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Review Article

Premature Ovarian Insufficiency and Ovarian Ageing: Exploring *Beeja Kshaya*, *Dhatukshaya* and *Rasayana*

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Abstract

Premature Ovarian Insufficiency (POI) is characterized by loss or marked disturbance of ovarian activity before 40 years of age. It may present with irregular or absent menstruation, hypoestrogenic symptoms, infertility, and increased long-term risks affecting bone, cardiovascular, sexual, and psychological health. Ovarian activity can be intermittent, which makes the condition biologically different from completed natural menopause. Contemporary research links POI and ovarian ageing with accelerated follicular depletion, genetic susceptibility, autoimmunity, iatrogenic injury, oxidative stress, mitochondrial dysfunction, genomic damage, inflammation, and changes in the ovarian microenvironment. *Ayurveda* describes declining reproductive capacity through *Beeja Kshaya*, *Artava Kshaya*, progressive *Dhatukshaya*, age-related *Vata* predominance, and reduced tissue resilience. *Rasayana* offers a preventive and restorative framework directed toward tissue nourishment, healthy ageing, and physiological adaptability. Experimental studies of selected *Rasayana* plants report antioxidant, anti-inflammatory, immunomodulatory, and cytoprotective effects, but clinical evidence for preservation or restoration of ovarian reserve remains limited. This review compares the two knowledge systems without treating their terms as biological synonyms. The most responsible integrative approach combines timely diagnosis, hormone and fertility counselling, long-term risk management, lifestyle support, and carefully standardized Ayurvedic adjuncts. Future studies should use reproducible Ayurvedic assessment, validated ovarian reserve measures, authenticated interventions, safety monitoring, and clinically meaningful outcomes.

Keywords

Premature Ovarian Insufficiency; ovarian ageing; *Beeja Kshaya*; *Artava Kshaya*; *Dhatukshaya*; *Rasayana*; infertility; reproductive ageing

1. Introduction

Female reproductive ageing begins years before natural menopause. The follicle pool diminishes continuously, oocyte competence changes, and endocrine coordination becomes less predictable. In a minority of women, this decline occurs unusually early and leads to Premature Ovarian Insufficiency (POI), often at a stage when pregnancy plans, education, employment, and relationships are still evolving.

Ayurvedic discussions of health, ageing, tissue integrity, and individual constitution provide a broad setting for understanding gradual decline [1]. The classical account of *Rasayana* places preservation of vitality and

healthy longevity alongside disease treatment [2]. Reproductive potential is discussed through *Beeja* and the quality of the maternal reproductive contribution [3]. Sushruta's account adds structural and reproductive observations relevant to female health [4], while the *Ashtanga Hridaya* presents these ideas within a later clinical synthesis [5]. Dravyaguna literature supplies the traditional pharmacological basis for selecting medicinal substances according to properties, actions, dose, and patient context [6].

Modern guidance has also changed the language and care of this condition. Earlier European guidance emphasized the multisystem consequences of POI and the need for long-term management [7]. Updated evidence-based recommendations now refine diagnosis, hormone therapy, fertility counselling, genetic evaluation, bone health, cardiovascular risk, and psychosocial care [8]. The joint international guideline reinforces that POI should be managed as more than an infertility diagnosis [9].

This review examines POI and ovarian ageing through both contemporary reproductive biology and the Ayurvedic concepts of *Beeja Kshaya*, *Artava Kshaya*, *Dhatukshaya*, and *Rasayana*. The comparison is intended to improve questions and care, not to rename molecular mechanisms in classical terminology.

2. Aim and Review Method

The review aims to evaluate the biological basis and clinical implications of POI and ovarian ageing, explore functional relationships with Ayurvedic accounts of reproductive and tissue decline, and assess the possible place of *Rasayana*-oriented care in an evidence-based integrative framework.

