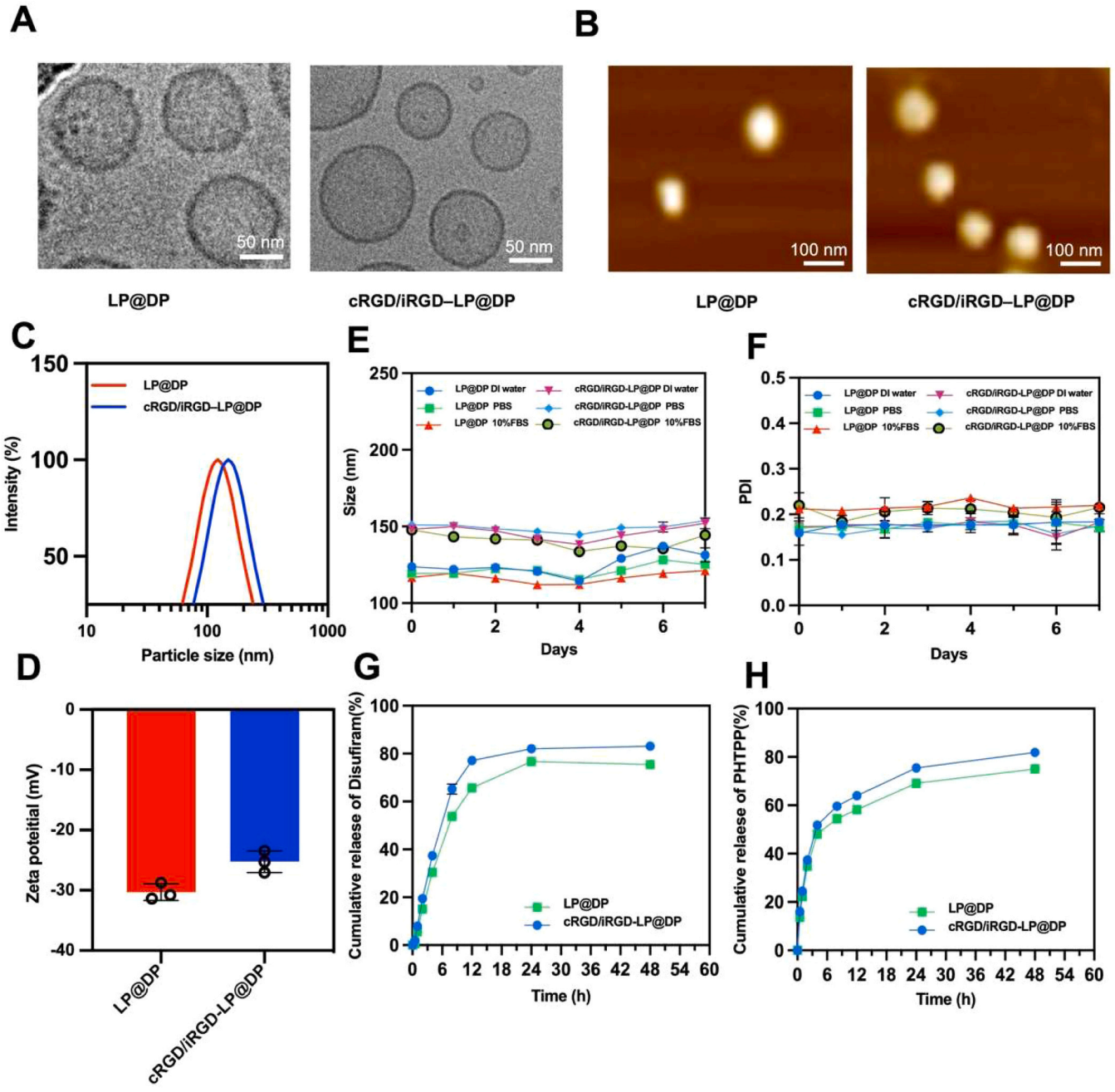

Fig. 3. Characterization of developed liposomal nanosystem modified with cRGD/iRGD peptide sequence obtained by thin layer method. Various methods of characterization (**A**) Cryo-TEM, (**B**) AFM, (**C**) hydrodynamic particle sizes (**D**) ζ potentials, (**E**,**F**) Stabilities of developed system in deionized water, PBS, and 10% FBS and (**G**,**H**) in vitro releases of drugs (disulfiram and PHTPP) show that physicochemically it can specifically and safely deliver drugs to endometriotic lesions. Reprinted from Ref. [147]. Copyright 2025. Elsevier.

VEGF-A gene expression *in vivo* [157]. Furthermore, pilot studies indicate that liposomal delivery of simvastatin to adenomyotic lesions

significantly reduces lesion size and proliferative markers such as Ki67 [100]. The results of Michel *et al.* show that adenomyotic xenografts grew at similar rates until day 14, when the xenografts from the simvastatin-NP group began shrinking compared to the two other groups. At the final measurement on day 28, the simvastatin-NP group had shrunk to a statistically significantly smaller volume compared to the control group and compared to the simvastatin group [100]. Given the shared inflammatory and genetic pathways between endometriosis and cancer (e.g., HOXA10 dysregulation) [16,158–161], oncological delivery strategies are being adapted for this condition. Specifically, lipid nanoparticles (LDE) exploit the upregulated low-density lipoprotein (LDL) receptors found in endometriotic foci [158–160]. Because LDL receptors are upregulated in cancer cell tissues. Badin *et al.* verified this idea for application in endometriosis treatment [149]. Results indicated that endometriotic foci showed significant LDE uptake, with increased LDL consumption by these cells, similar to cells in cancers and inflammatory diseases. Afterward, in 2023, a pilot clinical study on LDE-methotrexate (MTX) demonstrated symptomatic relief in pelvic pain and dysmenorrhea without significant adverse events, confirming the potential of this approach [162].

Although LNPs are currently widely used in medicine, due to their ability to protect the payload from degradation, improve solubility, and enable targeted delivery to specific sites, in endometriosis treatment is just beginning to be studied. The application of LNPs in endometriosis therapy represents a significant shift toward precision medicine, leveraging biomimetic properties to overcome the limitations of traditional hormonal and surgical interventions [163,164]. A critical advantage of LNPs and related lipid-based structures, such as micelles, is their ability to address the dense fibrotic interstitium characteristic of deep infiltrating endometriosis [100,156,157]. While bulkier biomaterial platforms like hydrogels often fail to penetrate deep into diseased tissues or cross cellular membranes, the small size and fluid lipid bilayer of LNPs facilitate membrane fusion and efficient cellular internalization. This enhanced tissue permeability is essential for delivering therapeutic payloads through the fibrotic barriers and adhesions that frequently distort the neighbourhood of endometriosis lesions. Furthermore, nanostructured lipid carriers (NLCs) offer a more stable iteration of these platforms, providing high encapsulation efficiency and sustained drug release profiles that can alleviate neuropathic and inflammatory pain over extended periods [100,157,165,166].

Despite these opportunities, significant limitations hinder the broad clinical adoption of LNP-based therapies. Compared to polymeric or metallic nanoparticles, lipid-based systems exhibit lower thermodynamic and physical stability [167]. They are highly susceptible to oxidation, hydrolysis, and premature drug leakage when exposed to lipases and surfactant proteins in biological fluids. Additionally, there are substantial concerns regarding the potential for LNPs to accumulate in the liver and other healthy organs, with the long-term consequences for a patient's overall health and future reproductive potential remaining largely unknown. In the case of endometriosis, local administration can also be used, which may be a solution to the above-mentioned problems related to the specificity of these materials. While RNA-LNP formulations show immense promise for gene editing and silencing overactive pathways in endometriosis, most research remains at the preclinical stage, and the gap between successful rodent models and confirmed clinical safety in humans is substantial [168]. Future development must therefore focus on enhancing the physical robustness of these carriers and ensuring targeted precision to minimize off-target toxicity before they can be considered a reliable clinical standard.

5.1.2. Synthetic polymer nanoparticles

Polymeric nanoparticles (NPs), comprising synthetic, natural, or copolymeric matrices, represent a versatile platform for the targeted management of endometriosis [169]. One such NPs is dendrimers – monodisperse, spherical, highly branched polymers. Wang *et al.* used PAMAM dendrimers as a gene vector [170]. Results showed that PAMAM provided greater DNA protection than the naked plasmid or Lipofectamine-protected plasmid, as the DNA level reduced marginally under PAMAM protection. Moreover, the use of PAMAM dendrimers inhibited the growth of the endometriotic lesion *in vivo* at days 15, 20, 25, and 30, as identified by noninvasive monitoring following the administration of a single dose of endostatin from different medications into the endometrial lesion. Immunohistochemistry results proved that endostatin-loaded PAMAM reduced the microvessel density through an antiangiogenic mechanism [170]. Beyond gene therapy, PLGA-based nanoparticles offer a robust framework for delivering anti-inflammatory and anti-angiogenic compounds. Recent evidence indicates that encapsulation of flavonoids, such as chrysin, into PLGA-NPs significantly improves their bioavailability and down-regulates pro-inflammatory cytokines, including IL-1β, IL-6, and Tnf-α, as well as Mmp9-mediated tissue remodeling [171]. Furthermore, innovative nanosystems, such as anti-CTLA−4-loaded PLGA-NPs, have been shown to modulate the immunological microenvironment in peritoneal fluid by regulating CD4 + CD25 + Treg cell populations, thereby inhibiting the proliferation and invasion of ectopic endometrial cells [172].

Gene therapy via miRNA and siRNA delivery represents an emerging frontier. MicroRNAs, which naturally regulate protein synthesis, have been successfully encapsulated into NPs to promote apoptosis in endometriotic cyst stromal cells (ECSCs). Moreover, several studies have reported aberrant miRNA expression in endometrial tissue cells from women affected by this disease [49,173]. Chaichian *et al.* encapsulated miR−503, as it is involved in the apoptosis of endometriotic cyst stromal cells (ECSCs) by inhibiting the cell cycle and thus preventing their proliferation [174]. This study demonstrates that nanoparticle-mediated drug delivery significantly reduces the viability of ectopic endometrial cells, driven by efficient intracellular accumulation in the nucleus and cytoplasm. Furthermore, *in vivo* assessment in murine models confirmed a significant regression of endometriotic lesions following a 3-week treatment protocol [174]. Furst *et al.* developed PEGylated DSPE-PEG2000 lipoplexes, incorporated into lyophilized hydroxyethyl cellulose (HEC) hydrogels, to facilitate vaginal siRNA delivery. These lipoplexes (approx. 200 nm) exhibited > 95% complexation efficiency, high stability in simulated vaginal fluid (SVF), and optimal diffusion characteristics without aggregation. The system maintained structural integrity post-lyophilization, suggesting that these engineered hydrogel-based vectors are a robust platform for siRNA-mediated endometriosis therapy [175].

In the treatment of endometriosis, achieving high therapeutic efficacy while minimizing systemic side effects necessitates the use of targeted drug delivery systems. Thus, modifying nanoparticles' surfaces yields the desired results, as the mechanism of cell uptake shifts from endocytosis to active targeting via membrane receptors [151] (Figs. 4 and 5). Experiment results showed that liposome application can improve the therapeutic effect of artesunate, a drug primarily used in malaria treatment, but which may find application in the treatment of endometriosis, as it exhibits anti-angiogenic properties. Moreover, the therapeutic efficacy of the drug delivery system *in vivo* showed a noticeable decrease in lesion volume, as developed liposomes were able to target these lesions [151] (Figs. 4 and 5).

Protein-based nanocarriers, particularly those utilizing albumin, offer a robust strategy for receptor-mediated drug delivery in endometriosis. Zhang *et al.* engineered a bovine serum albumin (BSA)-based system, loaded with mifepristone (BSA@Mif), designed to bind specifically to the SPARC receptor overexpressed on M2-like macrophages within ectopic lesions, which are highly abundant in ectopic endometrial tissue [176]. *In vitro* studies revealed that BSA@Mif conjugates not only improved cellular uptake but also promoted immunogenic cell death and the polarization of macrophages from an M2-like to an anti-inflammatory M1 phenotype. Concurrently, these nanoparticles effectively suppressed the proliferation of ectopic endometrial cells. *In vivo* findings validate this immunomodulatory strategy, demonstrating a

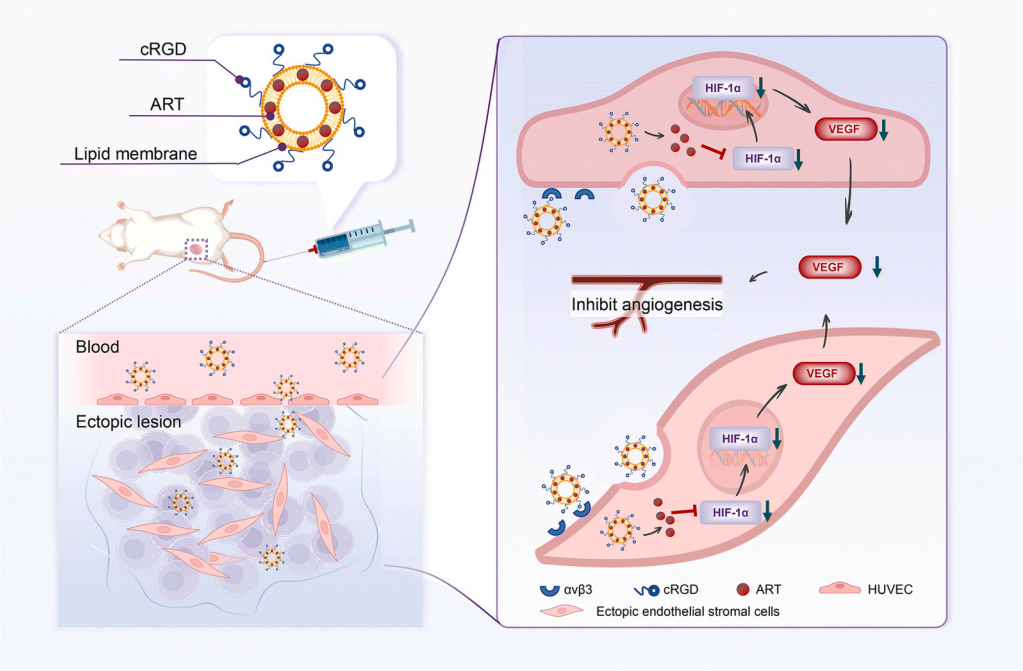

Fig. 4. Schematic illustration of targeted delivery of artesunate by the nanodrug cRGD-LP-ART to inhibit angiogenesis in endometriosis. Shortly, the nanosystem, after injection into the body, reaches the blood vessels around ectopic lesions, where it penetrates cells thanks to cRGD modification and releases the drug – artesunate. This drug suppresses HIF−1α and VEGF expression, leading to inhibited angiogenesis. Reprinted with permission from Ref. [148]. Copyright 2025. Royal Society of Chemistry.

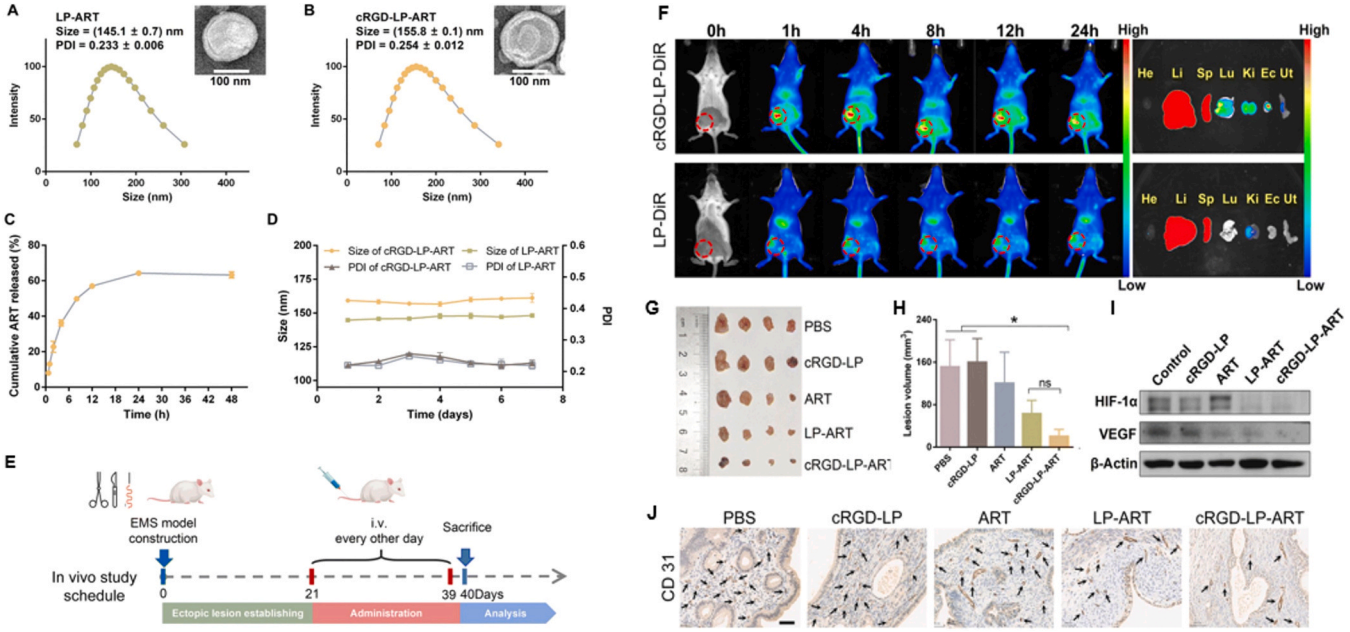

Fig. 5. TEM images and particle size of (**A**) liposome nanosystem loaded with artesunate (**B**) liposome nanosystem loaded with artesunate modified with cRGD. (**C**) In vitro release of the drug from cRGD-LP-ART in PBS (pH 7.4). (**D**) Stability changes in the particle sizes and PDI of LP-ART and cRGD-LP-ART within 7 days. (**E**) Schematic representation of the course of the experiment on the animal model (**F**) (left) In vivo real-time image of the distribution of two kinds of developed lipid nanoparticle based drug delivery system (the red circle indicates the location of the ectopic lesion) as well as ex vivo imaging of ectopic lesions, eutopic uteri and major organs harvested from endometriosis mice 24 h after administration of cRGD-LP-ART or LP-ART (right). (**G**) Photograph of ectopic lesions excised from endometriosis mice after applying different treatments. (**H**) Quantitative statistical analysis of the volume of ectopic lesions after different treatments. ns, no significance, and *$p < 0.05$. (**I**) The protein expression of HIF−1α and VEGF in ectopic lesions after receiving different treatments. (**J**) The typical images of CD31 immunohistochemical staining of ectopic lesions. Arrows indicate positive cells for CD31 (scale bar = 50 μm). Reprinted with permission from Ref. [148]. Copyright 2025. Royal Society of Chemistry.

reduced lesion burden and an effectively modulated immune microenvironment in murine models of endometriosis [176].

Synthetic polymer nanoparticles offer significant opportunities for precision medicine due to their customizable architectures and

tailorable degradation rates, which allow for the sustained and controlled release of therapeutic agents—such as hormonal drugs, antioxidants, or gene-silencing siRNA—over periods ranging from weeks to months [148,149,171,172,176,177]. By maintaining high local drug concentrations, these nanoparticles can effectively modulate the lesion microenvironment and reduce the need for frequent dosing, thereby minimizing the systemic side effects typically associated with conventional oral hormonal treatments [171,174]. Furthermore, their surfaces are highly amenable to functionalization with ligands like hyaluronic acid (HA) or RGD peptides, enabling targeted delivery to specific receptors (e.g., CD44 or integrins) that are overexpressed in endometriotic lesions [172].

However, the efficacy of synthetic polymeric nanoparticles is critically hindered by the dense fibrotic interstitium and pelvic adhesions characteristic of the disease [146,147,178,179]. These fibrotic barriers, resulting from chronic inflammation, create a mechanical blockade that severely restricts the passive diffusion and penetration of therapeutic molecules into the core of deep endometriotic implants [146]. While larger polymeric platforms and traditional nanoparticles often lack the inherent ability to deeply penetrate these thick tissues or cross cellular membranes, smaller structures like polymeric micelles are increasingly favored for their enhanced tissue permeability, which allows them to navigate the fibrotic barriers more effectively than bulkier carriers [146,147]. Consequently, the delivery of drugs through discrete polymeric nanoparticles remains largely limited to superficial peritoneal lesions unless they are specifically engineered for high tissue permeability [146].

