ameliorates local tissue injury and normalizes hemodynamic indices, supporting its use for pelvic "blood stasis" conditions that underlie dysmenorrhea and amenorrhea in traditional gynecology (Miao et al., 2019).

Leonurine and stachydrine also display vasodilatory, anti-platelet, and angiogenic activities, providing compound-level mechanisms for improved uterine blood supply and endometrial repair (Liao et al., 2023; Shi et al., 2022). Total alkaloid fractions from *L. japonicus* promote endothelial cell proliferation, migration, and tube formation via SRC/MEK/ERK signaling and accelerate wound healing *in vivo*, suggesting that enhanced neovascularization may contribute to the resolution of ischemic or stagnant uterine states associated with irregular menstruation and postpartum recovery (Li et al., 2019).

6.2 Anti-inflammatory and antioxidant activities

Motherwort total alkaloids attenuate bacteria-induced endometritis in rats, where treatment reduces inflammatory mediator overproduction and promotes endometrial repair through suppression of the PI3K/AKT/NF-κB axis and downstream cytokines (Ou et al., 2025). *in vitro*, these alkaloids inhibit lipopolysaccharide-triggered inflammatory responses in macrophages and human endometrial epithelial cells, highlighting a direct action on uterine immune-inflammatory microenvironments that are central to chronic endometrial pathology and infertility.

Broader pharmacological profiling shows that leonurine and stachydrine possess prominent anti-inflammatory and antioxidant properties, including inhibition of oxidative stress, modulation of NF-κB signaling, and reduction of tissue injury in cardiovascular and neuronal models (Liao et al., 2023; Wang et al., 2025). Crude *L. japonicus* extracts similarly downregulate TNF-α, IL-6, and IL-8 while enhancing anti-inflammatory IL-10 and antioxidant systems in trauma blood-stasis rats, indicating that both purified metabolites and complex mixtures can temper systemic and local inflammation relevant to pelvic pain, dysmenorrhea, and inflammatory gynecological disorders (Miao et al., 2019; Zhang et al., 2023).

6.3 Effects on uterine contraction and endocrine regulation

Classical and modern data converge to show that *L. japonicus* has marked effects on the uterus, including the ability to stimulate uterine smooth muscle and thereby assist in treating postpartum hemorrhage caused by uterine inertia (Shang et al., 2014). Bioassay-guided isolation has revealed that specific cyclopeptides and alkaloids, including leonurine, enhance contraction of rat uterine strips, while flavonoid glycosides exert the opposite, relaxing effect, explaining the herb's clinically observed bidirectional regulation of uterine activity in dysmenorrhea versus postpartum bleeding. More recently, coumarins isolated from *L. japonicus* were found to have similarly opposite effects on uterine smooth muscle: bergapten promotes contraction by increasing intracellular Ca^{2+} via L-type Ca^{2+} channels and α-adrenergic receptors, whereas osthole, an α-receptor antagonist, reduces Ca^{2+} influx and relaxes oxytocin-induced contractions (Fan et al., 2024). Beyond direct myometrial actions, network pharmacology analyses indicate that multiple motherwort components target endocrine-related molecules such as ESR1, AR, AKT1, and PPARG, suggesting integrated regulation of steroid hormone signaling in menstrual disorders (Wang et al., 2020).

Endocrine modulation by *L. japonicus* extends to ovarian steroidogenesis, where luteolin and luteolin-7-methylether suppress aromatase-mediated estrogen biosynthesis in human granulosa cells by inhibiting TPL2-MKK3/6-p38-CREB signaling (Shi et al., 2024). Luteolin-7-methylether (XLY29) decreases estradiol production in granulosa-like cells and downregulates aromatase promoter I.3/II without directly inhibiting catalytic activity, and *in vivo* lowers serum estradiol and alters estrous cycling in mice, suggesting potential applications in estrogen-excess conditions such as polycystic ovary syndrome (Du et al., 2020). A network pharmacology study focused on menstrual disorders further shows that 29 bioactive compounds from motherwort share core targets in endocrine, vascular, and inflammatory pathways, with hub genes including AKT1, PTGS2, ESR1, AR, and PPARG. Molecular docking indicates that many of these metabolites bind strongly to estrogen receptor and androgen receptor, providing a mechanistic bridge between traditional indications of "regulating menstruation" and modern concepts of hypothalamic-pituitary-ovarian axis and peripheral receptor modulation in gynecological endocrine disorders.