A narrative synthesis was prepared from classical Ayurvedic texts, clinical guidelines, reviews, and selected experimental and clinical literature concerning POI, ovarian reserve, reproductive ageing, oxidative stress, mitochondria, genetics, inflammation, and medicinal plants. The review was not preregistered and did not use a formal certainty-of-evidence instrument. It should therefore be read as a critical interdisciplinary overview rather than a systematic estimate of treatment effect.

3. POI: Definition and Clinical Meaning

POI describes impaired ovarian activity before 40 years of age. Menstrual disturbance, biochemical evidence of ovarian insufficiency, and the exclusion of alternative explanations form the basis of diagnosis. Current criteria and the need for repeat testing depend on the clinical context and the degree of diagnostic uncertainty.

A major clinical review established the importance of using the term insufficiency rather than failure because ovarian function can fluctuate [10]. Later updates emphasized the heterogeneity of presentation, cause, and residual activity [11]. A comprehensive review in the Lancet likewise distinguished POI from irreversible, completed menopause [12].

Population estimates vary with definition and sampling. A classic incidence study helped establish the often-quoted estimate of approximately 1% before 40 years [13], but prevalence differs among populations and may be higher under broader or more recent diagnostic approaches.

Common manifestations include oligomenorrhoea or amenorrhoea, infertility, vasomotor symptoms, sleep disturbance, vaginal dryness, sexual concerns, and emotional distress. The diagnosis also has implications for bone density and cardiovascular health. Because symptoms can be subtle or attributed to stress, pregnancy, weight change, thyroid disease, hyperprolactinaemia, polycystic ovarian syndrome, or hypothalamic disturbance, a structured evaluation is essential.

4. Ovarian Ageing: More Than Follicle Count

Ovarian ageing is driven by depletion of the follicular pool, but reserve alone does not explain the whole process. A major endocrine review described the interaction among follicle number, oocyte quality, endocrine feedback, and the timing of reproductive milestones [14]. Granulosa-cell ageing alters metabolic support, steroidogenesis, and communication within the follicle [15].

The oocyte has an unusually high dependence on mitochondrial energy. Age-related mitochondrial change can impair spindle formation, chromosome segregation, maturation, fertilization, and early embryonic development [16]. A later review placed mitochondrial DNA, bioenergetics, oxidative stress, and organelle quality control at the centre of ovarian ageing [17].

The free-radical theory of ageing provided an influential framework for cumulative oxidative injury [18]. More recent single-cell work has shown that ageing affects several ovarian cell populations and their signalling environment rather than the oocyte alone [19]. Stromal cells, immune cells, vasculature, granulosa cells, and extracellular matrix all contribute to the functional age of the ovary.

5. Causes and Accelerators of POI

POI is a syndrome with many possible causes. Genetic reviews describe variants affecting follicle formation, meiosis, DNA repair, mitochondrial function, hormone signalling, and follicular activation [20]. Continuing advances in molecular genetics have expanded the number of candidate genes and the opportunities for family counselling [21].

Autoimmune disease is another recognized pathway. Thyroid autoimmunity, adrenal autoimmunity, and less common immune-mediated conditions may coexist with POI. Earlier clinical reviews also highlighted iatrogenic causes, infections, metabolic disorders, and a large idiopathic group in whom no single explanation is found [22].

Chemotherapy, pelvic radiotherapy, ovarian surgery, severe endometriosis, and selected environmental exposures may reduce reserve or accelerate loss. The degree of risk depends on age, baseline reserve, treatment type and dose, operative technique, and individual susceptibility. Fertility-preservation counselling is most

useful before a gonadotoxic exposure whenever time and clinical circumstances permit.

6. Cellular Mechanisms of Reproductive Ageing

Ovarian ageing reflects a network of oxidative injury, mitochondrial dysfunction, genomic instability, altered autophagy, cellular senescence, inflammation, fibrosis, and dysregulated follicular activation. Sirtuins have attracted attention because they link cellular energy status with mitochondrial function, stress responses, DNA maintenance, and reproductive ageing [23].