Beyond tissue penetration, several significant limitations restrict the clinical translation of these structures. A primary concern is the generation of degradation products, such as glycolic and lactic acids, which can lower the local pH of the lesion microenvironment, potentially triggering further inflammation or accelerating the degradation of acid-sensitive therapeutic substances [146]. Finally, most current evidence is derived from rodent models, which are often incapable of predicting clinical efficacy or long-term safety in humans [180,181]. Future research must therefore focus on developing smart, stimuli-responsive polymers that can bypass fibrotic barriers while ensuring the biosafety of their degradation profiles before they can be established as a clinical standard [148,182]. This approach will be discussed later in the article.

5.1.3. Inorganic nanoparticles

5.1.3.1. Nanostructural cerium oxide. Literature shows many different approaches in this field covering a variety of inorganic nanostructures. One of them is nanoceria (nanostructural cerium oxide), working as the scavenging agent of free radicals that protects against oxidative stress in diseased tissues [178]. Rahman *et al.* propose a nanoceria-based composite in which nanoceria clusters grow on albumin substrate as a promising nanotherapeutic platform for endometriosis treatment. The effectiveness of albumin-nanoceria composite was investigated on tofacitinib-treated mice and compared to the bare tofacitinib effect. Importantly, despite anti-inflammatory activity and significant reduction of the lesions' growth, tofacitinib, as JAK/STAT pathway inhibitor, resulted in pregnancy loss due to its immunosuppressive activity. In the presence of nanoceria that modulates the local oxidative stress and inflammation, the adverse effect of tofacitinib was decreased, improving reproductive outcomes with maintained therapeutic effects [183].

Nevertheless, despite promising effectiveness in endometriosis treatment, nanoceria is also considered cytotoxic, which can lead to DNA damage [184]. Research by Courbiere *et al.* [185] and Ariu *et al.* [186] discuss the interactions between nanoceria and reproductive cells *in vitro*, particularly oocytes. Studies show that nanoparticles did not penetrate the oocyte cytoplasm but affected surrounding somatic cells and oocyte integrity. Higher concentrations of nanoceria were associated with increased DNA damage and disruption of cellular structures, while lower doses showed promising protective effects by reducing oxidative stress, cell apoptosis, preserving cytoskeletal organization, and improving blastocyst formation and cell viability. Ceria NPs can also cause genetic mutations, while their toxicity remains complex and requires a deeper understanding of the mechanisms behind the cellular uptake and studies after prolonged exposition [187]. Therefore, the role of the drug itself needs detailed studies covering long-term influence on the tissues.

5.1.3.2. Iron oxide nanoparticles (IONPs). In contrast to nanoceria, iron oxide offers high potential for biomedicine for its biocompatibility [188–190]. Iron oxide nanoparticles (IONPs) have become a powerful tool in disease treatment (i.e., cancer) due to their unique magnetic properties. Specifically, superparamagnetic iron oxide nanoparticles (SPIONs) can be manipulated using external magnetic fields, enabling targeted drug delivery and localized magnetic hyperthermia therapy. Iron oxide nanoparticles (IONPs) can effectively reduce the level of reactive oxygen species (ROS) by converting them into water molecules as potential cofactors for enzymatic antioxidants [191]. They can be easily modified onto the surface with various compounds, including drugs, enabling facile conjugation and incorporation into polymer matrices, broadening their functionalities [192].

IONs can also serve as efficient contrast agents as an alternative to classical gadolinium-based contrasts, enhancing resolution and maintaining high precision in recognition of diseased tissues. For the diagnosis of endometriosis, IONs were tested by, among others, Kalyani *et al.* [193]. Authors tested multi-walled carbon nanotubes and magnetite nanoparticles (MWCNT-Fe3O4) dispersed in chitosan (CS) with immobilized monoclonal antibodies for the selective electrochemical immuno-sensing of carbohydrate antigen 19–9 (CA19–9), a potential biomarker for endometriosis diagnostics. Moreover, biocompatibility and ability to respond to magnetic stimuli make IONs ideal candidates for controlled release systems and theranostic applications that combine diagnosis and therapy in a single platform [194–196]. Gao *et al.* proposed SPIONs as a cargo for miR−326 as a promising strategy for treating endometrial carcinoma, by targeting and silencing a major tumor-promoting signaling pathway [197]. *In vitro* and *in vivo* experiments prove that miR−326@SPIONs conjugate can significantly inhibit the growth of human endometrial carcinoma stem cells (HuECSCs), reducing the expression of members of the GPR91/STAT3/VEGF pathway, and concurrently limiting the phosphorylation of key molecules in this pathway in HuECSCs. Chen *et al.* demonstrated a SPIONs system for paclitaxel and irinotecan delivery to endometriotic cancer, proving the non-cytotoxicity of the bare matrix and enhanced reduction of cell viability for drugs modified SPIONs-containing PLGA with real-time monitoring of the controlled drug release [198]. The first article concerning magnetic hyperthermia for endometriosis treatment was published by Park *et al.* in 2022 [179]. The hexagonal SPIONs were modified with a peptide targeted to vascular endothelial growth factor receptor 2 (VEGFR−2) to promote its capture by endometriotic cells. Ultimately, the local hyperthermia caused by the external alternating magnetic field causes endometriotic cells' death. The authors developed a system targeted to endometriotic cells and intended for intravenous administration [179]. It is important to say that this concept is quite new, and it needs to be explored more extensively, especially its safety.

Lee *et al.* use ultrasmall superparamagnetic iron oxides (USPIO) as contrast agents in magnetic resonance imaging (MRI) [199], which are similar to nanostructural iron oxide agents that have been approved by the U.S. Food and Drug Admin-istration (FDA) for clinical diagnoses [200]. Authors demonstrated that USPIO administered intravenously into rats with induced endometriosis efficiently internalized into macrophages and other phagocytic cells after intravenous injection, enabling imaging of the ectopic uterine tissue (EUT) in autotransplanted rats. USPIO administration revealed inflammatory and degenerative changes with MRI. Similarly, hyaluronic acid (HA)-modified magnetic

iron oxide nanoparticles (HA-Fe_3O_4 NPs) were intravenously administered *via* tail vein into EUTs in the rodent model to detect the lesions [201]. The HA coating onto SPIONs prolonged the circulation in the bloodstream, increasing phagocytic activities by endothelial cells and leading to enhanced T_2-weighted MRI imaging. Given this, Jedryka *et al.* show the clinical studies on tracking early-stage endometrial cancer (EC) patients, where the SPIONs are used. As the EC spreads through the lymphatic system, the application of SPIONs enabled tracking of metastatic sentinel lymph nodes (SLNs) with high safety, no need to use other contrasting agents, and satisfactory accuracy parameters [202].

Iron oxide NPs can also be combined with other metal-based structures. Su *et al.* show that Fe3O4 encapsulated with guar gum, combined with Ag NPs, acts as an agent that reduces the viability of the AN3-CA endometrial cancer cell line without cytotoxicity to the normal cell line [203].

Due to the broad use of gadolinium-based compounds as T_1-weighted contrast agents for Magnetic Resonance Imaging (MRI), recent works show the Gd-based NPs for endometriosis diagnostics, like $NaGdF_4$@PEG@bevacizumab–Cy5.5 nanoparticles (NPBCNs) that offer targeted binding to endometrial cells, specifically through the vascular endothelial growth factor (VEGFR) [204]. Such a system proposed by Zhang *et al.* demonstrates accurate detection of endometriotic lesions in mice, not only by T_1-weighted imaging but also by fluorescence imaging, with no toxicity and adverse effects proven with histopathological examination [204].

As endometriosis is estrogen-dependent and its development is closely related to the elevated ROS level [205], recent studies also show novel solutions to inhibit the lesions' growth through the application of nanomaterials. Sun *et al.* proposed a manganese dioxide nanosheet decorated with macrophage membrane (MM-NS) that mimics the cell membrane as a novel type of nanozyme designed for the treatment of endometriosis [206]. The proposed system effectively scavenges ROS and alleviates the estrogen level, resulting in the inhibition of proliferation and inflammation of ectopic lesions in endometriosis mice.

5.1.3.3. Gold nanoparticles (AuNPs). Besides their cargo role, inorganic nanostructures also offer various functionalities, such as lesion visualization, enabling fast and effective diagnostics. Application of AuNPs also enables real-time photoacoustic imaging (PAI) through light absorption into sound waves. PAI is a non-invasive tool combining optical imaging that visualizes differences between different types of tissues, with ultrasound imaging that enhances fast and effective detection of diseased [207]. Imaging can be enhanced by coating AuNPs with fluorescent dyes for fluorescent imaging (FI). PAI offers high resolution and deep tissue penetration, while fluorescent dyes like fluorescein isothiocyanate (FITC) provide high sensitivity and molecular specificity [208]. The combination of these imaging techniques enables multimodal visualization, improving the diagnosis of endometriosis. Gold nanorods coated with silica (AuNR@silica) presented by Marquardt *et al.* were used for PAI, where the silica shell enhanced the FITC binding to NRs for FI in mice with induced endometriotic lesions as a facile way to separate diseased tissues for histopathological analyses [209]. Other work published by Kumar *et al.* presented using PEGylated, silica-coated gold nanorods tagged with (FITC) (AuNR@Si(F)-PEG) for PAI and FI combined with heat ablation *in situ* [210].

On the other hand, polyvinylpyrrolidone-capped gold nanorods (PVP-capped AuNRs) have a high potential for endometrial cancer treatment. These structures can bind VEGF165, which is a crucial endothelial cell function and angiogenesis regulator. The results show that binding reduces the proliferation, toxicity, and stimulatory effects of VEGF165 [211]. Au NPs also show high effectiveness to defeat anti-human endometrial cancer effects against Ishikawa, HEC−1-A, HEC−1-B, and KLE cell lines [212].

In the other work, Volpini *et al.* proposed the spherical and star-shaped AuNPs modification with lipoic acid-poly(ethylene glycol)-maleimide to target human endometriosis CD44(+) cells and reduce their viability by heat ablation. The *in vitro* studies in two HESC and NIH−3T3 non-endometriotic cell lines, and 12Z endometriotic cell lines show effective imaging [213] (Fig. 6). Nevertheless, the imaging of AuNPs is limited, requiring the application of agents enabling fluorescence detection.In contrast to the abovementioned AuNPs, Guo *et al.* Au-based reported hollow nanoshells (HAuNS) functionalized with TNYL peptides that specifically recognize and bind to EphB4 receptors, which are expressed in endometriotic lesions [214].

5.1.3.4. Silver and copper nanoparticles (AgNPs and CuNPs). Inorganic NPs can also work as highly effective drug delivery agents in endometriosis. Silver NPs (AgNPs) can work as cargo for PL1 (receptors: TNC-C and Fn-EDB), PL2 (Fn-EDB and NRP−1), PL3 (TNC-C and NRP−1), prototypic C-end Rule (CendR) peptide RPARPARPL1, and CendR peptides. The results show that PL1 targets not only ectopic endometriotic cells but also neovessels surrounding the endometriotic lesions. These structures show the highest effectiveness in promoting the internalization of nanoparticles in 12Z and HESC cells via interaction with proteins of the ECM and the NRP−1 receptor. Interestingly, biotin-modified AgNPs did not bind to endometriotic. lesions. Assuming that, Ag NPs may reduce endometriotic cell proliferation, with potential for therapy/diagnostic [215] (Fig. 7).

Ag NPs and silver oxide (Ag NPs) are strongly defeating or inhibiting the development of a wide range of microorganisms, including Gram-positive and Gram-negative bacteria and other pathogens that can affect patients, while undergoing surgical treatments. Aboelmaaty *et al.* propose AgO NPs to be used for *E. coli*-induced endometriosis in rats [216]. However, despite the high effectiveness, silver-based NPs can affect the functioning of the reproductive system [217]. The tissue damage is dose-dependent, relating to the collagen deposition, inflammation, cytoplasmic vacuolation, mitochondrial damage, and increased TNF-α expression. Therefore, the Ag NPS application in endometriosis treatment seems to be controversial [218].

The copper NPs reveal similar effectiveness in defeating pathogens, but they also offer different functionalities. Cu-polyphthalocyanine network-based spike-linked enzyme mimics (SLE-CuPPc) offer dual functionalities in combating endometrial infection. *S. aureus* effectively stimulates vascular proliferation, curbs fibrosis, and fosters endometrial repair. The spiky nanostructure of SLE-CuPPc adheres to bacterial surfaces, effectively trapping and causing visible morphological deformation and irreversible damage to *S. aureus* and *E. coli* induced by G-SLE-CuPPc [218].

Summarising, nanoparticles described above provide unique theranostic capabilities by functioning as both imaging contrast agents and active therapeutic media [183,186,197,200,213]. However, their efficacy is severely restricted by the dense fibrotic interstitium and pelvic adhesions characteristic of endometriosis, which create mechanical barriers to deep tissue penetration [147,168,182,187,188]. Although peptide functionalization (e.g., with iRGD or TNYL) can improve permeability, these structures face significant biocompatibility hurdles, specifically the risk of long-term heavy metal toxicity and accumulation in the liver, spleen, or reproductive organs [202]. Currently, clinical translation is limited by a lack of human trials; research remains strictly in the preclinical stage using rodent models, which may fail to predict human clinical outcomes. Bridging this gap requires rigorous long-term safety evaluations and more accurate animal-based testing.

5.2. Nanofibres

To date, nanofibers have not been extensively analyzed as a potential drug delivery system (DDS) for endometriosis treatment. PCL with PEG loaded with curcumin was proposed by Boroumand *et al.* curcumin-loaded nanofibers were proposed due to poor bioavailability using oral administration [219]. As it is known, curcumin is characterized by

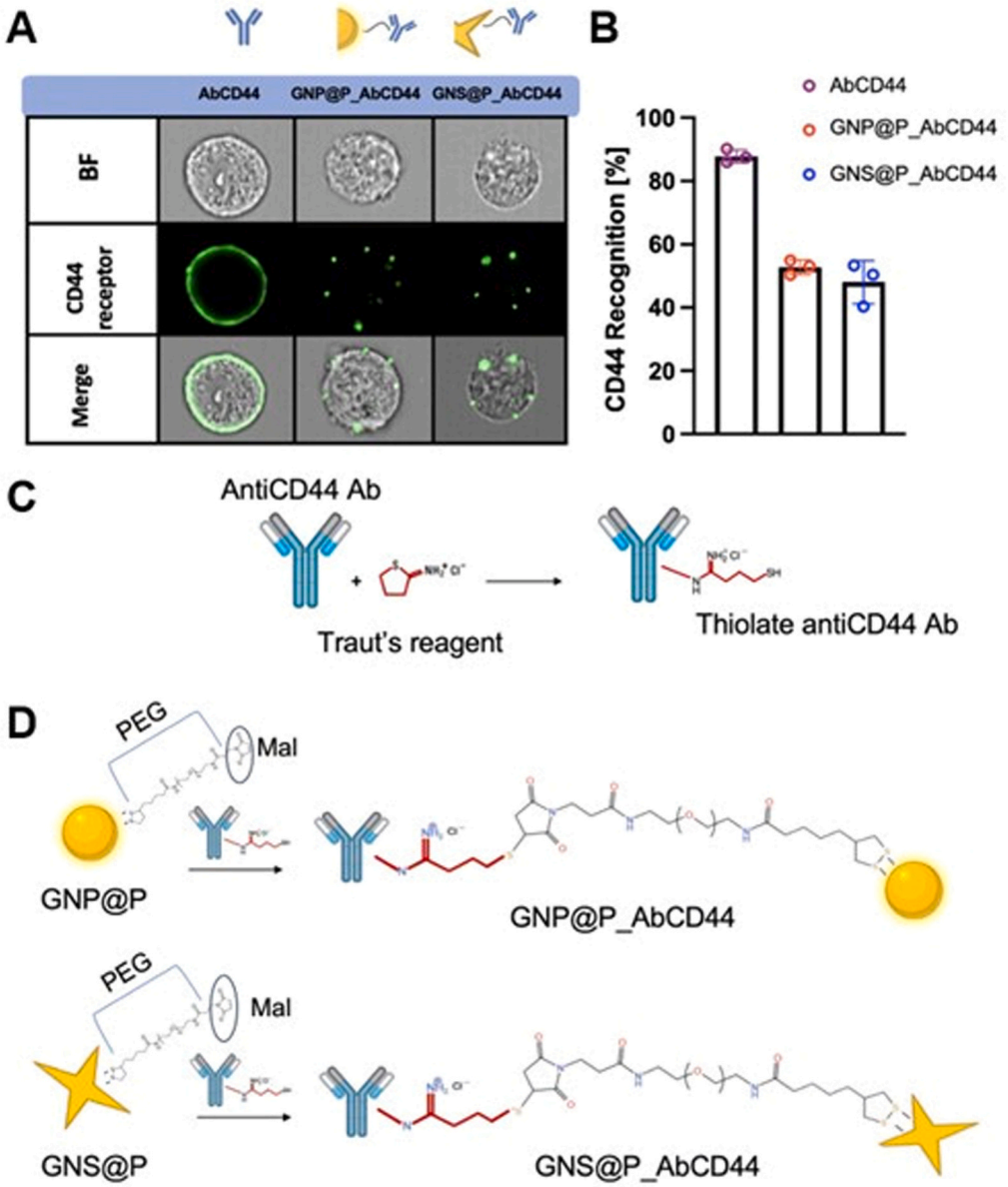

Fig. 6. Illustration of receptor recognition of Au@P_AbCD44 in endometriotic cell lines (top). (**A**) Images obtained via Flow cytometry images of 12Z cells incubated for 24 h with free AbCD44 and Au@P_AbCD44, respectively. Brightfield (BF) – cells; green colour – receptor. (**B**) Quantification of recognition via flow cytometry. (**C**) Scheme of gold nanosystem synthesis by firstly modification of the antiCD44 Ab with thiol group by using Traut reagent and then (**D**) gold nanoparticles and gold nanostars functionalization with the thiolated antiCD44 Ab to produce GNP@P_AbD44 and GNS@P_AbD44, respectively [200].

its anticancer, anti-inflammatory, and antioxidant properties. For this reason, it was proposed as a treatment for endometriosis. Experiments conducted on a mouse endometriosis model revealed that endometrial stroma and glands were reduced ca. 50% of curcumin was released during the first 24 h [219]. The nanofibres loaded with tenofovir (TFV) and levonorgestrel (LNG) up to 20% wt. were proposed by Blakney *et al.* [220]. So far, fibers loaded with progesterone have been analyzed by a few research groups [221–225]. Brako *et al.* focused on the analysis of mucosadhesive interactions of progesterone-loaded nanofibers with the mucosal membrane. The mucoadhesion of an artificial membrane (progesterone-loaded cellulose acetate) was compared to that of lamb esophageal mucosa and was found to be 10 times higher in magnitude. Detailed atomic force microscopy analysis (AFM) led to, e.g.determine the depth of interpenetration or unfilled voids [221]. Lavanya *et al.* utilized electrospinning to fabricate progesterone-loaded pullulan nanofibers, with FTIR spectroscopy confirming successful drug incorporation. The nanofibers exhibited a near-neutral zeta potential (ranging from 0.4 ± 0.01 to -0.5 ± 0.01 mV), suggesting potential for transmucosal administration. Given zeta potential value, suggest lack of colloidal stability, which calls into question the practical application of the system. Furthermore, the material demonstrated sustained progesterone release over 7 days, and cytotoxicity assays confirmed biocompatibility, underscoring its suitability for controlled therapeutic delivery [226]. For example, Chen *et al.* obtained a patient-tailored fibrous system for pelvic prolapse treatment. By integrating polycaprolactone (PCL) mesh, reinforced with nano-hydroxyapatite (nHA), along with drug-eluting poly(lactic-co-glycolic acid) (PLGA) nanofibers, they managed to show the effectiveness of release in vitro of metronidazole, ketorolac, bleomycin, and estradiol, respectively. Additionally, the mesh/nanofiber scaffolds released high drug amounts at the target location for over 28 days in vivo, while blood drug levels stayed low. This finding indicates that a resorbable scaffold may be an effective choice for addressing female pelvic organ prolapse [227]. Beyond virgin nanofibers, hybrid systems combining nanofibers with hydrogels offer

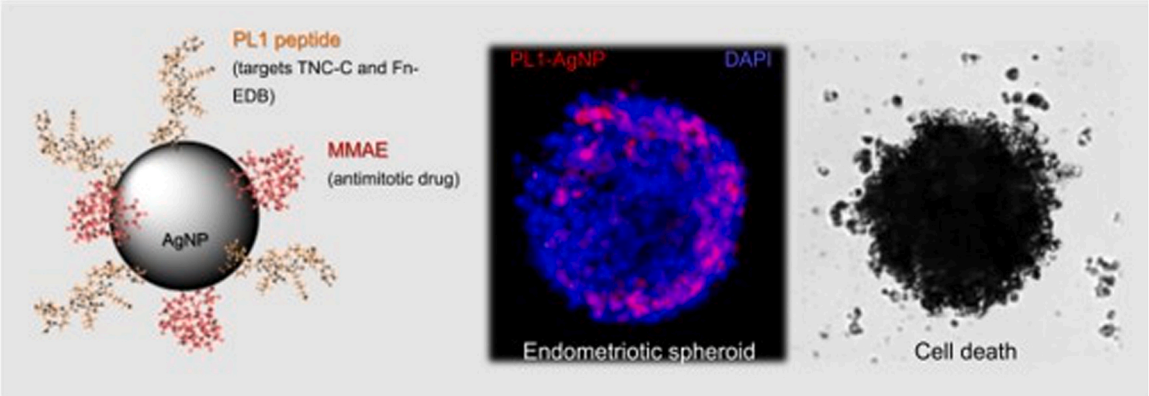

Fig. 7. Silver nanoparticles functionalized with synthetic PL1 peptide (left) showing specific internalization in endometriotic cells spheroid (center). The conjugation of PL1 peptide to Ag NPs loaded with the potent antimitotic drug decreases the viability of endometriotic cells, showing potential for therapy [202].

advanced therapeutic potential for endometriosis. Zhou *et al.* developed an injectable scaffold by homogenizing electrospun fibers and thermally crosslinking them into a porous, compressible framework. This system ensures minimally invasive administration, anatomical adaptation, and sustained drug release. Due to its biomimetic extracellular matrix (ECM) structure, the scaffold facilitates tissue repair by modulating cell proliferation, promoting hyperplastic cell apoptosis, and inhibiting angiogenesis, thereby effectively ameliorating endometrial hyperplasia [228].

In turn, Song *et al.* fabricated a nanobiomaterial by merging fibrinogen (Fg) and P(LLA-CL) via electrostatic spinning. Following the induction of physical injury to the rat endometrium, it was observed that Fg/P(LLA-CL) membranes inserted into the uterine cavities enhanced endometrial thickness, the quantity of glands post-injury, and neovascularization, while decreasing the extent of endometrial fibrosis. What is more, the expression of TGF-β1, a cytokine that facilitates fibrosis, was observed as its level reduced in the initial phase of injury. Ultimately, fertility tests validated that Fg/P(LLA-CL) enhanced the pregnancy rate in rats experiencing endometrial damage, with its safety confirmed through blood analyses and pathological evaluations of the heart, liver, spleen, lungs, and kidneys [229]. Endometriosis also may cause infertility, and to prevent that, restoration of native tissue may help fight this problem. Cao *et al.* developed injectable, bioactive short fibers derived from decellularized extracellular matrix (dECM). These fibers leverage electrostatic interactions to bind endometrial cells and facilitate sustained growth factor release. *In vitro*, the scaffold promotes the adhesion, proliferation, and angiogenic activity of human primary endometrial stromal cells (HESCs) and human umbilical vein endothelial cells (HUVECs). In vivo, dECM-based fibers significantly accelerated endometrial repair and vascularization. Notably, in a rat model of endometrial injury, fiber administration increased the live birth rate from 30% to 90%, demonstrating the therapeutic potential of this approach for treating endometrial factor infertility [230].

Functionalizing electrospun nanofibers offers a precise strategy to tune surface properties. For instance, aminolysis-assisted surface modification allows for the introduction of amine groups, facilitating carbohydrate conjugation such as maltose, which enhances bioactivity [231]. Such studies were conducted e.g. for uterine tissue engineering [131,147].

An approach that may bring a breakthrough in the effectiveness of treatment of female organ diseases might be targeting immune system cells such as neutrophils, macrophages, NK cells, and dendritic cells as they play a vital role in endometriosis by induscing e.g., angiogenesis and proliferation of endometrial cells [232]. The ability of these cells for the elimination of endometrial cells is limited, and abnormal cytokine secretion is observed, leading to the progression of lesions [233]. Moreover, the immune microenviroment may be stimulated by stem cells as they can secrete extracellular vesicles (EVs) and biomolecules e.g., chemokines, cytokines, and growth factors to employ proangiogenic as well as antifibrotic effects. Zhou *et al.* developed an ADMSC-laden silk fibroin/polycaprolactone (SF/PCL) nanofiber scaffold to promote endometrial regeneration []. The system supported ADMSC proliferation, restored endometrial morphology, and enhanced gland regeneration. It also promoted angiogenesis (CD31 upregulation) and attenuated fibrosis by suppressing the TGF-β/Smad signaling pathway. Furthermore, the scaffold upregulated critical decidualization markers (HOXA11, HAND2, FOXO1) and modulated the immune microenvironment by optimizing the Th1/Th2 balance and natural killer (NK) cell infiltration. Consequently, the ADMSC-SF/PCL system demonstrates significant potential as a therapeutic strategy for endometrial restoration and immune remodeling [234]. Darzi *et al.* developed composite PLACL/gelatin electrospun nanofiber meshes loaded with mesenchymal stem/stromal cells (eMSCs) in a mouse model [225]. This bioengineered construct enhanced mesh integration and attenuated the Foreign Body Response (FBR). Six weeks post-implantation, the nanomesh significantly upregulated 18 genes associated with ECM synthesis, cell adhesion, angiogenesis, and collagen remodeling. By modulating the immune microenvironment and promoting vascularization, these cell-engineered scaffolds offer a promising strategy to mitigate surgical complications associated with synthetic implants [235].

However, not only can nanoparticles or nanofibers be a promising tool to fight endometriosis, but a combined approach based on composite electrospun fibers containing nanoparticles inside fibers seems to be greatly beneficial. Krogstad *et al.* created the composite drug delivery system based on mucoadhesive fibers for improved retention in the vaginal tract (based on poly(vinyl alcohol) (PVA) and poly(vinyl pyrrolidone) (PVP)), and PEGylated etravirine-loaded PLGA nanoparticles that can readily diffuse through mucus [236]. Such an approach resulted in approximately 30xgreater retention of nanoparticles in the reproductive tract of mice at 24 h compared to aqueous suspensions. Moreover, those NPs within the fiber composites maintained higher, sustained etravirine concentrations for 24 h and up to 7 days. This highlights the platform's ability to provide sustained nanoparticle release for up to 3 days and drug retention for up to a week following a single dose [236].

There is a big similarity in the application of nanofibers for cervical cancer treatment. However, also in this case, nanofiber-based systems were not explored well. For example, Agarwal *et al.* proposed PCL/chitosan nanofibres loaded with cisplatin [237]. Very limited data are available on this topic; proposed systems are rather simple, the same drugs are analyzed, and these studies are usually finished on a mouse endometriosis model, making it difficult to conclude about the usefulness of the system for use on human cells [168,238].

The use of polymer or composite nanofibers as drug carriers for the

treatment of endometriosis has a critical limitation, which is the mechanical blockade posed by the dense fibrotic interstitium and pelvic adhesions. Unlike smaller nanoparticles, bulkier fibrous structures generally lack the inherent tissue permeability required to penetrate deep infiltrating lesions, often restricting their efficacy to superficial peritoneal surfaces. [239]. For this application, fibres are still in the minority. Furthermore, clinical translation remains at an early proof-of-concept stage. Current research is limited to rodent models, which cannot accurately predict human clinical outcomes or the long-term consequences of filament retention. Bridging the gap to clinical use requires overcoming administration complexities and conducting rigorous safety evaluations in more relevant animal models [168].

6. Hydrogels and therapies using external stimulation for drug release or endometriotic cells elimination

The drug release rate and its amount may be adjusted in order to personalize the therapy, among others. For this reason, on-demand drug delivery systems (DDS) are increasingly developed, often utilizing hydrogels not only as therapeutic carriers but also as physical barriers to prevent postoperative adhesion formation [240–244]. The external physical trigger, e.g., alternating magnetic field, ultrasound, or radiation, may be used to cause the local temperature increase, ultimately leading to drug release from the biomaterial [245,246]. Additionally, the local hyperthermia itself may also be used for the elimination of cancer or endometriosis cells [168]. For this purpose, the biomaterial should contain the nanoparticles sensitive to selected external triggers, like AuNPs or SPIONs. Gold nanoparticles are stimulated by near-infrared, which has limited tissue penetration (1–1.5 cm), limiting their application in endometriosis treatment, unless the use of this method during surgery is considered. For effective stimulation of materials placed in deeper parts of the body, for example, SPIONs are recommended [179]. The SPIONs are nanoparticles approved for biomedical use and commonly used for diagnostic purposes, i.e., Magnetic Resonance Imaging (MRI), or for treatment using magnetic hyperthermia.

So far, SPIONs have not been practically analyzed in the context of endometriosis treatment. In May 2022, the first article concerning magnetic hyperthermia for endometriosis treatment was published in Park *et al.* [179]. The hexagonal SPIONs doped with cobalt were modified with a peptide targeted to vascular endothelial growth factor receptor 2 (VEGFR−2), also known as KDR: kinase insert domain receptor, to promote its capture by endometriotic cells. Ultimately, the local hyperthermia caused by external alternating magnetic fields causes endometriotic cells' death [179]. The authors developed a system targeted to endometriotic cells and intended for intravenous administration. PEG-PCL-coated KDR-targeted NPs were administered intravenously with the clinically relevant dose of about 3 mg Fe/kg) offering dual functionality worked as a T_2-weighted contrast agent, enabling imaging with Magnetic Resonance Imaging (MRI) of endometriotic grafts in mice. Importantly, NPs did not show toxicity under a single 20-minute AMF session at 420 kHz, 26.9 kA/m. Nevertheless, the conditions that were used in magnetic hyperthermia (MH) exceed ($H \times f$ safety limits in MH), requiring further studies not only on long-term toxicity and biodistribution, but also effects in clinically tolerated field strengths [179]. The safety limit, so-called Atkinson-Brezovich limit, is about 4.85×10^5 A m^{-1} s^{-1} for the tissues with a diameter below 30 cm, while for the smaller regions the limit is increased even to 5×10^9 A m^{-1} s^{-1} [247].

One of the widely known inorganic nanostructures to be used in endometriosis that offer stimulus responsiveness is gold nanoparticles (Au NPs). AuNPs offer the use of photothermal therapy (PTT) to affect diseased tissues; they can be generated under irradiation with a specific wavelength. PTT has shown a significant effect in the management of various tumors in preclinical models and early-phase clinical studies [248], which makes them promising agents to treat other diseases like endometriosis.

The work published by Kumar *et al.* mentioned before on the AuNR@Si(F)-PEG) for PAI and FI combines imaging with on-demand photothermal treatment (PTT) *in vivo* on the endometriosis mouse model. Researchers show the controlled heat ablation up to 41–47 °C to reduce lesions due to the plasmonic properties of Au core [210]. Similarly, in the work presented by Volpini *et al.* spherical and star-shaped Au not only work as cargo for bioactive lipoic acid-poly(ethylene glycol)-maleimide to bind CD44(+), but also induce apoptosis with the increased temperature up to 42–44 °C induced by two different lasers on demand [213]. The PTT is also highly effective for the HAuNS when combined with TNYL peptides, enabling precise targeting and elimination of lesions with PTT [214].

Despite the broad development of imaging and targeting of endometriotic lesions with external stimuli through inorganic NPs, there is a big gap to be filled in the drug delivery covering endometriosis treatment [249].

Antsiferova *et al.* proposed that unmodified mesoporous silica NPs (UNPs) and aminopropyl modified silica NPs (AMNPs) were loaded with the immunomodulatory drug GMDP that would be administered topically to defeat endometriosis. Although UNPs effectively interact with peritoneal macrophages, they are not suitable for GMDP delivery in endometriosis, while AMNPs offer both high cellular uptake and increased immune activation, making AMNPs the effective cargo for GMDP delivery [250].

The synergistic effect can also be observed for the polymeric-based composites, where nanoparticles are incorporated in polymeric matrices to prepare platforms for endometrial regeneration. Dong *et al.* demonstrated shape memory polymer (SMP) poly(D, L-lactide-co-trimethylene carbonate) (PT) nanofibers containing cuprorivaite ($CaCuSi_4O_{10}$) nanosheets (CUPNSs) as the second near-infrared (NIR-II) photoresponsive shape memory composite that promotes both human endometrial endothelial cells (HEEC) and human umbilical vein endothelial cells (HUVEC) proliferation [251]. The photoresponsiveness improves the therapeutic effect. As the cuprorivaite can release Si and Cu ions, it also enhances the pro-angiogenesis of HUVECs due to the sustained release of bioactive ions (Si and Cu) [251].

The study presented by Moses *et al.* shows PEG-PCL spheres containing SiNc nanoplatform that effectively detect endometriotic lesions with NIR fluorescence and rapidly eliminate them by PTT [252]. Importantly, other work of these authors proves a similar effect on ovarian cancer xenografts [253]. Nevertheless, the limited depth of tissue penetration in nanoparticle-mediated PTT remains a concern and requires further development. Another work reveals the hydrogel (Vc-Ca/UFNs@Gel) containing calcium ascorbate (Vc-Ca) and ultrathin ferrous sulfide nanosheets (UFNs) that offers synergistic photothermal/ferroptosis/immune endometriosis therapy [244].

Importantly, the application of stimuli-responsive NPs to defeat endometriosis is a relatively new concept that needs more extensive exploration, especially regarding its safety. The research on on-demand drug delivery for endometriosis treatment is still at the preclinical or proof-of-concept stage. For this reason, in this area, a variety of research is needed to explore the efficiency of such ways of particular drug delivery, materials stability, biocompatibility, etc. [245,254].

Studies exploring the potential application of metal-based particles for endometriosis treatment mainly focus on the optimization of physicochemical properties, mainly discussing the correlation between synthesis parameters and the resulting morphology and structure of the proposed nanostructured materials. The studies also include *in vitro* biological assays like cell viability, cell proliferation, cellular uptake, and *in vivo* studies, including biocompatibility and biodistribution. Despite the promising findings, the clinical translation of metal-based nanostructures remains in its early stages. Progress is hindered by limited data on the long-term effect of applied particles and their retention from the organism, a detailed description of interaction

mechanisms between nanostructures within specific intracellular compartments, a lack of universal experimental protocols, and challenges related to scaling up synthesis for larger-scale use. Therefore, more comprehensive studies are needed to assess the long-term cellular and systemic effects of the metal-based materials on the organism [255].

7. Perspectives

Endometriosis is a chronic, potentially debilitating condition affecting individuals of reproductive age. From a clinical perspective, one of the most important factors is early diagnosis, which improves treatment efficacy and long-term prognosis. Also, selecting the appropriate personalized treatment program may be a good alternative. Unfortunately, the fact is that compared to other common diseases, standards of medical care, diagnosis, and treatment have been developed relatively recently. Consequently, there is an urgent need to intensify research and increase public awareness regarding the disease's impact on fertility and systemic health. Recent advancements in diagnostic modalities require validation through robust, large-scale clinical trials to establish their clinical utility. The researchers must shift focus toward the verification of promising pharmacological agents and advanced delivery systems, with an emphasis on direct comparative effectiveness studies. Future breakthroughs in endometriosis therapy rely on optimizing the physicochemical properties of carriers to circumvent biological barriers, thereby facilitating efficient drug diffusion into the lesion core (Table 2). Simultaneously, the development of intelligent nanostructures engineered for multifunctional synergy—integrating ablation techniques (e.g., photothermal therapy), the induction of controlled cell death (including ferroptosis), and precise modulation of the immune microenvironment within a single carrier—represents a strategy to eradicate lesions while remodeling the local niche. However, significant challenges persist. The integration of high-energy ablation carries a high risk of collateral thermal injury to adjacent healthy tissues. Furthermore, although inorganic and metallic nanoparticles provide unique theranostic capabilities, their long-term biocompatibility and the risks of heavy metal accumulation in reproductive organs must be rigorously addressed. Finally, bridging the translational gap requires moving beyond rodent models to primate-based validation to ensure long-term biosafety and clinical efficacy in humans. [63,64,66].

Deep infiltrative endometriosis (DIE) naturally brings to mind other disease entities, such as malignant tumors. These diseases are similar in the presence of distant foci, similar to metastases, promotion of a chronic inflammatory environment, the ability to adhere, invade, and cause tissue destruction, resistance to apoptosis, and the presence of lymphangiogenesis and lymph node foci [256]. Due to the endometriosis, the characteristic use of nanoparticles or locally injectable hydrogels is justified; however, in this matter, much more needs to be verified than in the preclinical stage [179,210,213,257] (Fig. 8). Technologies using the above-mentioned materials also have significant risks for patients, which need to be determined and studied as soon as possible. Currently, publication databases such as Scopus or PubMed contain few records regarding, for example, new drug delivery systems or therapies for endometriosis, compared to studies conducted on new therapies for other diseases with similar prevalence in the population (Fig. 2). This clearly demonstrates the scale of neglect in this area.

Recent advancements in biotechnology and genomics may revolutionize the management of endometriosis by enabling precision medicine strategies [258,259]. Patient-derived organoids now serve as robust models for personalized drug screening, allowing clinicians to evaluate therapeutic efficacy within patient-specific microenvironments [258]. Concurrently, 'gene expression fingerprinting' and the identification of somatic mutations—such as those in ARID1A or PIK3CA—offer critical insights into the molecular heterogeneity of the disease, guiding the selection of targeted therapies, including selective progesterone receptor modulators (SPRMs) [89]. Furthermore, integrating genomic data from GWAS with phenotypic profiling—specifically regarding fibrosis-related receptor expression (e.g., ERα) and neuropeptide levels—is essential for predicting treatment response and avoiding ineffective hormonal interventions [260]. These integrative approaches

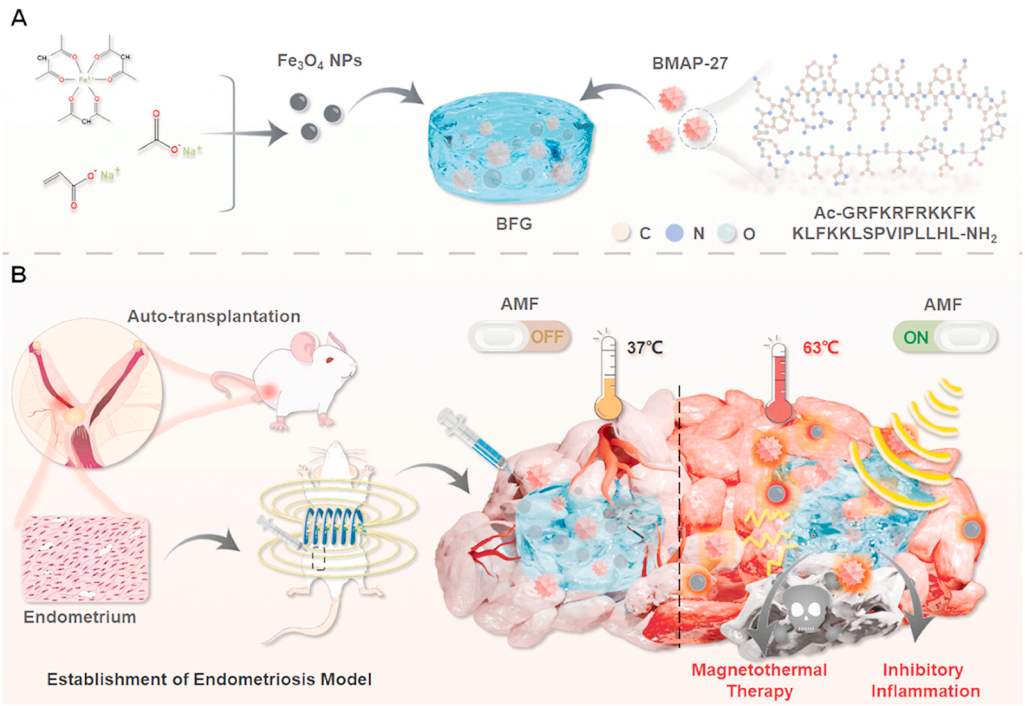

Fig. 8. Schematic representation of the combinational use of different nanomaterials for endometriosis treatment: (**A**) incorporation of Fe_3O_4 NPs and an anti-inflammatory peptide into a hydrogel, (**B**) injection of the created hybrid system into the lesion site of endometriosis, resulting in hydrogel melting and heating the lesion site to 63 °C due to the magnetic activation properties of Fe3O4. As a result, apoptosis of cells and rapid release of the BMAP−27 anti-inflammatory peptide happened [242].

provide a framework for developing customized therapeutic plans, thereby enhancing clinical outcomes and reducing the burden of adverse effects. Immunotherapy is also a promising approach for the development of new therapies in this area. Immunotherapy aims to treat the disease by correcting immune system dysfunction [30,250]. In both cases, nanomaterials are considered as vehicles for active substances, e.g., danazol or siRNA, and clinical data in endometriosis treatment are very limited and need to be explored further.