Age-related low-grade inflammation can alter the ovarian microenvironment, promote fibrosis, and disturb communication between follicles and surrounding tissue [24]. Oxidative stress is also relevant to female infertility more broadly, although its clinical measurement and therapeutic interpretation remain difficult [25].

These pathways interact. Mitochondrial dysfunction can increase reactive oxygen species; oxidative injury can damage mitochondrial and nuclear DNA; incomplete repair can promote senescence or apoptosis; inflammatory signalling can then reinforce tissue dysfunction. A single antioxidant is therefore unlikely to correct every dimension of ovarian ageing.

7. Clinical Assessment and Ovarian Reserve

Assessment begins with menstrual and reproductive history, pregnancy exclusion, medication and treatment history, symptoms of estrogen deficiency, family history, and examination guided by the presentation. Follicle-stimulating hormone and estradiol support diagnosis, while thyroid, prolactin, genetic, and autoimmune testing may be appropriate in selected women.

Anti-Mullerian hormone and antral follicle count estimate ovarian reserve but do not independently diagnose every case of POI and do not measure oocyte quality. A review of ovarian reserve markers explains the strengths and limitations of AMH, antral follicle count, FSH, inhibin B, and related tests [26]. Results must be interpreted with age, menstrual pattern, hormonal medicines, ovarian surgery, and the clinical question.

Evaluation should extend beyond fertility. Blood pressure, smoking, weight, physical activity, calcium and vitamin D status, bone density when indicated, sexual health, mood, sleep, and cardiovascular risk deserve attention. Genetic counselling and psychological support should be offered sensitively because the diagnosis may affect identity, family planning, and relatives.

8. *Beeja Kshaya* and *Artava Kshaya*

Beeja represents reproductive potential within the classical framework. *Beeja Kshaya* can therefore be used to describe quantitative or qualitative decline in the capacity for conception, while *Beeja Dushti* emphasizes impaired quality. The terms are broader than follicle number and should not be equated with a single laboratory result.

Artava is associated with female reproductive function and the menstrual expression of that function. *Artava Kshaya* is described through reduced, delayed, or absent menstruation and impaired fertility. These features resemble common manifestations of POI, but the similarity is clinical rather than mechanistic.

A woman with a low AMH value does not automatically have *Beeja Kshaya* in a standardized research sense, because no universally validated cross-system definition exists. Integrative studies should define Ayurvedic criteria prospectively and assess agreement among clinicians before correlating them with ovarian reserve measures.

9. *Dhatukshaya*, *Jara*, and *Vata*

Dhatukshaya describes progressive decline in tissue quantity, quality, nourishment, or function. The sequence of *Rasa*, *Rakta*, *Mamsa*, *Meda*, *Asthi*, *Majja*, and *Shukra Dhatu* situates reproductive health within the condition of the whole organism. In this view, impaired reproductive capacity may coexist with reduced strength, dryness, sleep disturbance, bone vulnerability, or reduced resilience.

Jara describes ageing, while age-related *Vata* predominance helps explain increasing dryness, variability, depletion, and functional instability. POI can present with menstrual irregularity, vaginal dryness, sleep disturbance, anxiety, and bone loss, which makes a *Vata-Dhatukshaya* interpretation clinically meaningful within *Ayurveda*.

The comparison should retain its boundaries. *Vata* is not follicle-stimulating hormone, *Dhatukshaya* is not mitochondrial dysfunction, and *Artava Kshaya* is not hypoestrogenism. Their value lies in organizing a patient-centred pattern that can be studied alongside, rather than substituted for, endocrine and genetic findings.

10. Conceptual Correlation

The following comparison summarizes plausible functional relationships. It is designed for interdisciplinary discussion and does not imply that either system validates the terminology of the other.