Furthermore, it is essential to standardize clinical trial design and long-term follow-up protocols to rigorously assess safety profiles—including metabolic effects and bone mineral density—and to support the development of truly personalized therapeutic strategies [63,64,261].

Clinical studies on novel therapies using nanomaterials as drug carriers or PTT agents are still rare for endometriosis treatment. It is important to collect data on, e.g., lipid nanoparticles, clinical complaints related to nanoparticle delivery, toxicity, and the long-term effectiveness of the therapy. Without the determination to move research into the clinical phase, new ideas will not be verified, and development in this area will not happen [196,213,214].

8. Conclusions

Endometriosis research largely focuses on disease mechanisms, whereas current clinical treatments mainly focus on direct symptom management. In the most difficult cases, such as DIE, when other treatments have been exhausted, radical procedures such as hysterectomy may be required. As demonstrated in this review, preclinical research on new endometriosis treatments (e.g., drug delivery methods, hyperthermia) is still in the very early stages of development. Often, many of these studies are not followed up and never reach the clinical trial phase, highlighting the limited availability of alternative therapeutic pathways for effective endometriosis treatment for patients suffering from this common conditionThe scientific community has already proposed several promising approaches to developing new methods for treating this disease, such as magnetic hyperthermia. However, for the proposed development paths to undergothorough verification, it is necessary to undertake systematic research efforts and engage multidisciplinary teams of researchers to support their potential translation into clinical trials and future clinical applications.

CRediT authorship contribution statement

Olga Urbanek: Writing – review & editing, Writing – original draft, Visualization, Supervision, Funding acquisition, Formal analysis, Conceptualization. **Magdalena Osial:** Writing – review & editing, Writing – original draft. **Angelika Zaszczyńska:** Writing – review & editing, Writing – original draft. **Łukasz Luśtyk:** Writing – review &

Table 2
Overview of engineered material systems for localized endometriosis therapy, categorized by disease subtype and therapeutic mechanism.

TYPE	PROPOSED MATERIAL	STRATEGY	APPLICATION	REF.
SUPERFICIAL PERITONEAL LESIONS	Mifepristone-loaded polymeric implant	Controlled and sustained local drug release of progesterone receptor antagonist	Long-term suppression of superficial lesions with reduced systemic toxicity	[90]
	Levonorgestrel-releasing polymeric intrauterine device	Localized progestin delivery reduces inflammation and ectopic tissue proliferation	Chronic pain management and recurrence prevention	[85]
	Circulating miRNA nanodiagnostic platform	Detection of disease-specific circulating miRNA signatures	Non-invasive early diagnosis and monitoring	[66]
	PLGA nanoparticles coated with bacterial outer membrane vesicles (OMV-PLGA NPs)	Immunomodulation and macrophage reprogramming to suppress inflammatory lesion establishment	Prevention of lesion implantation and inflammatory progression	[262]
	PLGA/gold-core ionic liquid-coated nanoparticles (Au-PLGA-IL NPs)	Neutrophil hitchhiking, photothermal-targeted delivery to inflammatory lesions	Targeted nanotherapy and lesion ablation	[263]
	Cell penetrating peptides (PF6 and NF70) nanoparticles combined with siRNA	Downregulation of ribonucleotide reductase subunit M2 (RRM2) and vascular endothelial growth factor (VEGF)	Targeted delivery to inhibit endometriotic primary cell proliferation and invasion	[107]
	Chrysin-loaded PLGA nanoparticles	Downregulating NF-κB activation-driven expression of angiogenic factors	Reduction of endometriotic lesion implantation and progression	[171]
	Anti-CD44 antibody-conjugated gold nanoparticles	Photothermal-targeted delivery to inflammatory lesions	Targeted nanotherapy and lesion ablation	[213]
OVARIAN ENDOMETRIOMA	Danazol co-crystal drug-delivery system	Crystal engineering improves dissolution rate and oral bioavailability	Improved pharmacological treatment of ovarian endometrioma	[95]
	Aromatase inhibitor-loaded intrauterine delivery system	Local hormonal suppression with minimized systemic exposure	Reduction of cyst growth and estrogen-driven progression	[85]
	cRGD-modified liposome nanodrug containing artesunate	Targeting HIF−1α in the HIF−1α/VEGF pathway	Targeted delivery to inhibit angiogenesis in ectopic lesions	[151]
	PLGA nanoparticles with miRNA	Gene delivery to endometriotic cells	Apoptosis of stromal cells of ovarian endometrium cysts by use of gene therapy	[174]
DEEP INFILTRATING ENDOMETRIOSIS	Selective progesterone receptor modulator (SPRM)-based biomaterials	Modulation of progesterone resistance and inflammatory pathways	Treatment of hormonally resistant infiltrating lesions	[76, 88]
	FUT4 mRNA biosensing platform	Molecular detection of altered glycosylation-associated gene expression	Biomarker-assisted diagnosis and lesion stratification	[63]
	LDL nanoemulsion containing lipid nanoparticles	Uptake of labeled lipid nanoparticles (LDE) by overexpressed LDL receptors in endometriotic foci	Effective treatment of deep endometriosis using nanotechnology as an alternative to surgery	[149]
	lipid nanoparticles composed of cholesteryl oleate, phosphatidylcholine, free cholesterol, and triolein combined with didodecyl-methotrexate	Injection of the developed nanosystem into the arm vein	Lower the pain intensity during the treatment of deep infiltrative endometriosis	[162]
	FITC-tagged, silica-coated gold nanorods	Laser-induced thermal ablation	Imaging of endometric tissues and lesion stratification	[210]
ADENOMYOSIS	Simvastatin-loaded liposomal nanoparticles	Nanocarrier-mediated targeted anti-angiogenic and anti-inflammatory therapy	Experimental localized treatment of adenomyosis	[100]
	Epigenetic biomarker system based on HOXA10 DNA methylation	Detection of aberrant methylation associated with impaired endometrial receptivity	Precision diagnostics and molecular disease characterization	[16]

editing, Writing – original draft, Visualization. **Matteo Pavone:** Writing – review & editing, Writing – original draft.

Ethical approval

Not applicable.

Declaration of Generative AI and AI-assisted technologies in the writing process

Generative artificial intelligence (AI) tools were used in the preparation of this manuscript for language refinement, grammar correction, and figure generation. Specifically, Gemini was utilised to improve the clarity and readability of the text and to assist in the conceptual development of schematic scientific figures. All scientific content, literature interpretation, figure verification, critical analysis and conclusions were developed, reviewed and validated by the authors. The authors accept full responsibility for the accuracy, originality and integrity of the manuscript and all associated figures.

Declaration of Competing Interest

The authors declare no conflict of interest.

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Data availability

No data was used for the research described in the article.

References

[1] World Population Dashboard | United Nations Population Fund, (n.d.). ⟨https://www.unfpa.org/data/world-population-dashboard⟩ (accessed January 8, 2026).
[2] K. Singh, R. Swarup, Women are poorly represented in clinical trials. That's problematic, Natindia (2025), https://doi.org/10.1038/d44151-025-00036-y.
[3] I. Zucker, B.J. Prendergast, Sex differences in pharmacokinetics predict adverse drug reactions in women, Biol. Sex. Differ. 11 (2020) 32, https://doi.org/10.1186/s13293-020-00308-5.
[4] J.R. Steinberg, C.J. Magnani, B.E. Turner, B.T. Weeks, A.M.P. Young, C.F. Lu, N. Zhang, M.T. Richardson, A.C. Fitzgerald, Z. Mekonnen, T. Redman, M. Adetunji, S.A. Martin, J.N. Anderson, K.S. Chan, M.P. Milad, Early discontinuation, results reporting, and publication of gynecology clinical trials from 2007 to 2020, Obstet. Gynecol. 139 (2022) 821–831, https://doi.org/10.1097/AOG.0000000000004735.
[5] Home | ClinicalTrials.gov, (n.d.). ⟨https://clinicaltrials.gov/⟩ (accessed January 8, 2026).
[6] A.-M. Matei, A.-M. Draghici-Ionescu, M. Cioplea, S. Zurac, D. Boda, I. Serban, C. Caruntu, M. Ilie, L. Gyula, Skin endometriosis: a case report and review of the literature, Exp. Ther. Med. 21 (2021) 532, https://doi.org/10.3892/etm.2021.9964.
[7] J. Yao, H. Zheng, H. Nie, C.-F. Li, W. Zhang, J.-J. Wang, Endometriosis of the lung: a case report and review of literature, World J. Clin. Cases 11 (2023) 4326–4333, https://doi.org/10.12998/wjcc.v11.i18.4326.
[8] K. Upson, S.A. Missmer, Epidemiology of Adenomyosis, Semin. Reprod. Med. 38 (2020) 089–107, https://doi.org/10.1055/s-0040-1718920.
[9] C. Cricco, A. Daugenti, D. Angilecchia, D. Ceron, Differential diagnosis of endometriosis in patient with nonspecific low back pain: A case report, J. Bodyw. Mov. Ther. 27 (2021) 227–232, https://doi.org/10.1016/j.jbmt.2021.02.019.
[10] Endometriosis, (n.d.). ⟨https://www.who.int/news-room/fact-sheets/detail/endometriosis⟩ (accessed January 8, 2026).
[11] ReproductiveFacts.org homepage, (n.d.). ⟨https://www.reproductivefacts.org/⟩ (accessed January 8, 2026).
[12] P. Parasar, P. Ozcan, K.L. Terry, Endometriosis: Epidemiology, Diagnosis and Clinical Management, Curr. Obstet. Gynecol. Rep. 6 (2017) 34–41, https://doi.org/10.1007/s13669-017-0187-1.
[13] S. Harris, L.J. Tata, N. Qureshi, K. Read, M. Bains, The Experiences of Endometriosis Patients During Primary Healthcare Encounters: A Systematic Review of Qualitative Evidence, Women'S. Reprod. Health (2025) 1–14, https://doi.org/10.1080/23293691.2025.2545308.
[14] M. Gabriel, V. Fey, T. Heinosalo, P. Adhikari, K. Rytkönen, T. Komulainen, K. Huhtinen, T.D. Laajala, H. Siitari, A. Virkki, P. Suvitie, H. Kujari, T. Aittokallio, A. Perheentupa, M. Poutanen, A relational database to identify differentially expressed genes in the endometrium and endometriosis lesions, Sci. Data 7 (2020) 284, https://doi.org/10.1038/s41597-020-00623-x.
[15] Home, Clinical Trials Arena (n.d.). ⟨https://www.clinicaltrialsarena.com/⟩ (accessed January 8, 2026).
[16] M.H. Elias, N. Lazim, Z. Sutaji, M.A. Abu, A.K. Abdul Karim, A. Ugusman, S. E. Syafruddin, M.H. Mokhtar, M.F. Ahmad, HOXA10 DNA Methylation Level in the Endometrium Women with Endometriosis: A Systematic Review, Biology 12 (2023) 474, https://doi.org/10.3390/biology12030474.
[17] S. Asghari, A. Valizadeh, L. Aghebati-Maleki, M. Nouri, M. Yousefi, Endometriosis: Perspective, lights, and shadows of etiology, Biomed. & Pharmacother. 106 (2018) 163–174, https://doi.org/10.1016/j.biopha.2018.06.109.
[18] F. Liu, S. Yuan, Q. Yan, S. Yang, W. Yan, T. Xiang, Z. Wu, G. Li, W. Ren, W. Wang, Global Trends in Endometriosis Burden, 1990–2021: A Sociodemographic Analysis Using GBD 2021 Data and Projections to 2036, IJWH 18 (2026) 1–13, https://doi.org/10.2147/IJWH.S560463.
[19] K.E. Nnoaham, L. Hummelshoj, P. Webster, T. d'Hooghe, F. De Cicco Nardone, C. De Cicco Nardone, C. Jenkinson, S.H. Kennedy, K.T. Zondervan, Impact of endometriosis on quality of life and work productivity: a multicenter study across ten countries, Fertil. Steril. 96 (2011) 366–373.e8, https://doi.org/10.1016/j.fertnstert.2011.05.090.
[20] B. Swift, B. Taneri, C.M. Becker, H. Basarir, H. Naci, S.A. Missmer, K. T. Zondervan, N. Rahmioglu, Prevalence, diagnostic delay and economic burden of endometriosis and its impact on quality of life: results from an Eastern Mediterranean population, Eur. J. Public. Health 34 (2024) 244–252, https://doi.org/10.1093/eurpub/ckad216.
[21] World Endometriosis Society - leading the way in endometriosis, World Endometriosis Society (n.d.). ⟨https://www.worldendosociety.org/⟩ (accessed January 8, 2026).
[22] Homepage, European Endometriosis League (n.d.). ⟨https://euroendometriosis.com/⟩ (accessed January 8, 2026).
[23] Endometriosis, Foundation, Endometriosis Foundation Of America | EndoFound, (n.d.). ⟨https://www.endofound.org/⟩ (accessed January 8, 2026).
[24] Strona główna, Fundacja "Pokonać Endometriozę" (n.d.). ⟨https://pokonacendometrioze.pl/⟩ (accessed January 8, 2026).
[25] Ending endometriosis starts by saying it | Endometriosis UK, (n.d.). ⟨https://www.endometriosis-uk.org/⟩ (accessed January 8, 2026).
[26] Endometriosis Association of Ireland, (n.d.). ⟨https://www.endometriosis.ie/⟩ (accessed January 8, 2026).
[27] Welcome to Endometriosis NZ | Endometriosis New Zealand, (n.d.). ⟨https://nzendo.org.nz/⟩ (accessed January 8, 2026).
[28] S.-W. Guo, Recurrence of endometriosis and its control, Human. Reprod. Update 15 (2009) 441–461, https://doi.org/10.1093/humupd/dmp007.
[29] C. Chapron, L. Marcellin, B. Borghese, P. Santulli, Rethinking mechanisms, diagnosis and management of endometriosis, Nat. Rev. Endocrinol. 15 (2019) 666–682, https://doi.org/10.1038/s41574-019-0245-z.
[30] S. Amidifar, D. Jafari, A.H. Mansourabadi, S. Sadaghian, A. Esmaeilzadeh, Immunopathology of Endometriosis, Molecular Approaches, Am. J. Rep. Immunol. 93 (2025) e70056, https://doi.org/10.1111/aji.70056.
[31] D.C. Rodríguez-Lozano, M.D.P. Meza-Rodríguez, O.P. Cruz-Orozco, B. Sánchez-Ramírez, A. Olguin-Ortega, J.R. Silvestri-Tomassoni, G. Corona-Barsse, L. F. Escobar-Ponce, J.M. Solis-Paredes, B. Dominguez-Trejo, I. Camacho-Arroyo, Emotional dysregulation in women with endometriosis with cyclical and non-cyclical chronic pelvic pain, BMC Women'S. Health 22 (2022) 525, https://doi.org/10.1186/s12905-022-02066-5.
[32] H. Nassiri Kigloo, R. Itani, T. Montreuil, I. Feferkorn, J. Raina, T. Tulandi, F. Mansour, S. Krishnamurthy, E. Suarthana, Endometriosis, chronic pain, anxiety, and depression: A retrospective study among 12 million women, J. Affect. Disord. 346 (2024) 260–265, https://doi.org/10.1016/j.jad.2023.11.034.
[33] B. Smolarz, K. Szyłło, H. Romanowicz, Endometriosis: Epidemiology, Classification, Pathogenesis, Treatment and Genetics (Review of Literature), IJMS 22 (2021) 10554, https://doi.org/10.3390/ijms221910554.
[34] H.M. Arsalan, H. Mumtaz, A.S. Lagana, Biomarkers of endometriosis. in: Advances in Clinical Chemistry, Elsevier, 2025, pp. 73–120, https://doi.org/10.1016/bs.acc.2025.01.004.
[35] J.A. Sampson, PERFORATING HEMORRHAGIC (CHOCOLATE) CYSTS OF THE OVARY: THEIR IMPORTANCE AND ESPECIALLY THEIR RELATION TO PELVIC ADENOMAS OF ENDOMETRIAL TYPE ("ADENOMYOMA" OF THE UTERUS, RECTOVAGINAL SEPTUM, SIGMOID, ETC.), Arch. Surg. 3 (1921) 245, https://doi.org/10.1001/archsurg.1921.01110080003001.
[36] R.F.P.M. Kruitwagen, Endometriosis and retrograde menstruation, 1991.
[37] J. Lamceva, R. Uljanovs, I. Strumfa, The Main Theories on the Pathogenesis of Endometriosis, IJMS 24 (2023) 4254, https://doi.org/10.3390/ijms24054254.
[38] J. Halme, M.G. Hammond, J.F. Hulka, S.G. Raj, L.M. Talbert, Retrograde Menstruation in Healthy Women and in Patients With Endometriosis, J. Am. Coll. Obstet. Gynecol. (1984).
[39] P. Vercellini, N. Salmeri, E. Somigliana, M. Piccini, F. Caprara, P. Viganò, S. De Matteis, Müllerian anomalies and endometriosis as potential explanatory models

for the retrograde menstruation/implantation and the embryonic remnants/celomic metaplasia pathogenic theories: a systematic review and meta-analysis, Human. Reprod. 39 (2024) 1460–1470, https://doi.org/10.1093/humrep/deae086.
[40] M.A. Pitot, C.A. Bookwalter, K.M. Dudiak, Müllerian duct anomalies coincident with endometriosis: a review, Abdom. Radiol. 45 (2020) 1723–1740, https://doi.org/10.1007/s00261-020-02465-y.
[41] J.N. Painter, C.A. Anderson, D.R. Nyholt, S. Macgregor, J. Lin, S.H. Lee, A. Lambert, Z.Z. Zhao, F. Roseman, Q. Guo, S.D. Gordon, L. Wallace, A. K. Henders, P.M. Visscher, P. Kraft, N.G. Martin, A.P. Morris, S.A. Treloar, S. H. Kennedy, S.A. Missmer, G.W. Montgomery, K.T. Zondervan, Genome-wide association study identifies a locus at 7p15.2 associated with endometriosis, Nat. Genet. 43 (2011) 51–54, https://doi.org/10.1038/ng.731.
[42] The Role of Hormone Imbalance in the Pathogenesis of Endometriosis, AJMHS 5 (2024), https://doi.org/10.25236/AJMHS.2024.050707.
[43] H. Ansariniya, A. Yavari, A. Javaheri, F. Zare, Oxidative stress-related effects on various aspects of endometriosis, Am. J. Rep. Immunol. 88 (2022) e13593, https://doi.org/10.1111/aji.13593.
[44] N. Santanam, A.A. Murphy, S. Parthasarathy, Macrophages, Oxidation, and Endometriosis, Ann. New. Y. Acad. Sci. 955 (2002) 183–198, https://doi.org/10.1111/j.1749-6632.2002.tb02779.x.
[45] A.D. Greene, S.A. Lang, J.A. Kendziorski, J.M. Sroga-Rios, T.J. Herzog, K. A. Burns, Endometriosis: where are we and where are we going? Reproduction 152 (2016) R63–R78, https://doi.org/10.1530/REP-16-0052.
[46] Z. Lu, W. Zhang, S. Jiang, J. Zou, Y. Li, Effect of oxygen tensions on the proliferation and angiogenesis of endometriosis heterograft in severe combined immunodeficiency mice, Fertil. Steril. 101 (2014) 568–576, https://doi.org/10.1016/j.fertnstert.2013.10.039.
[47] A.L.L. Rocha, F.M. Reis, R.N. Taylor, Angiogenesis and Endometriosis, Obstet. Gynecol. Int. 2013 (2013) 1–8, https://doi.org/10.1155/2013/859619.
[48] E. Coiplet, B. Courbiere, A. Agostini, L. Boubli, F. Bretelle, A. Netter, Endometriosis and environmental factors: A critical review, J. Gynecol. Obstet. Human. Reprod. 51 (2022) 102418, https://doi.org/10.1016/j.jogoh.2022.102418.
[49] A. Chandrakanth, S. Firdous, R. Vasantharekha, W. Santosh, B. Seetharaman, Exploring the Effects of Endocrine-Disrupting Chemicals and miRNA Expression in the Pathogenesis of Endometriosis by Unveiling the Pathways: a Systematic Review, Reprod. Sci. 31 (2024) 932–941, https://doi.org/10.1007/s43032-023-01412-8.
[50] B.S. Bedrick, L. Courtright, J. Zhang, M. Snow, I.L. Sampaio Amendola, E. Nylander, K. Cayton-Vaught, J. Segars, B. Singh, A systematic review of epigenetics of endometriosis, F. &S Rev. 5 (2024) 100070, https://doi.org/10.1016/j.xfnr.2024.01.003.
[51] Y. Zhuang, T. Lyu, Y. Chen, W. Li, L. Tang, S. Xian, P. Yang, L. Wang, Q. Zhang, C. Mei, Y. Lin, Z. Yan, Z. Li, J. He, F. Zeng, Mechanistic insights into endometriosis: roles of Streptococcus agalactiae and L-carnitine in lesion development and angiogenesis, Angiogenesis 28 (2025) 38, https://doi.org/10.1007/s10456-025-09991-7.
[52] A. Muraoka, M. Suzuki, T. Hamaguchi, S. Watanabe, K. Iijima, Y. Murofushi, K. Shinjo, S. Osuka, Y. Hariyama, M. Ito, K. Ohno, T. Kiyono, S. Kyo, A. Iwase, F. Kikkawa, H. Kajiyama, Y. Kondo, *Fusobacterium* infection facilitates the development of endometriosis through the phenotypic transition of endometrial fibroblasts, Sci. Transl. Med. 15 (2023) eadd1531, https://doi.org/10.1126/scitranslmed.add1531.
[53] E. Pascoal, J.M. Wessels, M.K. Aas-Eng, M.S. Abrao, G. Condous, D. Jurkovic, M. Espada, C. Exacoustos, S. Ferrero, S. Guerriero, G. Hudelist, M. Malzoni, S. Reid, S. Tang, C. Tomassetti, S.S. Singh, T. Van Den Bosch, M. Leonardi, Strengths and limitations of diagnostic tools for endometriosis and relevance in diagnostic test accuracy research, Ultrasound Obstet. &amp Gyne 60 (2022) 309–327, https://doi.org/10.1002/uog.24892.
[54] C.M. Becker, A. Bokor, O. Heikinheimo, A. Horne, F. Jansen, L. Kiesel, K. King, M. Kvaskoff, A. Nap, K. Petersen, E. Saridogan, C. Tomassetti, N. Van Hanegem, N. Vulliemoz, N. Vermeulen, ESHRE Endometriosis Guideline Group, S. Altmäe, B. Ata, E. Ball, F. Barra, E. Bastu, A. Bianco-Anil, U.B. Knudsen, R. Brubel, J. Cambitzi, A. Cantineau, Y. Cheong, A. Daniilidis, B. De Bie, C. Exacoustos, S. Ferrero, T. Gelbaya, J. Goetz-Collinet, G. Hudelist, M. Hussain, T. Indrielle-Kelly, S. Khazali, S.L. Kumar, U. Leone Roberti Maggiore, J.W.M. Maas, H. McLaughlin, J. Metello, V. Mijatovic, Y. Miremadi, C. Muteshi, M. Nisolle, E. Oral, G. Pados, D. Parades, N. Pluchino, P.R. Supramaniam, M. Schick, B. Seeber, R. Seracchioli, A.S. Laganà, A. Stavroulis, L. Tebache, G. Uncu, U. Van Den Broeck, A. Van Peperstraten, A. Vereczkey, A. Wolthuis, P.Y. Bahat, C. Yazbeck, ESHRE guideline: endometriosis, 2022, Human. Reprod. Open. (2022), https://doi.org/10.1093/hropen/hoac009.
[55] A. Fassbender, D.O. B. De Moor, E. Waelkens, C. Meuleman, C. Tomassetti, K. Peeraer, T. D'Hooghe, Biomarkers of Endometriosis, in: T. Harada (Ed.), Endometriosis, Springer Japan, Tokyo, 2014, pp. 321–339, https://doi.org/10.1007/978-4-431-54421-0_20.
[56] B.D. Yilmaz, S.E. Bulun, Endometriosis and nuclear receptors, Human. Reprod. Update 25 (2019) 473–485, https://doi.org/10.1093/humupd/dmz005.
[57] J. Nie, Y. Yi, X. Liu, S.-W. Guo, Progressively diminished estrogen signaling concordant with increased fibrosis in ectopic endometrium, Human. Reprod. Open. 2025 (2025) hoaf028, https://doi.org/10.1093/hropen/hoaf028.
[58] D.E. Machado, A. Palumbo Jr., J.M. Santos, R.M. Mattos, T. Alves dos Santos, S. H. Seabra, L. da Cunha Boldrioni, J.A. Perini, L.E. Nasciutti, A. GFP, endometriosis model reveals important morphological characteristics of the angiogenic process that govern benign and malignant diseases, Histol. Histopathol. (2014) 903–912, https://doi.org/10.14670/HH-29.903.
[59] H. Xu, T. Zhang, G.C.W. Man, K.E. May, C.M. Becker, T.N. Davis, A.L. Kung, A. E. Birsner, R.J. D'Amato, A.W.Y. Wong, C.C. Wang, Vascular endothelial growth factor C is increased in endometrium and promotes endothelial functions, vascular permeability and angiogenesis and growth of endometriosis, Angiogenesis 16 (2013) 541–551, https://doi.org/10.1007/s10456-013-9333-1.
[60] M. Szubert, J. Suzin, M. Duechler, A. Szulawska, M. Czyz, K. Kowalczyk-Amico, Evaluation of selected angiogenic and inflammatory markers in endometriosis before and after danazol treatment, Reprod. Fertil. Dev. 26 (2014) 414–420, https://doi.org/10.1071/RD12258.
[61] A.L. Hsu, I. Khachikyan, P. Stratton, Invasive and Noninvasive Methods for the Diagnosis of Endometriosis, Clin. Obstet. & Gynecol. 53 (2010) 413–419, https://doi.org/10.1097/GRF.0b013e3181db7ce8.
[62] G. Condous, B. Gerges, I. Thomassin-Naggara, C. Becker, C. Tomassetti, H. Krentel, B.J. Van Herendael, M. Malzoni, M.S. Abrao, E. Saridogan, J. Keckstein, G. Hudelist, Intersociety Consensus Group §, K. Aas-Eng, J. L. Alcazar, C. Bafort, M. Bazot, D. Bielen, A. Bokor, T. Bourne, F. Carmona, A. Di Giovanni, D. Djokovic, A. Egekvist, J. English, C. Exacoustos, H. Ferreira, S. Ferrero, R. Forstner, S. Freeman, M. Goncalves, G. Grimbizis, A. Guerra, S. Guerriero, F.W. Jansen, D. Jurkovic, S. Khazali, M. Leonardi, C. Maciel, L. Manganaro, M. Mueller, M. Nisolle, G. Noe, S. Reid, H. Roman, P. Rousset, M. Seyer Hansen, S. Singh, V. Thomas, D. Timmerman, U.A. Ulrich, T. Van Den Bosch, D. Van Schoubroeck, A. Wattiez, Non-invasive imaging techniques for diagnosis of pelvic deep endometriosis and endometriosis classification systems: an International Consensus Statement. Human Reproduction Open, 2024, https://doi.org/10.1093/hropen/hoae029.
[63] M. Żeberkiewicz, A. Hyc, A. Iwan, A. Zwierzchowska, A. Ścieżyńska, I. Kalaszczyńska, E. Barcz, J. Malejczyk, Expression of Fucosyltransferase 4 (FUT4) mRNA Is Increased in Endometrium from Women with Endometriosis, JCM 11 (2022) 5606, https://doi.org/10.3390/jcm11195606.
[64] endometrioza.abm.gov.pl, O badaniu, Endometrioza (n.d.). ⟨https://endometrioza.abm.gov.pl/end/o-badaniu/2862,O-badaniu.html⟩ (accessed January 23, 2026).
[65] C. Ferrier, S. Bendifallah, S. Suisse, Y. Dabi, C. Touboul, A. Puchar, K. Zarca, I. Durand Zaleski, Saliva microRNA signature to diagnose endometriosis: A cost-effectiveness evaluation of the Endotest®, BJOG 130 (2023) 396–406, https://doi.org/10.1111/1471-0528.17348.
[66] S. Bendifallah, Y. Dabi, S. Suisse, L. Delbos, M. Poilblanc, P. Descamps, F. Golfier, L. Jornea, D. Bouteiller, C. Touboul, A. Puchar, E. Daraï, Endometriosis Associated-miRNome Analysis of Blood Samples: A Prospective Study, Diagnostics 12 (2022) 1150, https://doi.org/10.3390/diagnostics12051150.
[67] J.T. Jensen, W. Schlaff, K. Gordon, Use of combined hormonal contraceptives for the treatment of endometriosis-related pain: a systematic review of the evidence, Fertil. Steril. 110 (2018) 137–152.e1, https://doi.org/10.1016/j.fertnstert.2018.03.012.
[68] V. Zajec, M. Mikuš, S.G. Vitale, M.N. D'alterio, M. Gregov, M.J. Šarić, J. Carugno, S. Angioni, M. Ćorić, Current status and challenges of drug development for hormonal treatment of endometriosis: a systematic review of randomized control trials, Gynecol. Endocrinol. 38 (2022) 713–720, https://doi.org/10.1080/09513590.2022.2109145.
[69] L. Troìa, S. Luisi, Estro-Progestins and Pain Relief in Endometriosis, Endocrines 3 (2022) 349–366, https://doi.org/10.3390/endocrines3020028.
[70] J.-B. Mitchell, S. Chetty, F. Kathrada, Progestins in the symptomatic management of endometriosis: a meta-analysis on their effectiveness and safety, BMC Women'S. Health 22 (2022) 526, https://doi.org/10.1186/s12905-022-02122-0.
[71] P. Vercellini, L. Buggio, N. Berlanda, G. Barbara, E. Somigliana, S. Bosari, Estrogen-progestins and progestins for the management of endometriosis, Fertil. Steril. 106 (2016) 1552–1571.e2, https://doi.org/10.1016/j.fertnstert.2016.10.022.
[72] A.M. Soliman, K.S. Coyne, E. Zaiser, J. Castelli-Haley, M.J. Fuldeore, The burden of endometriosis symptoms on health-related quality of life in women in the United States: a cross-sectional study, J. Psychosom. Obstet. & Gynecol. 38 (2017) 238–248, https://doi.org/10.1080/0167482X.2017.1289512.
[73] G. Kamergorodsky, A.L. Invitti, P. D'Amora, R.M. Parreira, A. Kopelman, T.C. S. Bonetti, M.J.B.C. Girão, E. Schor, Progesterone's role in deep infiltrating endometriosis: Progesterone receptor and estrogen metabolism enzymes expression and physiological changes in primary endometrial stromal cell culture, Mol. Cell. Endocrinol. 505 (2020) 110743, https://doi.org/10.1016/j.mce.2020.110743.
[74] P. Vierikko, A. Kauppila, L. Rönnberg, R. Vihko, Steroidal regulation of endometriosis tissue: lack of induction of 17β-hydroxysteroid dehydrogenase activity by progesterone, medroxyprogesterone acetate, or danazol, Fertil. Steril. 43 (1985) 218–224, https://doi.org/10.1016/S0015-0282(16)48376-7.
[75] G.R. Attia, K. Zeitoun, D. Edwards, A. Johns, B.R. Carr, S.E. Bulun, Progesterone Receptor Isoform A But Not B Is Expressed in Endometriosis1, J. Clin. Endocrinol. & Metab. 85 (2000) 2897–2902, https://doi.org/10.1210/jcem.85.8.6739.
[76] H. Tang, T. Lin, M. Wu, S. Tsai, Progesterone resistance in endometriosis: A pathophysiological perspective and potential treatment alternatives, Reprod. Med. & Biol. 23 (2024) e12588, https://doi.org/10.1002/rmb2.12588.
[77] J. Donnez, M.-M. Dolmans, Endometriosis and Medical Therapy: From Progestogens to Progesterone Resistance to GnRH Antagonists: A Review, JCM 10 (2021) 1085, https://doi.org/10.3390/jcm10051085.
[78] E.S. Surrey, GnRH agonists in the treatment of symptomatic endometriosis: a review, F. &S Rep. 4 (2023) 40–45, https://doi.org/10.1016/j.xfre.2022.11.009.

[79] E. Surrey, Endometriosis and Assisted Reproductive Technologies: Maximizing Outcomes, Semin. Reprod. Med. 31 (2013) 154–163, https://doi.org/10.1055/s-0032-1333481.
[80] J.Y. Wang, Y. Zhang, J. Ding, Oral Gonadotropin-Releasing Hormone Antagonists in the Treatment of Endometriosis: Advances in Research, J. Clin. Med. Res. 17 (2025) 299–308, https://doi.org/10.14740/jocmr6236.
[81] Y. Osuga, P.-L. Torng, C.-J. Jeng, Clinical studies investigating the use of leuprorelin in Asian women with endometriosis: a review, J. Obstet. Gynaecol. 39 (2019) 291–296, https://doi.org/10.1080/01443615.2018.1460584.
[82] A. Amirudin, S. Tjandra, Leuprorelin acetate hormone therapy in the management of ovarian endometriosis: A case report, Intern. Jrnl 8 (2025) 638–643, https://doi.org/10.33024/minh.v8i5.852.
[83] K. Techatraisak, A. Hestiantoro, R. Soon, M.J. Banal-Silao, M.-R. Kim, S.J. Seong, S.T. Hidayat, L. Cai, S. Shin, B.S. Lee, Impact of Long-Term Dienogest Therapy on Quality of Life in Asian Women with Endometriosis: the Prospective Non-Interventional Study ENVISIOeN, Reprod. Sci. 29 (2022) 1157–1169, https://doi.org/10.1007/s43032-021-00787-w.
[84] Committee Opinion No. 663: Aromatase Inhibitors in Gynecologic Practice, Obstet. Gynecol. 127 (2016) e170–e174, https://doi.org/10.1097/AOG.0000000000001484.
[85] P. Acién, I. Velasco, M. Acién, Anastrozole and levonorgestrel-releasing intrauterine device in the treatment of endometriosis: a randomized clinical trial, BMC Women'S. Health 21 (2021) 211, https://doi.org/10.1186/s12905-021-01347-9.
[86] F.M. Reis, S. Chouzenoux, M. Bourdon, M. Jeljeli, C. Chapron, F. Batteux, Effects of Ulipristal Acetate on Reactive Oxygen Species and Proinflammatory Cytokine Release by Epithelial and Stromal Cells from Human Endometrium and Endometriosis, Reprod. Sci. 31 (2024) 260–266, https://doi.org/10.1007/s43032-023-01341-6.
[87] Y.X. Zhang, Effect of mifepristone in the different treatments of endometriosis, Clin. Exp. Obstet. Gynecol. 43 (2016) 350–353, https://doi.org/10.12891/ceog2086.2016.
[88] M.S. Islam, S. Afrin, S.I. Jones, J. Segars, Selective Progesterone Receptor Modulators—Mechanisms and Therapeutic Utility, Endocr. Rev. 41 (2020) bnaa012, https://doi.org/10.1210/endrev/bnaa012.
[89] A. Wagenfeld, P.T.K. Saunders, L. Whitaker, H.O.D. Critchley, Selective progesterone receptor modulators (SPRMs): progesterone receptor action, mode of action on the endometrium and treatment options in gynecological therapies, Expert. Opin. Ther. Targets 20 (2016) 1045–1054, https://doi.org/10.1080/14728222.2016.1180368.
[90] L. Mei, J. Bao, L. Tang, C. Zhang, H. Wang, L. Sun, G. Ma, L. Huang, J. Yang, L. Zhang, K. Liu, C. Song, H. Sun, A novel mifepristone-loaded implant for long-term treatment of endometriosis: In vitro and in vivo studies, Eur. J. Pharm. Sci. 39 (2010) 421–427, https://doi.org/10.1016/j.ejps.2010.01.012.
[91] J. Słowik, W. Mika, I. Sieradzka, K. Wajda, W. Kostyniak, Current Approaches to the Treatment of Endometriosis: A Narrative Review, J. Educ. Health Sport. 87 (2026) 67581, https://doi.org/10.12775/JEHS.2026.87.67581.
[92] E. Lopez-Saldivar, Y. Gallardo-Castañeda, D. Glossman-Mitnik, N. Flores-Holguin, Fluorine-Modified SERMs: A DFT, ADMET, and Statistical Analysis of Toremifene and Raloxifene, ChemistrySelect 11 (2026) e02899, https://doi.org/10.1002/slct.202502899.
[93] T. Harada, I. Ohta, Y. Endo, H. Sunada, H. Noma, F. Taniguchi, SR-16234, a Novel Selective Estrogen Receptor Modulator for Pain Symptoms with Endometriosis: An Open-label Clinical Trial, Yonago Acta Med. 60 (2017) 227–233, https://doi.org/10.33160/yam.2017.12.003.
[94] S.N. Shapna, S. Das, S. Akter, M.R. Khan, Evidence from a Favorable Clinical Outcome, Ther. Role Danazol Scar Endometr. (2025), https://doi.org/10.5281/ZENODO.17256757.
[95] V. Patil, S. Jadhav, S. Mahajan, DEVELOPMENT AND OPTIMIZATION OF DANAZOL CO-CRYSTAL LOADED TABLET TO TREAT ENDOMETRIOSIS, Prospect. Pharm. Sci. (2025), https://doi.org/10.56782/pps.525.
[96] H.S. Taylor, M. Alderman Iii, T.M. D'Hooghe, A.T. Fazleabas, A.J. Duleba, Effect of simvastatin on baboon endometriosis, Biol. Reprod. 97 (2017) 32–38, https://doi.org/10.1093/biolre/iox058.
[97] K.-H. Wang, Y.-H. Chang, D.-C. Ding, Simvastatin inhibits the immunosuppressive effects of endometrial cancer-associated mesenchymal stem cells through TGF-β2/SMAD2/3 signaling and reduces tumor growth, Sci. Rep. 15 (2025) 21533, https://doi.org/10.1038/s41598-025-08686-9.
[98] S. Salam, F. Deeba, J. Banu, S. Ishrat, C. Saha, S. Sinha, P. Patel, M. Haque, Statins: Is it New Weaponry against Endometriosis? Adv. Human. Biol. 15 (2025) 267–277, https://doi.org/10.4103/aihb.aihb_25_25.
[99] L. Gibran, R.C. Maranhão, M.S. Abrão, E.C. Baracat, S. Podgaec, Could statins constitute a novel treatment for endometriosis? Systematic review of the literature, Eur. J. Obstet. & Gynecol. Reprod. Biol. 179 (2014) 153–158, https://doi.org/10.1016/j.ejogrb.2014.05.028.
[100] R. Michel, K.L. Vincent, G.W. Kirschen, M. Motamedi, J. Saada, J. Yang, B. Ozpolat, G.S. Kilic, M.A. Borahay, Simvastatin-loaded liposomal nanoparticles as treatment for adenomyosis in a patient-derived xenograft mouse model: a pilot study, J. Obstet. Gynaecol. 45 (2025) 2502083, https://doi.org/10.1080/01443615.2025.2502083.
[101] S. Afrin, M. Ali, M. El Sabeh, Q. Yang, A. Al-Hendy, M.A. Borahay, Simvastatin inhibits stem cell proliferation in human leiomyoma via TGF-β3 and Wnt/β-Catenin pathways, J. Cell. Mol. Med. 26 (2022) 1684–1698, https://doi.org/10.1111/jcmm.17211.
[102] M. Madlener, W.C. Parks, S. Werner, Matrix Metalloproteinases (MMPs) and Their Physiological Inhibitors (TIMPs) Are Differentially Expressed during Excisional Skin Wound Repair, Exp. Cell. Res. 242 (1998) 201–210, https://doi.org/10.1006/excr.1998.4049.
[103] A. Szóstek-Mioduchowska, M. Słowińska, J. Pacewicz, D.J. Skarzynski, K. Okuda, Matrix metallopeptidase expression and modulation by transforming growth factor-β1 in equine endometrosis, Sci. Rep. 10 (2020) 1119, https://doi.org/10.1038/s41598-020-58109-0.
[104] J. Ke, J. Ye, M. Li, Z. Zhu, The Role of Matrix Metalloproteinases in Endometriosis: A Potential Target, Biomolecules 11 (2021) 1739, https://doi.org/10.3390/biom11111739.
[105] T. Shimizu, Y. Iwamoto, Y. Yanagihara, K. Ikeda, K. Achiwa, Combined effects of synthetic lipid a analogs or bacterial lipopolysaccharide with glucosaminylmuramyl dipeptide on antitumor activity against meth a fibrosarcoma in mice, Int. J. Immunopharmacol. 14 (1992) 1415–1420, https://doi.org/10.1016/0192-0561(92)90013-B.
[106] G. Mittica, E. Ghisoni, G. Giannone, M. Aglietta, S. Genta, G. Valabrega, Checkpoint inhibitors in endometrial cancer: preclinical rationale and clinical activity, Oncotarget 8 (2017) 90532–90544, https://doi.org/10.18632/oncotarget.20042.
[107] K. Kiisholts, K. Kurrikoff, P. Arukuusk, L. Porosk, M. Peters, A. Salumets, Ü. Langel, Cell-Penetrating Peptide and siRNA-Mediated Therapeutic Effects on Endometriosis and Cancer In Vitro Models, Pharmaceutics 13 (2021) 1618, https://doi.org/10.3390/pharmaceutics13101618.
[108] L. Wei, X. Ma, Y. Hou, T. Zhao, R. Sun, C. Qiu, Y. Liu, Z. Qiu, Z. Liu, J. Jiang, Verteporfin reverses progestin resistance through YAP/TAZ-PI3K-Akt pathway in endometrial carcinoma, Cell. Death Discov. 9 (2023) 30, https://doi.org/10.1038/s41420-023-01319-y.
[109] F.J.M.E. Roumen, M.M.T. Op Ten Berg, E.H.M. Hoomans, The combined contraceptive vaginal ring (NuvaRing®): First experience in daily clinical practice in The Netherlands, Eur. J. Contracept. & Reprod. Health Care 11 (2006) 14–22, https://doi.org/10.1080/13625180500389547.
[110] J. Algorta, M. Diaz, R. De Benito, M. Lefebvre, E. Sicard, M. Furtado, P.A. Regidor, C. Ronchi, Pharmacokinetic bioequivalence, safety and acceptability of Ornibel®, a new polymer composition contraceptive vaginal ring (etonogestrel/ethinylestradiol 11.00/3.474 mg) compared with Nuvaring® (etonogestrel/ethinylestradiol 11.7/2.7 mg), Eur. J. Contracept. & Reprod. Health Care 22 (2017) 429–438, https://doi.org/10.1080/13625187.2017.1413179.
[111] R.K. Malcolm, K.-L. Edwards, P. Kiser, J. Romano, T.J. Smith, Advances in microbicide vaginal rings, Antivir. Res. 88 (2010) S30–S39, https://doi.org/10.1016/j.antiviral.2010.09.003.
[112] J.W. McBride, P. Boyd, N. Dias, D. Cameron, R.E. Offord, O. Hartley, V.L. Kett, R. K. Malcolm, Vaginal rings with exposed cores for sustained delivery of the HIV CCR5 inhibitor 5P12-RANTES, J. Control. Release 298 (2019) 1–11, https://doi.org/10.1016/j.jconrel.2019.02.003.
[113] R.I. Bjarnadóttir, M. Tuppurainen, S.R. Killick, Comparison of cycle control with a combined contraceptive vaginal ring and oral levonorgestrel/ethinyl estradiol, Am. J. Obstet. Gynecol. 186 (2002) 389–395, https://doi.org/10.1067/mob.2002.121103.
[114] G. Schmidt, S.-B. Andersson, Ö. Nordle, C.-J. Johansson, P.O. Gunnarsson, Release of 17-Beta-Oestradiol from a Vaginal Ring in Postmenopausal Women: Pharmacokinetic Evaluation, Gynecol. Obstet. Invest. 38 (1994) 253–260, https://doi.org/10.1159/000292492.
[115] F. Casper, E. Petri, Local Treatment of Urogenital Atrophy with an Estradiol-Releasing Vaginal Ring: A Comparative and a Placebo-Controlled Multicenter Study, Int. Urogynecology J. Pelvic Floor. Dysfunct. 10 (1999) 171–176, https://doi.org/10.1007/s001920050040.
[116] P. Boyd, B. Variano, P. Spence, C.F. McCoy, D.J. Murphy, Y.H. Dallal Bashi, R. K. Malcolm, vitro release testing methods for drug-releasing vaginal rings, J. Control. Release 313 (2019) 54–69, https://doi.org/10.1016/j.jconrel.2019.10.015.
[117] S. Koetsawang, J. Gao, U. Krishna, A. Cuadros, G.I. Dhall, R. Wyss, J.R. La Puenta, A.T.L. Andrade, T. Khan, E.S. Kononova, J.P. Lawson, U. Parekh, M. Elstein, V. Hingorani, N. Wang, Z. Yao, B.-M. Landgren, R. Boukhris, L. Lo, S. Boccard, D. Machin, A. Pinol, P.J. Rowe, Microdose intravaginal levonorgestrel contraception: A multicentre clinical trial, Contraception 41 (1990) 105–124, https://doi.org/10.1016/0010-7824(90)90141-H.
[118] V. Brache, Progestin-only contraceptive rings, Steroids 65 (2000) 687–691, https://doi.org/10.1016/S0039-128X(00)00175-6.
[119] R. Massai, E. Quinteros, M.V. Reyes, R. Caviedes, A. Zepeda, J.C. Montero, H. B. Croxatto, Extended use of a progesterone-releasing vaginal ring in nursing women: a phase II clinical trial, Contraception 72 (2005) 352–357, https://doi.org/10.1016/j.contraception.2005.05.004.
[120] A.L. Nelson, Transdermal contraception methods: today's patches and new options on the horizon, Expert. Opin. Pharmacother. 16 (2015) 863–873, https://doi.org/10.1517/14656566.2015.1022531.
[121] M. Notelovitz, D. Casselb, D. Hilleb, K.W. Furstb, M.-P. Dain, C. VandePol, D. Skarinskyb, Efficacy of continuous sequential transdermal estradiol and norethindrone acetate in relieving vasomotor symptoms associated with menopause, Am. J. Obstet. Gynecol. 182 (2000) 7–12, https://doi.org/10.1016/S0002-9378(00)70483-2.
[122] A. Marklund, A. Sjövall, L. Blomqvist, J. Carlson, K.A. Rodriguez-Wallberg, Endometriosis, the great imitator – a successful case of fertility preservation in a woman receiving sterilizing treatment due to a diagnosis of rectosigmoid carcinoma, Gynecol. Endocrinol. 35 (2019) 945–948, https://doi.org/10.1080/09513590.2019.1633298.