Modern observation	Ayurvedic concept	Interpretive limit
Declining ovarian reserve	*Beeja Kshaya*	Not defined by AMH alone
Reduced oocyte competence	*Beeja Dushti*	No direct molecular equivalence
Irregular or absent menstruation	*Artava Kshaya*	Requires endocrine diagnosis
Systemic tissue decline	*Dhatukshaya*	Broader than ovarian ageing
Age-related functional change	*Jara* and *Vata* predominance	A clinical framework, not a biomarker

Modern observation	Ayurvedic concept	Interpretive limit
Reduced fertility	*Vandhyatva*	Many causes require differentiation
Loss of resilience	Reduced *Ojas* and *Dhatu* quality	Needs operational research criteria

Table 1. Functional correlations between ovarian ageing and selected Ayurvedic concepts.

11. *Rasayana* and Reproductive Resilience

Rasayana is a broad strategy for preserving tissue quality, physiological adaptability, and healthy ageing. Its application may include food, sleep, behaviour, stress regulation, medicinal substances, and individualized correction of factors that impair nourishment. In reproductive ageing, this orientation is attractive because it begins before severe functional loss.

A review of *Ashwagandha* (*Withania somnifera*) describes antioxidant, adaptogenic, immunomodulatory, and stress-related actions associated with its traditional *Rasayana* use [27]. A broader review of *Rasayana* places such interventions within a traditional model of healthy ageing rather than a single-drug treatment [28].

Shatavari (*Asparagus racemosus*) is widely discussed in female reproductive care and has demonstrated pharmacological activities relevant to inflammation, oxidative stress, and reproductive physiology in preclinical research [29]. *Amalaki* (*Emblica officinalis*) contains polyphenols and tannins with antioxidant and cytoprotective properties [30].

Guduchi (*Tinospora cordifolia*) has yielded compounds with immunomodulatory activity [31]. *Yashtimadhu* (*Glycyrrhiza glabra*) also has antioxidant and endocrine-relevant pharmacology, but liquorice can cause clinically important mineralocorticoid effects, including hypertension and hypokalaemia, when exposure is excessive or prolonged [32].

These findings support further research, not a claim that any plant regenerates the human follicle pool. Extract, identity, dose, duration, formulation, co-medication, and patient selection substantially affect benefit and risk.

12. Possible Biological Actions of *Rasayana*

Antioxidant and cytoprotective effects may be relevant where oxidative burden contributes to cellular damage. Anti-inflammatory and immunomodulatory effects could be explored in defined inflammatory or autoimmune contexts. Adaptogenic effects may support sleep, stress tolerance, and quality of life, all of which matter to women coping with POI.

Mitochondrial protection is a plausible experimental target, but improvement in a cell or animal marker does not establish restoration of ovarian reserve in humans. Likewise, a change in AMH should not be interpreted as improved fertility unless supported by appropriate reproductive outcomes and an understanding of normal assay variability.

The value of *Rasayana* may ultimately be multidimensional: supporting general health, treatment adherence, symptom burden, psychological resilience, and healthy behaviours while established medical care addresses estrogen deficiency, bone health, cardiovascular risk, and fertility planning.

***Rasayana* principle**	**Researchable modern domain**	**Evidence boundary**
Dhatu Poshana	Nutrition and tissue metabolism	Requires measurable outcomes
Vayasthapana	Healthy-ageing pathways	Does not imply reversal of age
Ojovardhana	Immune regulation and resilience	Not equivalent to one immune marker
Antioxidant action	Oxidative-stress modulation	Biomarker change is not restored fertility
Adaptogenic action	Stress and neuroendocrine regulation	Clinical relevance must be tested
Cytoprotection	Mitochondrial and cellular integrity	Predominantly preclinical evidence

Table 2. Researchable *Rasayana* domains and the limits of current interpretation.

13. Follicle Pool and Reproductive Timing

Quantitative modelling of human ovarian reserve illustrates the steep decline from fetal life to menopause and the wide uncertainty around any individual's trajectory [33]. Reproductive ageing varies considerably among women, and chronological age alone cannot predict the exact timing of diminished fertility or menopause [34].