[123] A. Graham, Drugs in Gynaecology and Contraception, in: A. Khalil, A. Griffiths (Eds.), Part 1 MRCOG Synoptic Revision Guide, 1st ed., Cambridge University Press, 2023, pp. 186–209, https://doi.org/10.1017/9781108644464.020.
[124] C. Blacker, N. Brion, F. Caulin, C. Mayolle, J.Y. Reginster, A. Regnard, R. Scholler, Plasma Concentration of Estradiol After Transdermal Administration of Systen®50 (Evorel®) or Menorest®50, Clin. Drug. Investig. 11 (1996) 339–346, https://doi.org/10.2165/00044011-199611060-00004.
[125] L.J. Middleton, R. Champaneria, J.P. Daniels, S. Bhattacharya, K.G. Cooper, N. H. Hilken, P. O'Donovan, M. Gannon, R. Gray, K.S. Khan, on behalf of the International Heavy Menstrual Bleeding Individual Patient Data Meta-analysis Collaborative Group, Hysterectomy, endometrial destruction, and levonorgestrel releasing intrauterine system (Mirena) for heavy menstrual bleeding: systematic review and meta-analysis of data from individual patients, c3929–c3929, BMJ 341 (2010), https://doi.org/10.1136/bmj.c3929.
[126] Z. Qin, D. Zhang, G. Cao, H. Li, Progestin-based pharmacotherapy in fertility preservation in early endometrial cancer, Front. Oncol. 14 (2024) 1487008, https://doi.org/10.3389/fonc.2024.1487008.
[127] M. Mawet, F. Nollevaux, D. Nizet, F. Wijzen, V. Gordenne, N. Tasev, D. Segedi, B. Marinescu, A. Enache, V. Parhomenko, F. Frankenne, J.-M. Foidart, Impact of a new levonorgestrel intrauterine system, Levosert®, on heavy menstrual bleeding: results of a one-year randomised controlled trial, Eur. J. Contracept. & Reprod. Health Care 19 (2014) 169–179, https://doi.org/10.3109/13625187.2014.894184.
[128] S.B. Yisa, A.A. Okenwa, R.P. Husemeyer, Treatment of pelvic endometriosis with etonogestrel subdermal implant (Implanon®), J. Fam. Plann Reprod. Health Care 31 (2005) 67–70, https://doi.org/10.1783/0000000052972799.
[129] I. Reinecke, M. Schultze-Mosgau, R. Nave, H. Schmitz, B.A. Ploeger, Model-Based Dose Selection for Intravaginal Ring Formulations Releasing Anastrozole and Levonorgestrel Intended for the Treatment of Endometriosis Symptoms, J. Clin. Pharma 57 (2017) 640–651, https://doi.org/10.1002/jcph.846.
[130] M.J. Chen, M.D. Creinin, Removal of a Nonpalpable Etonogestrel Implant With Preprocedure Ultrasonography and Modified Vasectomy Clamp, Obstet. & Gynecol. 126 (2015) 935–938, https://doi.org/10.1097/AOG.0000000000001082.
[131] S. Fanse, Q. Bao, D.J. Burgess, Long-acting intrauterine systems: Recent advances, current challenges, and future opportunities, Adv. Drug. Deliv. Rev. 191 (2022) 114581, https://doi.org/10.1016/j.addr.2022.114581.
[132] V. Halpern, V. Brache, D. Taylor, A. Lendvay, L. Cochón, J.T. Jensen, L. J. Dorflinger, Clinical trial to evaluate pharmacokinetics and pharmacodynamics of medroxyprogesterone acetate after subcutaneous administration of Depo-Provera, Fertil. Steril. 115 (2021) 1035–1043, https://doi.org/10.1016/j.fertnstert.2020.11.002.
[133] A.M. Dlugi, J.D. Miller, J. Knittle, Lupron depot (leuprolide acetate for depot suspension) in the treatment of endometriosis: a randomized, placebo-controlled, double-blind study, Fertil. Steril. 54 (1990) 419–427, https://doi.org/10.1016/S0015-0282(16)53755-8.
[134] J.A. Rock, J.A. Truglia, R.J. Caplan, Zoladex (goserelin acetate implant) in the treatment of endometriosis: a randomized comparison with danazol. The Zoladex Endometriosis Study Group, Obstet. Gynecol. 82 (1993) 198–205.
[135] Leuprorelin-containing depot medicinal products - referral | European Medicines Agency (EMA), (2019). ⟨https://www.ema.europa.eu/en/medicines/human/referrals/leuprorelin-containing-depot-medicinal-products⟩ (accessed February 12, 2026).
[136] B.E. Barton, J.A. Erickson, S.I. Allred, J.M. Jeffries, K.K. Stephens, M.I. Hunter, K. A. Woodall, W. Winuthayanon, Reversible female contraceptives: historical, current, and future perspectives, Biol. Reprod. 110 (2024) 14–32, https://doi.org/10.1093/biolre/ioad154.
[137] B. Liang, L. Wu, H. Xu, C.W. Cheung, W.Y. Fung, S.W. Wong, C.C. Wang, Efficacy, safety and recurrence of new progestins and selective progesterone receptor modulator for the treatment of endometriosis: a comparison study in mice, Reprod. Biol. Endocrinol. 16 (2018) 32, https://doi.org/10.1186/s12958-018-0347-9.
[138] B. Cho, J.-W. Roh, J. Park, K. Jeong, T.-H. Kim, Y.S. Kim, Y.-S. Kwon, C.-H. Cho, S. H. Park, S.H. Kim, Safety and Effectiveness of Dienogest (Visanne®) for Treatment of Endometriosis: A Large Prospective Cohort Study, Reprod. Sci. 27 (2020) 905–915, https://doi.org/10.1007/s43032-019-00094-5.
[139] M.D.P. Andres, L.A. Lopes, E.C. Baracat, S. Podgaec, Dienogest in the treatment of endometriosis: systematic review, Arch. Gynecol. Obstet. 292 (2015) 523–529, https://doi.org/10.1007/s00404-015-3681-6.
[140] P. Wright, Healing Pelvic Pain, 2023.
[141] X. Yang, G. Wu, L. Luo, Q. He, X. Wu, R. Xu, The effects of the combination of Yasmin and shaofuzhuyu capsules on MBV, endometrial thickness, and disease recurrence in hysteroscopic polypectomy patients, (n.d.).
[142] L.C. Gemmell, K.E. Webster, S. Kirtley, K. Vincent, K.T. Zondervan, C.M. Becker, The management of menopause in women with a history of endometriosis: a systematic review, Human. Reprod. Update 23 (2017) 481–500, https://doi.org/10.1093/humupd/dmx011.
[143] Northwestern University, Phase IV Pilot. Study Ulipristal Acetate Treat. Endometr. -Relat. Pelvic Pain. Clin. Gov. (2024). ⟨https://clinicaltrials.gov/study/NCT02213081⟩ (accessed February 12, 2026).
[144] Mansoura University, gov, Goserline Acetate Versus Dienogest Treat. Pain. Assoc. Endometr. Clin. (2021). ⟨https://clinicaltrials.gov/study/NCT05013242⟩ (accessed February 12, 2026).
[145] Assistance Publique - Hôpitaux de Paris, Pilot Phase II, Randomized, and Control in Double Blind Placebo Effectiveness a 3 Months on Bleeding Fibroids Treatment With ULIPRISTAL ACETATE 10 mg/Day in Patients Suffering From Symptomatic Endometriosis, clinicaltrials.gov, 2022. ⟨https://clinicaltrials.gov/study/NCT02587000⟩ (accessed February 12, 2026).
[146] G. Vissers, M. Giacomozzi, W. Verdurmen, R. Peek, A. Nap, The role of fibrosis in endometriosis: a systematic review, Human. Reprod. Update 30 (2024) 706–750, https://doi.org/10.1093/humupd/dmae023.
[147] D.R. Friend, Drug delivery for the treatment of endometriosis and uterine fibroids, Drug. Deliv. Transl. Res. 7 (2017) 829–839, https://doi.org/10.1007/s13346-017-0423-2.
[148] O.S. Fenton, K.N. Olafson, P.S. Pillai, M.J. Mitchell, R. Langer, Advances in Biomaterials for Drug Delivery, Adv. Mater. 30 (2018) 1705328, https://doi.org/10.1002/adma.201705328.
[149] A. Bedin, R.C. Maranhão, E.R. Tavares, P.O. Carvalho, E.C. Baracat, S. Podgaec, Nanotechnology for the treatment of deep endometriosis: uptake of lipid core nanoparticles by LDL receptors in endometriotic foci, Clinics 74 (2019) e989, https://doi.org/10.6061/clinics/2019/e989.
[150] Z. Liao, J. Li, S. Xian, J. Huang, W. Tian, Q. Zhong, W. Shi, X. Li, X. Shuai, S. Chen, A dual-targeted liposomal nanosystem for co-delivery of estrogen receptor β antagonist and disulfiram for the non-hormonal treatment of endometriosis, Acta Biomater. 208 (2025) 456–471, https://doi.org/10.1016/j.actbio.2025.10.054.
[151] J. Ma, Z. Liao, J. Li, X. Li, H. Guo, Q. Zhong, J. Huang, X. Shuai, S. Chen, A cRGD-modified liposome for targeted delivery of artesunate to inhibit angiogenesis in endometriosis, Biomater. Sci. 13 (2025) 1045–1058, https://doi.org/10.1039/D4BM01506A.
[152] Q. Chen, J. Wang, W. Li, L. Shang, D. Wang, P. Duan, Drug Screening of Primary Human Endometriotic Cells Based on Micro-Encapsulating Microfluidic Chip, Adv. Sci. 12 (2025) 2504647, https://doi.org/10.1002/advs.202504647.
[153] S. Teworte, M.C. Behrens, M. Widhe, L. Gurzeler, M. Hedhammar, P. Luciani, A Fibronectin (FN)-Silk 3D Cell Culture Model as a Screening Tool for Repurposed Antifibrotic Drug Candidates for Endometriosis, Small (2025) 2409126, https://doi.org/10.1002/smll.202409126.
[154] C. Puglia, F. Bonina, Lipid nanoparticles as novel delivery systems for cosmetics and dermal pharmaceuticals, Expert. Opin. Drug. Deliv. 9 (2012) 429–441, https://doi.org/10.1517/17425247.2012.666967.
[155] M. Mehta, T.A. Bui, X. Yang, Y. Aksoy, E.M. Goldys, W. Deng, Lipid-Based Nanoparticles for Drug/Gene Delivery: An Overview of the Production Techniques and Difficulties Encountered in Their Industrial Development, ACS Mater. Au 3 (2023) 600–619, https://doi.org/10.1021/acsmaterialsau.3c00032.
[156] H. Hajipour, R. Sambrani, M. Ghorbani, Z. Mirzamohammadi, M. Nouri, Sildenafil citrate–loaded targeted nanostructured lipid carrier enhances receptivity potential of endometrial cells via LIF and VEGF upregulation, Naunyn-Schmiede 'S. Arch. Pharmacol. 394 (2021) 2323–2331, https://doi.org/10.1007/s00210-021-02153-8.
[157] S. Javid, N. Ziamajidi, S. Foroughi, R. Abbasalipourkabir, Effects of tamoxifen-loaded solid lipid nanoparticles on the estrogen receptor-α (ER-α) and vascular endothelial growth factor-A (VEGF-A) genes expression in the endometrial tissue of ovariectomized female Sprague-Dawley rats, Int. J. Biol. Macromol. 96 (2017) 706–712, https://doi.org/10.1016/j.ijbiomac.2016.12.055.
[158] R.C. Maranhão, I.A. Roland, O. Toffoletto, J. Antonio Ramires, R.P. Gonçalves, C. H. Mesquita, F. Pileggi, Plasma kinetic behavior in hyperlipidemic subjects of a lipidic microemulsion that binds to low density lipoprotein receptors, Lipids 32 (1997) 627–633, https://doi.org/10.1007/s11745-997-0080-6.
[159] R.C. Maranhão, T.B. Cesar, S.R. Pedroso-Mariani, M.H. Hirata, C.H. Mesquita, Metabolic behavior in rats of a nonprotein microemulsion resembling low-density lipoprotein, Lipids 28 (1993) 691–696, https://doi.org/10.1007/BF02535988.
[160] R.C. Maranhão, B. Garicochea, E.L. Silva, P. Dorlhiac-Llacer, S.M.S. Cadena, I.J. C. Coelho, J.C. Meneghetti, F.J.C. Pileggi, D.A.F. Chamone, Plasma Kinetics and Biodistribution of a Lipid Emulsion Resembling Low-Density Lipoprotein in Patients with Acute Leukemia, Cancer Res. 54 (1994) 4660–4666.
[161] R. Maranhão, S. Graziani, N. Yamaguchi, R. Melo, M. Latrilha, D. Rodrigues, R. Couto, S. Schreier, A. Buzaid, Association of carmustine with a lipid emulsion: in vitro, in vivo and preliminary studies in cancer patients, Cancer Chemother. Pharmacol. 49 (2002) 487–498, https://doi.org/10.1007/s00280-002-0437-3.
[162] R. Avila-Tavares, L. Gibran, L.G.O. Brito, T.M. Tavoni, M.O. Gonçalves, E. C. Baracat, R.C. Maranhão, S. Podgaec, Pilot study of treatment of patients with deep infiltrative endometriosis with methotrexate carried in lipid nanoparticles, Arch. Gynecol. Obstet. 309 (2023) 659–667, https://doi.org/10.1007/s00404-023-07246-8.
[163] Y. Peng, M. Zhang, J. Yan, R. Wang, Y. Xin, X. Zheng, L. Zhu, W. Fei, M. Zhao, Emerging bioengineering breakthroughs in precision diagnosis and therapy for endometriosis and adenomyosis, J. Mater. Chem. B 13 (2025) 742–762, https://doi.org/10.1039/D4TB01755B.
[164] V. Herrara, D. Tarab-Ravski, S.C. Chauhan, N. Narang, M. Mirazul Islam, D. Peer, R. Prasad, M.M. Yallapu, Nanotechnology strategies for endometrium health: Are we on the right track? Bioact. Mater. 54 (2025) 423–449, https://doi.org/10.1016/j.bioactmat.2025.08.016.
[165] P. Yuan, B. Chen, Y. Huang, X. Xin, Long-term regression of experimental endometriosis in a rat model treated with local application of levonorgestrel-loaded biodegradable microspheres, Human. Reprod. 27 (2012) 2089–2095, https://doi.org/10.1093/humrep/des142.
[166] Z. Tang, X. Zhang, S. Meng, X. Yi, Y. Liu, K. Wu, Y. Li, S. Peng, H. Guo, M. Du, Y. Z. Zhu, X. Wang, Cell membrane camouflaged and ROS responsive nanosomes for targeted endometriosis therapy via reversing inflammatory, low-autophagy, and immunotolerant microenvironment, Chem. Eng. J. 493 (2024) 152697, https://doi.org/10.1016/j.cej.2024.152697.

[167] L. Xu, X. Wang, Y. Liu, G. Yang, R.J. Falconer, C.-X. Zhao, Lipid Nanoparticles for Drug Delivery, Adv. NanoBiomed Res. 2 (2022) 2100109, https://doi.org/10.1002/anbr.202100109.
[168] S. Garzon, A.S. Laganà, F. Barra, J. Casarin, A. Cromi, R. Raffaelli, S. Uccella, M. Franchi, F. Ghezzi, S. Ferrero, Novel drug delivery methods for improving efficacy of endometriosis treatments, Expert. Opin. Drug. Deliv. 18 (2021) 355–367, https://doi.org/10.1080/17425247.2021.1829589.
[169] M.A. Beach, U. Nayanathara, Y. Gao, C. Zhang, Y. Xiong, Y. Wang, G.K. Such, Polymeric Nanoparticles for Drug Delivery, Chem. Rev. 124 (2024) 5505–5616, https://doi.org/10.1021/acs.chemrev.3c00705.
[170] N. Wang, B. Liu, L. Liang, Y. Wu, H. Xie, J. Huang, X. Guo, J. Tan, X. Zhan, Y. Liu, L. Wang, P. Ke, Antiangiogenesis Therapy of Endometriosis Using PAMAM as a Gene Vector in a Noninvasive Animal Model, BioMed. Res. Int. 2014 (2014) 1–11, https://doi.org/10.1155/2014/546479.
[171] M.A. Kotb, I.A. Abdelmawgood, A.A. WalyEldeen, M.H. Abdelaziz, M.L. Khalaf, A. S. Mohamed, A.E. Dakrory, S.A. Ibrahim, Chrysin-loaded PLGA nanoparticles alleviate the implantation of endometriotic lesions via attenuation of peritoneal inflammation and downregulating NF-κB activation-driven expression of angiogenic factors, J. Drug. Deliv. Sci. Technol. 109 (2025) 106984, https://doi.org/10.1016/j.jddst.2025.106984.
[172] Q. Liu, P. Ma, L. Liu, G. Ma, J. Ma, X. Liu, Y. Liu, W. Lin, Y. Zhu, Evaluation of PLGA containing anti -CTLA4 inhibited endometriosis progression by regulating CD4 + CD25 + Treg cells in peritoneal fluid of mouse endometriosis model, Eur. J. Pharm. Sci. 96 (2017) 542–550, https://doi.org/10.1016/j.ejps.2016.10.031.
[173] T. Hirakawa, K. Nasu, W. Abe, Y. Aoyagi, M. Okamoto, K. Kai, K. Takebayashi, H. Narahara, miR-503, a microRNA epigenetically repressed in endometriosis, induces apoptosis and cell-cycle arrest and inhibits cell proliferation, angiogenesis, and contractility of human ovarian endometriotic stromal cells, Hum. Reprod. 31 (2016) 2587–2597, https://doi.org/10.1093/humrep/dew217.
[174] S. Chaichian, A. Mehdizadeh Kashi, kobra, V. Tehermanesh, S. pirhajati Mahabadi, N. Minaeian, Eslahi, Effect of PLGA nanoparticle-mediated delivery of miRNA 503 on the apoptosis of ovarian endometriosis cells, Cell. J. (2022), https://doi.org/10.22074/cellj.2022.557554.1069.
[175] T. Furst, G.R. Dakwar, E. Zagato, A. Lechanteur, K. Remaut, B. Evrard, K. Braeckmans, G. Piel, Freeze-dried mucoadhesive polymeric system containing pegylated lipoplexes: Towards a vaginal sustained released system for siRNA, J. Control. Release 236 (2016) 68–78, https://doi.org/10.1016/j.jconrel.2016.06.028.
[176] M. Zhang, Y. Ye, Z. Chen, X. Wu, Y. Chen, P. Zhao, M. Zhao, C. Zheng, Targeting delivery of mifepristone to endometrial dysfunctional macrophages for endometriosis therapy, Acta Biomater. 189 (2024) 505–518, https://doi.org/10.1016/j.actbio.2024.09.037.
[177] M. Zhao, J.-L. Cheng, J.-J. Yan, F.-Y. Chen, J.-Z. Sheng, D.-L. Sun, J. Chen, J. Miao, R.-J. Zhang, C. Zheng, H.-F. Huang, Hyaluronic acid reagent functional chitosan-PEI conjugate with AQP2-siRNA suppressed endometriotic lesion formation, IJN (2016) 1323, https://doi.org/10.2147/IJN.S99692.
[178] M. Aloisi, G. Rossi, S. Cecconi, The Dual Role of Nanomaterials in Ovarian Cancer and Female Fertility as Anti- and Prooxidants, Antioxidants 14 (2025) 1066, https://doi.org/10.3390/antiox14091066.
[179] Y. Park, A.A. Demessie, A. Luo, O.R. Taratula, A.S. Moses, P. Do, L. Campos, Y. Jahangiri, C.R. Wyatt, H.A. Albarqi, K. Farsad, O.D. Slayden, O. Taratula, Targeted Nanoparticles with High Heating Efficiency for the Treatment of Endometriosis with Systemically Delivered Magnetic Hyperthermia, Small 18 (2022) 2107808, https://doi.org/10.1002/smll.202107808.
[180] K.N. Dodds, V. Fattori, N.A. Andrews, C.B. Appleyard, J.A. Christianson, R. Gomez, S.L. McAllister, S.A. Missmer, J. Nagel, P. Nunez-Badinez, M.S. Rogers, P.T.K. Saunders, M.A. Tejada, K. Vincent, L. Hummelshoj, K.L. Bruner-Tran, E. Greaves, for the EPHect Experimental Models Working Group, N.A. Andrews, M.S. Anglesio, C.B. Appleyard, J. Arosh, C.M. Becker, K.L. Bruner-Tran, K. A. Burns, R.L. Chandler, J.A. Christianson, F.L. Cousins, K.N. Dodds, V. Fattori, A. Fazleabas, C. Gargett, J.S. Gnecco, R. Gomez, M. Götte, E. Greaves, L. G. Griffith, P.G. Groothuis, R. Grümmer, S.-W. Guo, S.M. Hawkins, M.L. Hull, L. Hummelshoj, M. Hutchinson, M.G. Ibrahim, E.E. Marr, S.L. McAllister, S. A. Missmer, J. Mogill, J. Nagel, W.B. Nothnick, P. Nunez-Badinez, K.G. Osteen, D. Peterse, M.S. Rogers, A. Romano, P.T.K. Saunders, M.Á. Tejada, K.L. Sharpe-Timms, W.A. Verri, P. Viganó, K. Vincent, WERF Endometriosis Phenome and Biobanking Harmonisation Project for Experimental Models in Endometriosis Research (EPHect-EM-Pain): methods to assess pain behaviour in rodent models of endometriosis, in: Molecular Human Reproduction, 31, 2025, https://doi.org/10.1093/molehr/gaaf023.
[181] A. Tamadon, A. Zare, M. Mahdipour, A. Salehpour, N.M. Mussin, A.A. Mussina, R. A. Aringazina, A. Duisenova, K.R. Zhilisbayeva, M.A. Kurmanalina, C. Fu, From Mice to Primates: Assessing Hormone-Based Endometriosis Models for Preclinical and Therapeutic Insights, Iran. J. Med. Sci. 50 (2025), https://doi.org/10.30476/ijms.2025.105805.3975.
[182] Y. Liu, L.-N. Tian, Z.-Y. Wu, Z.-X. Wang, M.K. Khan, J. Ding, R. Jia, F.-G. Wu, Biomaterials for endometriosis treatment: Design, advances, and prospects, Acta Biomater. 216 (2026) 1–21, https://doi.org/10.1016/j.actbio.2026.03.034.
[183] M.S. Rahman, K. Hadrick, S.-J. Chung, I. Carley, J.-Y. Yoo, S. Nahar, T.H. Kim, T. Kim, J.-W. Jeong, Nanoceria as a non-steroidal anti-inflammatory drug for endometriosis theranostics, J. Control. Release 378 (2025) 1015–1029, https://doi.org/10.1016/j.jconrel.2024.12.074.
[184] L. Benameur, M. Auffan, M. Cassien, W. Liu, M. Culcasi, H. Rahmouni, P. Stocker, V. Tassistro, J.-Y. Bottero, J. Rose, A. Botta, S. Pietri, DNA damage and oxidative stress induced by CeO_2 nanoparticles in human dermal fibroblasts: Evidence of a clastogenic effect as a mechanism of genotoxicity, Nanotoxicology 9 (2015) 696–705, https://doi.org/10.3109/17435390.2014.968889.
[185] B. Courbiere, M. Auffan, R. Rollais, V. Tassistro, A. Bonnefoy, A. Botta, J. Rose, T. Orsière, J. Perrin, Ultrastructural Interactions and Genotoxicity Assay of Cerium Dioxide Nanoparticles on Mouse Oocytes, IJMS 14 (2013) 21613–21628, https://doi.org/10.3390/ijms141121613.
[186] F. Ariu, L. Bogliolo, A. Pinna, L. Malfatti, P. Innocenzi, L. Falchi, D. Bebbere, S. Ledda, Cerium oxide nanoparticles (CeO2 NPs) improve the developmental competence of in vitro-matured prepubertal ovine oocytes, Reprod. Fertil. Dev. 29 (2017) 1046–1056, https://doi.org/10.1071/RD15521.
[187] M. Lakshmanan, M. Saini, M. Nune, Exploring the innovative application of cerium oxide nanoparticles for addressing oxidative stress in ovarian tissue regeneration, J. Ovarian Res. 17 (2024) 241, https://doi.org/10.1186/s13048-024-01566-2.
[188] G. Wyszogrodzka-Gaweł, M. Stróżyk, M. Skoda, M. Osial, E. Baran, A. Mendyk, Target, Treat, and Track: Superparamagnetic Iron Oxide Nanoparticles (SPION) Driven Theranostic Delivery of Antimicrobials to the Lungs, NSA 18 (2025) 405–421, https://doi.org/10.2147/NSA.S539424.
[189] N. Elahi, M. Rizwan, Progress and prospects of magnetic iron oxide nanoparticles in biomedical applications: A review, Artif. Organs 45 (2021) 1272–1299, https://doi.org/10.1111/aor.14027.
[190] Y.A. Fahim, I.W. Hasani, W. Mahmoud Ragab, Promising biomedical applications using superparamagnetic nanoparticles, Eur. J. Med. Res. 30 (2025) 441, https://doi.org/10.1186/s40001-025-02696-z.
[191] S. Nejadali Chaleshtari, E. Amini, F. Baniasadi, S. Tavana, M. Ghalamboran, Oocyte maturation, fertilization, and embryo development in vitro by green and chemical iron oxide nanoparticles: a comparative study, Sci. Rep. 14 (2024) 14157, https://doi.org/10.1038/s41598-024-65121-1.
[192] M. Osial, G.N. Ha, V.H. Vu, P.T. Nguyen, D. Nieciecka, P. Pietrzyk-Thel, O. Urbanek, S.J. Olusegun, S. Wilczewski, M. Giersig, H.T. Do, T.T.M. Dinh, One-pot synthesis of magnetic hydroxyapatite (SPION/HAp) for 5-fluorouracil delivery and magnetic hyperthermia, J. Nanopart. Res. 26 (2024) 7, https://doi.org/10.1007/s11051-023-05916-x.
[193] T. Kalyani, A. Sangili, A. Nanda, S. Prakash, A. Kaushik, S. Kumar Jana, Bio-nanocomposite based highly sensitive and label-free electrochemical immunosensor for endometriosis diagnostics application, Bioelectrochemistry 139 (2021) 107740, https://doi.org/10.1016/j.bioelechem.2021.107740.
[194] T.J. Carter, G. Agliardi, F. Lin, M. Ellis, C. Jones, M. Robson, A. Richard-Londt, P. Southern, M. Lythgoe, M. Zaw Thin, V. Ryzhov, R.T.M. De Rosales, C. Gruettner, M.R.A. Abdollah, R.B. Pedley, Q.A. Pankhurst, T.L. Kalber, S. Brandner, S. Quezada, P. Mulholland, M. Shevtsov, K. Chester, Potential of Magnetic Hyperthermia to Stimulate Localized Immune Activation, Small 17 (2021) 2005241, https://doi.org/10.1002/smll.202005241.
[195] M. Osial, A. Pregowska, The Application of Artificial Intelligence in Magnetic Hyperthermia Based Research, Future Internet 14 (2022) 356, https://doi.org/10.3390/fi14120356.
[196] J. Santos, J.C. Silva, M.A. Valente, T. Vieira, P.I.P. Soares, Enhancing magnetic hyperthermia: Investigating iron oxide nanoparticle coating and stability, Nanotechnology 7 (2025) 100141, https://doi.org/10.1016/j.nxnano.2025.100141.
[197] Y. Gao, H. Qian, X. Tang, X. Du, G. Wang, H. Zhang, F. Ye, T. Liu, Superparamagnetic iron oxide nanoparticle-mediated expression of miR-326 inhibits human endometrial carcinoma stem cell growth, IJN 14 (2019) 2719–2731, https://doi.org/10.2147/IJN.S200480.
[198] M. Chen, Q. Zhou, C. Chen, Y. Liu, X. Wang, Synergic combination of paclitaxel and irinotecan loaded poly (lactic-co-glycolic acid) nanocomplexes for MRI and the treatment of endometrial cancer, Mater. Express (2021).
[199] H.J. Lee, H.J. Lee, J.M. Lee, Y. Chang, S.T. Woo, Ultrasmall superparamagnetic iron oxides enhanced MR imaging in rats with experimentally induced endometriosis, Magn. Reson. Imaging 30 (2012) 860–868, https://doi.org/10.1016/j.mri.2012.02.020.
[200] K. Lu, R. Zhang, H. Wang, C. Li, Z. Yang, K. Xu, X. Cao, N. Wang, W. Cai, J. Zeng, M. Gao, PEGylated Ultrasmall Iron Oxide Nanoparticles as MRI Contrast Agents for Vascular Imaging and Real-Time Monitoring, ACS Nano 19 (2025) 3519–3530, https://doi.org/10.1021/acsnano.4c13356.
[201] H. Zhang, J. Li, W. Sun, Y. Hu, G. Zhang, M. Shen, X. Shi, Hyaluronic Acid-Modified Magnetic Iron Oxide Nanoparticles for MR Imaging of Surgically Induced Endometriosis Model in Rats, PLoS. ONE 9 (2014) e94718, https://doi.org/10.1371/journal.pone.0094718.
[202] M.A. Jedryka, P. Klimczak, M. Kryszpin, T. Poprawski, A. Czekanski, P. Lepka, R. Matkowski, Superparamagnetic Iron Oxide Nanoparticles as a Tracer for Sentinel Lymph Node Mapping in Endometrial Cancer, IJMS 26 (2025) 781, https://doi.org/10.3390/ijms26020781.
[203] J. Su, P. Zhang, X. Han, C. Sui, A.F. El-kott, A.S. Alshehri, M.A. AlShehri, K. Morsy, S. Negm, Decorated of silver nanoparticles overguar gum-encapsulated Fe3O4 NPs for the catalytic reduction of 4-nitrophenol followed by study of anti-endometrial cancer potential, J. Organomet. Chem. 1015 (2024) 123225, https://doi.org/10.1016/j.jorganchem.2024.123225.
[204] Q. Zhang, S. Wu, Y. Li, M. Lai, Q. Li, C. Fu, Z. Yao, J. Zhang, Endometriosis-targeted MRI imaging using bevacizumab-modified nanoparticles aimed at vascular endothelial growth factor, Nanoscale Adv. 5 (2023) 3994–4001, https://doi.org/10.1039/D2NA00787H.
[205] J. Lee, S.G. Yeo, J.M. Lee, S.S. Kim, J.-W. Lee, N. Chung, D.C. Park, Expression of Free Radicals and Reactive Oxygen Species in Endometriosis: Current Knowledge and Its Implications, Antioxidants 14 (2025) 877, https://doi.org/10.3390/antiox14070877.