Foundational histological work counted germ cells across stages of human development and remains important to the understanding of the finite follicle pool [35]. Modern estimates have refined the numbers, but the central observation remains: most follicles are lost through atresia, not ovulation.

Residual follicles may remain in some women with POI, and intermittent ovulation is possible. This does not mean that ovarian reserve can be reliably reactivated. Counselling should preserve realistic hope without offering a predictable spontaneous pregnancy rate or an unproven rejuvenation claim.

14. Standard Clinical Management

Management should be individualized and shared with the patient. Unless contraindicated, systemic hormone therapy is commonly recommended until approximately the usual age of natural menopause to treat estrogen

deficiency and reduce long-term health consequences. The regimen should account for the presence of a uterus, symptoms, bleeding pattern, contraindications, preferences, and the need for contraception.

Hormone therapy for POI is replacement of hormones lost unusually early; it is not identical in purpose or risk context to initiating menopausal hormone therapy at an older age. Regular review should address adherence, bleeding, blood pressure, migraine, thrombotic risk, breast and cervical screening as appropriate, bone health, and sexual symptoms.

Lifestyle care includes resistance and weight-bearing activity, adequate nutrition, tobacco avoidance, moderation of alcohol, sleep support, and management of cardiovascular risk. Vaginal estrogen or other local measures may be considered for genitourinary symptoms according to clinical suitability.

15. Fertility Counselling

Fertility counselling should begin early and be honest about uncertainty. Intermittent ovarian activity can occur, but no current treatment reliably restores the depleted follicle pool or guarantees natural conception. Donor-oocyte in vitro fertilization is an established option for many women, while adoption, embryo donation, or a decision not to pursue parenthood may also be relevant.

Fertility preservation is most effective before gonadotoxic treatment or substantial loss of reserve. Oocyte or embryo cryopreservation, ovarian tissue cryopreservation, and specialist referral depend on age, diagnosis, treatment urgency, available expertise, and patient preference.

Any Ayurvedic intervention used during fertility treatment should be disclosed to the reproductive team. Potential endocrine effects, liver injury, herb-drug interactions, contamination, and product variability must be considered, particularly around ovarian stimulation, anaesthesia, pregnancy, or autoimmune disease.

16. An Integrative Care Framework

Integrative care can add value when it coordinates rather than fragments treatment. A useful plan may combine guideline-based endocrine management with individualized diet, sleep, exercise, stress reduction, counselling, and a carefully selected Ayurvedic regimen. Goals should be explicit: symptom relief, general wellbeing, bone and cardiovascular protection, fertility support, or investigation of a biological marker.

Rasayana should be framed as supportive care unless a specific therapeutic claim has adequate clinical evidence. A woman should not be advised to stop hormone replacement, postpone fertility referral, or rely on herbs to restore follicles. At the same time, the Ayurvedic emphasis on tissue nourishment, daily routine, and long-term resilience can strengthen patient engagement and whole-person care.

Follow-up should document menstrual pattern, symptoms, adherence, adverse effects, blood pressure, relevant laboratory findings, bone health, and patient-reported outcomes. Product name, ingredients, manufacturer, batch, dose, duration, and co-interventions should be recorded to make both care and research reproducible.

17. Evidence Gaps and Research Priorities

Most *Rasayana* evidence relevant to ovarian ageing is preclinical or indirect. Human studies often involve heterogeneous infertility populations, small samples, variable formulations, short treatment periods, and surrogate outcomes. Few trials are designed specifically for well-defined POI.

Future studies should standardize diagnostic criteria, distinguish POI from diminished ovarian reserve and hypothalamic amenorrhoea, and stratify participants by cause. Ayurvedic assessments of *Beeja Kshaya*, *Artava Kshaya*, *Dhatukshaya*, and *Vata* should use prespecified criteria and report inter-rater reliability.

Interventions require authenticated botanical ingredients, quality testing, dose justification, manufacturing standards, pharmacovigilance, and transparent co-treatment. Outcomes should include menstrual activity, symptoms, bone and cardiovascular markers, quality of life, adverse events, and fertility outcomes. AMH and antral follicle count can be included, but neither should stand alone as proof of ovarian rejuvenation.

Mechanistic substudies may examine oxidative stress, inflammatory signalling, mitochondrial function, metabolomics, or cellular senescence. Preregistration, adequate controls, blinded outcome assessment, and long-term follow-up would substantially improve credibility.

18. Critical Appraisal

The relationship between POI and *Beeja Kshaya*, *Artava Kshaya*, or *Dhatukshaya* is clinically suggestive but not experimentally established. The frameworks operate at different levels: one describes follicles, hormones, genes, and cells; the other organizes reproductive potential, tissue nourishment, ageing, and individual pattern.

The comparison becomes unhelpful when terms are presented as exact equivalents or when experimental antioxidant activity is converted into a clinical claim of restored fertility. It becomes useful when it produces testable questions, encourages earlier preventive care, and brings symptoms, long-term health, and patient experience into the same consultation.

A balanced conclusion is therefore possible. *Ayurveda* offers a coherent model of reproductive decline and a constructive strategy for supporting healthy ageing. Modern reproductive medicine provides the diagnostic, hormonal, genetic, and fertility tools required for safe care. Rigorous integration should preserve both strengths.

19. Conclusion

POI is a heterogeneous condition with reproductive, endocrine, skeletal, cardiovascular, sexual, and

psychological consequences. Ovarian ageing involves follicular depletion together with changes in oocytes, granulosa cells, mitochondria, DNA maintenance, immunity, stroma, and vascular function. Intermittent activity may persist, but reliable restoration of depleted reserve is not currently available.

Beeja Kshaya, *Artava Kshaya*, *Dhatukshaya*, *Jara*, and *Vata* offer a systemic Ayurvedic account of declining reproductive capacity. *Rasayana* provides a positive framework for tissue support, resilience, and healthy ageing. Selected plants have promising biological activities, yet their role in POI requires direct, standardized clinical evaluation.

The most responsible approach combines early diagnosis, guideline-based hormone and fertility care, protection of long-term health, psychosocial support, and carefully monitored Ayurvedic adjuncts. This model respects classical knowledge while keeping claims proportionate to the evidence.

20.References

[1] Charaka. *Charaka Samhita*. *Sutra Sthana*, Chapter 1. In: Shastri K, Chaturvedi GN, editors. *Vidyotini* Hindi Commentary. Reprint ed. Varanasi: Chaukhambha Bharati Academy; 2023. p. 5-38.

[2] Charaka. *Charaka Samhita*. *Chikitsa Sthana*, Chapter 1 (*Rasayana Adhyaya*). In: Shastri K, Chaturvedi GN, editors. *Vidyotini* Hindi Commentary. Reprint ed. Varanasi: Chaukhambha Bharati Academy; 2023. p. 1-39.

[3] Charaka. *Charaka Samhita*. *Sharira Sthana*, Chapter 2. In: Shastri K, Chaturvedi GN, editors. *Vidyotini* Hindi Commentary. Reprint ed. Varanasi: Chaukhambha Bharati Academy; 2023. p. 845-872.

[4] Sushruta. *Sushruta Samhita*. *Sharira Sthana*, Chapter 2. In: Shastri AD, editor. *Ayurveda Tatva Sandipika*. Reprint ed. Varanasi: Chaukhambha Sanskrit Sansthan; 2023. p. 15-38.

[5] Vagbhata. *Ashtanga Hridaya*. *Sharira Sthana*, Chapter 1. In: Gupta A, editor. *Vidyotini* Hindi Commentary. Reprint ed. Varanasi: Chaukhambha Prakashan; 2022. p. 227-246.