[206] Q. Sun, J. Chen, M. Yang, X. Ding, H. Zhang, Z. Huang, Q. Huang, Q. Chen, Macrophage membrane-decorated MnO2 nanozyme catalyzed the scavenging of estradiol for endometriosis treatment, Colloids Surf. B Biointerfaces 233 (2024) 113633, https://doi.org/10.1016/j.colsurfb.2023.113633.
[207] J.V. Jokerst, M. Thangaraj, P.J. Kempen, R. Sinclair, S.S. Gambhir, Photoacoustic Imaging of Mesenchymal Stem Cells in Living Mice *via* Silica-Coated Gold Nanorods, ACS Nano 6 (2012) 5920–5930, https://doi.org/10.1021/nn302042y.
[208] T.T. Nguyen, H.N. Nguyen, T.H.L. Nghiem, X.-H. Do, T.T. To, T.X.P. Do, D.L. Do, H.G. Nguyen, H.M. Nguyen, N.D. Nguyen, M.Q. Luu, T.N. Nguyen, T.B.N. Nguyen, V.T. Nguyen, V.T. Pham, U.T.T. Than, T.M.N. Hoang, Author Correction: High biocompatible FITC-conjugated silica nanoparticles for cell labeling in both in vitro and in vivo models, Sci. Rep. 15 (2025) 25104, https://doi.org/10.1038/s41598-025-10067-1.
[209] R.M. Marquardt, M. Nafiujjaman, T.H. Kim, S.-J. Chung, K. Hadrick, T. Kim, J.-W. Jeong, A Mouse Model of Endometriosis with Nanoparticle Labeling for In Vivo Photoacoustic Imaging, Reprod. Sci. 29 (2022) 2947–2959, https://doi.org/10.1007/s43032-022-00980-5.
[210] P.P.P. Kumar, S. Chung, K. Hadrick, M.L. Hill, M. Lee, T.H. Kim, J. Jeong, T. Kim, Noninvasive Detection and Thermal Ablation Therapy of Endometriosis Using Silica-Coated Gold Nanorods, Adv. NanoBiomed Res. 5 (2025) 2500101, https://doi.org/10.1002/anbr.202500101.
[211] H. Gamal, W. Tawfik, H.H. El-Sayyad, H.M. Fahmy, A.N. Emam, H.A. El-Ghaweet, Efficacy of polyvinylpyrrolidone-capped gold nanorods against 7,12 dimethylbenz(a)anthracene-induced oviduct and endometrial cancers in albino rats, Egypt. J. Basic. Appl. Sci. 10 (2023) 274–289, https://doi.org/10.1080/2314808X.2023.2185615.
[212] D. Ke, W. Li, Q. Chen, L. Luo, Y. Wang, F. Meng, Y. Sun, Application of nanoparticles in the therapeutic management of endometrial cancer, Eur. J. Med. Res. 31 (2026) 201, https://doi.org/10.1186/s40001-025-03623-y.
[213] C. Volpini, N. Bloise, C. Casali, B. Albini, M. Dominoni, F. Barra, M. Biggiogera, P. Galinetto, B. Gardella, V.G. Vellone, S. Ferrero, P. Minzioni, L. Visai, AntiCD44 antibody-conjugated gold nanoparticles for targeted photothermal therapy of endometriotic cells, Biomater. Sci. 13 (2025) 5164–5183, https://doi.org/10.1039/D5BM00701A.
[214] X. Guo, W. Li, J. Zhou, W. Hou, X. Wen, H. Zhang, F. Kong, L. Luo, Q. Li, Y. Du, J. You, Specific Photothermal Ablation Therapy of Endometriosis by Targeting Delivery of Gold Nanospheres, Small 13 (2017) 1603270, https://doi.org/10.1002/smll.201603270.
[215] L. Simón-Gracia, K. Kiisholts, V. Petrikaitė, A. Tobi, M. Saare, P. Lingasamy, M. Peters, A. Salumets, T. Teesalu, Homing Peptide-Based Targeting of Tenascin-C and Fibronectin in Endometriosis, Nanomaterials 11 (2021) 3257, https://doi.org/10.3390/nano11123257.
[216] A.M. Aboelmaaty, M.A. Sayed, M.A. Elgabry, M.S. Kotp, G.I. Fouad, M.E. El-Shamarka, S.T. Omara, Therapeutic effects of silver nanoparticles on-induced endometritis in rats, Egyptian Pharmaceutical Journal 21(4), 456–471 (n.d.).
[217] A.P. Lytvynenko, L.S. Rieznichenko, V.A. Sribna, M.I. Stupchuk, N.G. Grushka, A. A. Shepel, T.Yu Voznesenska, T.V. Blashkiv, O.N. Kaleynykova, Functional status of reproductive system under treatment of silver nanoparticles in female mice, Int. J. Reprod. Contracept. Obstet. Gynecol. 6 (2017) 1713, https://doi.org/10.18203/2320-1770.ijrcog20171930.
[218] A. Chinnathambi, T. Awad Alahmadi, S. Ali Alharbi, Biogenesis of copper nanoparticles (Cu-NPs) using leaf extract of *Allium noeanum*, antioxidant and *in-vitro* cytotoxicity, Artif. Cells Nanomed. Biotechnol. 49 (2021) 500–510, https://doi.org/10.1080/21691401.2021.1926275.
[219] S. Boroumand, S. Hosseini, Z. Pashandi, R. Faridi-Majidi, M. Salehi, Curcumin-loaded nanofibers for targeting endometriosis in the peritoneum of a mouse model, J. Mater. Sci Mater. Med. 31 (2020) 8, https://doi.org/10.1007/s10856-019-6337-4.
[220] A. Blakney, Y. Jiang, K. Woodrow, E. Krogstad, Delivery of multipurpose prevention drug combinations from electrospun nanofibers using composite microarchitectures, IJN (2014) 2967, https://doi.org/10.2147/IJN.S61664.
[221] F. Brako, R. Thorogate, S. Mahalingam, B. Raimi-Abraham, D.Q.M. Craig, M. Edirisinghe, Mucoadhesion of Progesterone-Loaded Drug Delivery Nanofiber Constructs, ACS Appl. Mater. Interfaces 10 (2018) 13381–13389, https://doi.org/10.1021/acsami.8b03329.
[222] C. Karuppannan, M. Sivaraj, J.G. Kumar, R. Seerangan, S. Balasubramanian, D. R. Gopal, Fabrication of Progesterone-Loaded Nanofibers for the Drug Delivery Applications in Bovine, Nanoscale Res. Lett. 12 (2017) 116, https://doi.org/10.1186/s11671-016-1781-2.
[223] F. Brako, B.T. Raimi-Abraham, S. Mahalingam, D.Q.M. Craig, M. Edirisinghe, The development of progesterone-loaded nanofibers using pressurized gyration: A novel approach to vaginal delivery for the prevention of pre-term birth, Int. J. Pharm. 540 (2018) 31–39, https://doi.org/10.1016/j.ijpharm.2018.01.043.
[224] J.E. Oliveira, E.S. Medeiros, L. Cardozo, F. Voll, E.H. Madureira, L.H.C. Mattoso, O.B.G. Assis, Development of poly(lactic acid) nanostructured membranes for the controlled delivery of progesterone to livestock animals, Materials Science Engineering C 33 (2013) 844–849, https://doi.org/10.1016/j.msec.2012.10.032.
[225] G.O. Do Nascimento Soares, R. Ribeiro Lima Machado, M. Mendonça Diniz, A. B. Da Silva, Electrospun progesterone-loaded cellulose acetate nanofibers and their drug sustained-release profiles, Polym. Eng. & Sci. 60 (2020) 3231–3243, https://doi.org/10.1002/pen.25549.
[226] M. Lavanya, S. Jeyakumar, V.G. Veerappa, H.A. Pushpadhas, K.P. Ramesha, A. Kumaresan, A. Manimaran, F.M. Eljeeva Emerald, Fabrication and characterization of progesterone loaded pullulan nanofibers for controlled release, J. Drug. Deliv. Sci. Technol. 91 (2024) 105193, https://doi.org/10.1016/j.jddst.2023.105193.
[227] Y.-P. Chen, T.-S. Lo, Y.-H. Chien, Y.-H. Kuo, S.-J. Liu, Vitro and In Vivo Drug Release from a Nano-Hydroxyapatite Reinforced Resorbable Nanofibrous Scaffold for Treating Female Pelvic Organ Prolapse, Polymers 16 (2024) 1667, https://doi.org/10.3390/polym16121667.
[228] Y. Zhou, M. Liu, J. Duan, C. He, M. Xu, J. Huang, A. Zhang, W. Cui, B. Xu, Injectable self-expanding short-fiber scaffold reduces endometrial hyperplasia, J. Control. Release 387 (2025) 114172, https://doi.org/10.1016/j.jconrel.2025.114172.
[229] S. Song, S. Wu, D. Meiduo, P. Chen, H. Li, H. He, Nano-biomaterial Fibrinogen/P(LLA-CL) for prevention of intrauterine adhesion and restoration of fertility, J. Biomed. Mater. Res. 112 (2024) 167–179, https://doi.org/10.1002/jbm.a.37604.
[230] Y. Cao, J. Qi, J. Wang, L. Chen, Y. Wang, Y. Long, B. Li, J. Lai, Y. Yao, Y. Meng, X. Yu, X. Chen, L.G. Ng, X. Li, Y. Lu, X. Cheng, W. Cui, Y. Sun, Injectable "Homing-Like" Bioactive Short-Fibers for Endometrial Repair and Efficient Live Births, Adv. Sci. 11 (2024) 2306507, https://doi.org/10.1002/advs.202306507.
[231] S. Hanuman, M. Nune, Design and Characterization of Maltose-Conjugated Polycaprolactone Nanofibrous Scaffolds for Uterine Tissue Engineering, Regen. Eng. Transl. Med. 8 (2022) 334–344, https://doi.org/10.1007/s40883-021-00231-0.
[232] L.K. Symons, J.E. Miller, V.R. Kay, R.M. Marks, K. Liblik, M. Koti, C. Tayade, The Immunopathophysiology of Endometriosis, Trends Mol. Med. 24 (2018) 748–762, https://doi.org/10.1016/j.molmed.2018.07.004.
[233] Y. Tan, W.F. Flynn, S. Sivajothi, D. Luo, S.B. Bozal, M. Davé, A.A. Luciano, P. Robson, D.E. Luciano, E.T. Courtois, Single-cell analysis of endometriosis reveals a coordinated transcriptional programme driving immunotolerance and angiogenesis across eutopic and ectopic tissues, Nat. Cell. Biol. 24 (2022) 1306–1318, https://doi.org/10.1038/s41556-022-00961-5.
[234] L. Zhou, H. Wang, D. Shen, J. Xiang, N. Yu, X. He, W. Zhao, R. Wang, H. Wang, H. Yu, X. Ding, Z. Liu, Y. He, Stem cells implanted with nanofibrous mats for injured endometrial regeneration and immune-microenvironment remodeling, Mater. Today Bio 23 (2023) 100855, https://doi.org/10.1016/j.mtbio.2023.100855.
[235] S. Darzi, J. Alappadan, K. Paul, P. Mazdumder, A. Rosamilia, Y.B. Truong, C. Gargett, J. Werkmeister, S. Mukherjee, Immunobiology of foreign body response to composite PLACL/gelatin electrospun nanofiber meshes with mesenchymal stem/stromal cells in a mouse model: Implications in pelvic floor tissue engineering and regeneration, Biomater. Adv. 155 (2023) 213669, https://doi.org/10.1016/j.bioadv.2023.213669.
[236] E.A. Krogstad, R. Ramanathan, C. Nhan, J.C. Kraft, A.K. Blakney, S. Cao, R.J. Y. Ho, K.A. Woodrow, Nanoparticle-releasing nanofiber composites for enhanced in vivo vaginal retention, Biomaterials 144 (2017) 1–16, https://doi.org/10.1016/j.biomaterials.2017.07.034.
[237] U. Aggarwal, A.K. Goyal, G. Rath, Development and characterization of the cisplatin loaded nanofibers for the treatment of cervical cancer, Materials Science Engineering C 75 (2017) 125–132, https://doi.org/10.1016/j.msec.2017.02.013.
[238] X. Wang, S. Liu, Y. Guan, J. Ding, C. Ma, Z. Xie, Vaginal drug delivery approaches for localized management of cervical cancer, Adv. Drug. Deliv. Rev. 174 (2021) 114–126, https://doi.org/10.1016/j.addr.2021.04.009.
[239] P. Nakielski, C. Rinoldi, M. Pruchniewski, S. Pawłowska, M. Gazińska, B. Strojny, D. Rybak, K. Jezierska-Woźniak, O. Urbanek, P. Denis, E. Sinderewicz, W. Czelejewska, J. Staszkiewicz-Chodor, M. Grodzik, Y. Ziai, M. Barczewska, W. Maksymowicz, F. Pierini, Laser-Assisted Fabrication of Injectable Nanofibrous Cell Carriers, Small 18 (2022) 2104971, https://doi.org/10.1002/smll.202104971.
[240] A.H.C. Anthis, S. Kilchenmann, M. Murdeu, P.J. LeValley, M. Wolf, C. Meyer, O. Cipolato, M.W. Tibbitt, J. Rosendorf, V. Liska, T. Rduch, I.K. Herrmann, Reversible Mechanical Contraception and Endometriosis Treatment Using Stimuli-Responsive Hydrogels, Adv. Mater. 36 (2024) 2310301, https://doi.org/10.1002/adma.202310301.
[241] W. Tian, C. Wang, R. Chu, H. Ge, X. Sun, M. Li, Injectable hydrogel nanoarchitectonics with near-infrared controlled drug delivery for in situ photothermal/endocrine synergistic endometriosis therapy, Biomater. Res. 27 (2023) 100, https://doi.org/10.1186/s40824-023-00442-2.
[242] M.S. De Wilde, R. Devassy, H. Krentel, R.L. De Wilde, L.A. Torres-de La Roche, Self-Cross-Linked Hyaluronic Acid Gel for Adhesion Prophylaxis in Laparoscopic Deep Endometriosis Removal: Safety Report of a Prospective Pilot Study, JCM 13 (2024) 6284, https://doi.org/10.3390/jcm13206284.
[243] I.S. Ermiş, E. Deveci, F. Aşır, Effects of Quince Gel and Hesperidin Mixture on Experimental Endometriosis, Molecules 28 (2023) 5945, https://doi.org/10.3390/molecules28165945.
[244] C. Wang, W. Tian, X. Dai, J. Yuan, N. Ni, Q. Fan, H. Liu, H. Sun, J. Wan, X. Sun, Calcium ascorbate loaded ultrathin ferrous sulfide nanosheets thermo-sensitive hydrogels for near-infrared light activation of synergistic endometriosis therapy, Chem. Eng. J. 496 (2024) 153740, https://doi.org/10.1016/j.cej.2024.153740.
[245] F. Pierini, P. Nakielski, O. Urbanek, S. Pawłowska, M. Lanzi, L. De Sio, T. A. Kowalewski, Polymer-Based Nanomaterials for Photothermal Therapy: From Light-Responsive to Multifunctional Nanoplatforms for Synergistically Combined Technologies, Biomacromolecules 19 (2018) 4147–4167, https://doi.org/10.1021/acs.biomac.8b01138.
[246] X. Liu, S. Yan, H. Wu, M. Chen, H. Dai, Z. Wang, M. Chai, Q. Hu, D. Li, L. Chen, R. Diao, S. Chen, L. Wang, X. Shi, Interventional Hydrogel Microsphere Controlled-Releasing Curcumin for Photothermal Therapy against Endometriosis, Adv. Funct. Mater. 34 (2024) 2315907, https://doi.org/10.1002/adfm.202315907.

[247] R. Hergt, S. Dutz, Magnetic particle hyperthermia—biophysical limitations of a visionary tumour therapy, J. Magn. Magn. Mater. 311 (2007) 187–192, https://doi.org/10.1016/j.jmmm.2006.10.1156.
[248] L. Luo, H. Zhou, S. Wang, M. Pang, J. Zhang, Y. Hu, J. You, The Application of Nanoparticle-Based Imaging and Phototherapy for Female Reproductive Organs Diseases, Small (2023) 2207694, https://doi.org/10.1002/smll.202207694.
[249] V.D. Cuomo, C. Romano, D.J. Procter, Direct Activation of Sulfides by C–H Oxidation with Photoexcited Nitroarenes: Formal Manipulations of the C—S Bond, Angew. Chem. Int. Ed. 64 (2025) e202509244, https://doi.org/10.1002/anie.202509244.
[250] Y. Antsiferova, N. Sotnikova, E. Parfenyuk, Different Effects of the Immunomodulatory Drug GMDP Immobilized onto Aminopropyl Modified and Unmodified Mesoporous Silica Nanoparticles upon Peritoneal Macrophages of Women with Endometriosis, BioMed. Res. Int. 2013 (2013) 1–10, https://doi.org/10.1155/2013/924362.
[251] C. Dong, C. Yang, M.R. Younis, J. Zhang, G. He, X. Qiu, L. Fu, D. Zhang, H. Wang, W. Hong, J. Lin, X. Wu, P. Huang, Bioactive NIR-II Light-Responsive Shape Memory Composite Based on Cuprorivaite Nanosheets for Endometrial Regeneration, Adv. Sci. 9 (2022) 2102220, https://doi.org/10.1002/advs.202102220.
[252] A.S. Moses, O.R. Taratula, H. Lee, F. Luo, T. Grenz, T. Korzun, A.S. Lorenz, F. Y. Sabei, S. Bracha, A.W.G. Alani, O.D. Slayden, O. Taratula, Nanoparticle-Based Platform for Activatable Fluorescence Imaging and Photothermal Ablation of Endometriosis, Small 16 (2020) 1906936, https://doi.org/10.1002/smll.201906936.
[253] X. Li, C. Schumann, H.A. Albarqi, C.J. Lee, A.W.G. Alani, S. Bracha, M. Milovancev, O. Taratula, O. Taratula, A Tumor-Activatable Theranostic Nanomedicine Platform for NIR Fluorescence-Guided Surgery and Combinatorial Phototherapy, Theranostics 8 (2018) 767–784, https://doi.org/10.7150/thno.21209.
[254] J. Dulińska-Litewka, A. Łazarczyk, P. Hałubiec, O. Szafrański, K. Karnas, A. Karewicz, Superparamagnetic Iron Oxide Nanoparticles—Current and Prospective Medical Applications, Materials 12 (2019) 617, https://doi.org/10.3390/ma12040617.
[255] Y.-C. Wang, R.-H. Fu, H.-J. Hsieh, H.-T. Chao, S.-H. Kao, Polyglycolic acid/chitosan glue and apoptosis of endometriotic cells, Fertil. Steril. 84 (2005) 75–81, https://doi.org/10.1016/j.fertnstert.2005.01.127.
[256] M. Kvaskoff, Y. Mahamat-Saleh, L.V. Farland, N. Shigesi, K.L. Terry, H.R. Harris, H. Roman, C.M. Becker, S. As-Sanie, K.T. Zondervan, A.W. Horne, S.A. Missmer, Endometriosis and cancer: a systematic review and meta-analysis, Human. Reprod. Update 27 (2021) 393–420, https://doi.org/10.1093/humupd/dmaa045.
[257] H. Liu, X. Dai, N. Li, L. Zhang, Z. Wang, K. Ren, Y. Li, X. Sun, J. Wan, Injectable Magnetic Hydrogel Incorporated with Anti-Inflammatory Peptide for Efficient Magnetothermal Treatment of Endometriosis, Adv. Sci. 11 (2024) 2409778, https://doi.org/10.1002/advs.202409778.
[258] M. Agustina-Hernández, E. Francés-Herrero, M. Gómez-Álvarez, P. Alonso-Frías, M. Romeu, A. Monzó, H. Ferrero, C. Bueno-Fernandez, I. Cervelló, Biotechnological progresses in modelling the human endometrium: the evolution of current in vitro techniques and emerging trends, Front. Bioeng. Biotechnol. 12 (2024) 1495338, https://doi.org/10.3389/fbioe.2024.1495338.
[259] N. Rahmioglu, S. Mortlock, M. Ghiasi, P.L. Møller, L. Stefansdottir, G. Galarneau, C. Turman, R. Danning, M.H. Law, Y. Sapkota, P. Christofidou, S. Skarp, A. Giri, K. Banasik, M. Krassowski, M. Lepamets, B. Marciniak, M. Nõukas, D. Perro, E. Sliz, M. Sobalska-Kwapis, G. Thorleifsson, N.F. Topbas-Selcuki, A. Vitonis, D. Westergaard, R. Arnadottir, K.S. Burgdorf, A. Campbell, C.S.K. Cheuk, C. Clementi, J. Cook, I. De Vivo, A. DiVasta, O. Dorien, J.F. Donoghue, T. Edwards, P. Fontanillas, J.N. Fung, R.T. Geirsson, J.E. Girling, P. Harkki, H. R. Harris, M. Healey, O. Heikinheimo, S. Holdsworth-Carson, I.C. Hostettler, H. Houlden, S. Houshdaran, J.C. Irwin, M.-R. Jarvelin, Y. Kamatani, S. H. Kennedy, E. Kepka, J. Kettunen, M. Kubo, B. Kulig, V. Kurra, H. Laivuori, M. R. Laufer, C.M. Lindgren, S. MacGregor, M. Mangino, N.G. Martin, C. Matalliotaki, M. Matalliotakis, A.D. Murray, A. Ndungu, C. Nezhat, C.M. Olsen, J. Opoku-Anane, S. Padmanabhan, M. Paranjpe, M. Peters, G. Polak, D. J. Porteous, J. Rabban, K.M. Rexrode, H. Romanowicz, M. Saare, L. Saavalainen, A.J. Schork, S. Sen, A.L. Shafrir, A. Siewierska-Górska, M. Słomka, B.H. Smith, B. Smolarz, T. Szaflik, K. Szyłło, A. Takahashi, K.L. Terry, C. Tomassetti, S. A. Treloar, A. Vanhie, K. Vincent, K.C. Vo, D.J. Werring, E. Zeggini, M.I. Zervou, DBDS Genomic Consortium, K. Stefansson, M. Nyegaard, FinnGen Study, P. Harkki, O. Heikinheimo, J. Kettunen, V. Kurra, H. Laivuori, O. Uimari, FinnGen Endometriosis Taskforce, The Celmatix Research Team, G. Galarneau, C. Clementi, P. Yurttas-Beim, The 23andMe Research Team, P. Fontanillas, J. Y. Tung, S. Adachi, J.E. Buring, P.M. Ridker, T. D'Hooghe, G.N. Goulielmos, D. K. Hapangama, C. Hayward, A.W. Horne, S.-K. Low, H. Martikainen, D. I. Chasman, P.A.W. Rogers, P.T. Saunders, M. Sirota, T. Spector, D. Strapagiel, J. Y. Tung, D.C. Whiteman, L.C. Giudice, D.R. Velez-Edwards, O. Uimari, P. Kraft, A. Salumets, D.R. Nyholt, R. Mägi, K. Stefansson, C.M. Becker, P. Yurttas-Beim, V. Steinthorsdottir, M. Nyegaard, S.A. Missmer, G.W. Montgomery, A.P. Morris, K.T. Zondervan, The genetic basis of endometriosis and comorbidity with other pain and inflammatory conditions, Nat. Genet. 55 (2023) 423–436, https://doi.org/10.1038/s41588-023-01323-z.
[260] P.T.K. Saunders, A.W. Horne, Endometriosis: etiology, pathobiology, and therapeutic prospects, Cell 184 (2021) 2807–2824, https://doi.org/10.1016/j.cell.2021.04.041.
[261] Home | The Doctors Laboratory, (n.d.). ⟨https://www.tdlpathology.com/⟩ (accessed January 23, 2026).
[262] L. Wang, W. Peng, J. Wang, J. Chen, M. Liu, H. Huang, R. Jia, J. Ding, Macrophage membrane-biomimetic nanovehicles delivering amygdalin halt pyroptosis propagation and alleviate endometriosis-associated neuropathic pain, Mater. Today Bio 38 (2026) 103141, https://doi.org/10.1016/j.mtbio.2026.103141.
[263] P. Vashisth, L.T.D. Clerc, D. Hu, W. Jones, T. Shaikh, C.M. Hamadani, G. S. Dasanyake, G. Singh, C.M. Chism, B. Gamboa, A.C. Wall, N. Whitehead, T. Gilmer, S.X. Edgecomb, M.C. Pride, N.C. Fitzkee, E.E.L. Tanner, Ionic liquid-coated gold core polymeric nanoparticles for selective neutrophil hitchhiking towards endometriosis treatment, Commun. Chem. 9 (2026) 119, https://doi.org/10.1038/s42004-026-01909-8.