[6] Sharma PV. *Dravyaguna Vijnana*. Vol. II. Reprint ed. Varanasi: Chaukhambha Bharati Academy; 2022.

[7] Webber L, Davies M, Anderson R, Bartlett J, Braat D, Cartwright B, et al. ESHRE Guideline: management of women with premature ovarian insufficiency. Hum Reprod. 2016;31(5):926-937.

[8] Panay N, Anderson RA, Bennie A, Cedars M, Davies M, Ee C, et al. Evidence-based guideline: premature ovarian insufficiency. Hum Reprod Open. 2024;2024(4):hoae065.

[9] ESHRE, ASRM, CREWHIRL and IMS Guideline Group on POI. Evidence-based guideline: premature ovarian insufficiency. Climacteric. 2024;27(6):510-520.

[10] Nelson LM. Clinical practice. Primary ovarian insufficiency. N Engl J Med. 2009;360(6):606-614.

[11] Torrealday S, Kodaman P, Pal L. Premature ovarian insufficiency—an update on recent advances in understanding and management. F1000Res. 2017;6:2069.

[12] De Vos M, Devroey P, Fauser BCJM. Primary ovarian insufficiency. Lancet. 2010;376(9744):911-921.

[13] Coulam CB, Adamson SC, Annegers JF. Incidence of premature ovarian failure. Obstet Gynecol. 1986;67(4):604-606.

[14] Broekmans FJ, Soules MR, Fauser BCJM. Ovarian ageing: mechanisms and clinical consequences. Endocr Rev. 2009;30(5):465-493.

[15] Tatone C, Amicarelli F. The aging ovary—the poor granulosa cells. Fertil Steril. 2013;99(1):12-17.

[16] Bentov Y, Casper RF. The aging oocyte—can mitochondrial function be improved? Fertil Steril. 2013;99(1):18-22.

[17] May-Panloup P, Boucret L, Chao de la Barca JM, et al. Ovarian ageing: the role of mitochondria. Hum Reprod Update. 2016;22(6):725-743.

[18] Harman D. Free radical theory of aging: an update. Ann N Y Acad Sci. 2006;1067:10-21.

[19] Wang S, Zheng Y, Li J, et al. Single-cell transcriptomic atlas of primate ovarian ageing. Cell. 2020;180(3):585-600.

[20] Jiao X, Ke H, Qin Y, Chen ZJ. Molecular genetics of premature ovarian insufficiency. Trends Endocrinol Metab. 2018;29(11):795-807.

[21] Qin Y, Jiao X, Simpson JL, Chen ZJ. Genetics of primary ovarian insufficiency: new developments and opportunities. Hum Reprod Update. 2015;21(6):787-808.

[22] Goswami D, Conway GS. Premature ovarian failure. Hum Reprod Update. 2005;11(4):391-410.

[23] Tatone C, Di Emidio G, Vitti M, et al. Sirtuins in female fertility and reproductive ageing. Free Radic Biol Med. 2018;117:293-307.

[24] Lord JM, Midwinter MJ, Chen YF, et al. The ageing ovary and chronic inflammation. Ageing Res Rev. 2020;62:101091.

[25] Agarwal A, Gupta S, Sharma RK. Oxidative stress and its implications in female infertility—a clinician's perspective. Reprod Biomed Online. 2005;11(5):641-650.

[26] Bhide A, Shah PS, Acharya G. A review of ovarian reserve markers. Facts Views Vis Obgyn. 2018;10(2):95-106.

[27] Singh N, Bhalla M, de Jager P, Gilca M. An overview on *Ashwagandha* (*Withania somnifera*): a *Rasayana* (rejuvenator) of *Ayurveda*. Afr J Tradit Complement Altern Med. 2011;8(5 Suppl):208-213.

[28] Tiwari AK. *Rasayana*: a traditional herbal approach to healthy ageing. Pharmacogn Rev. 2008;2(4):263-272.

[29] Thakur M, Lochab S. Phytopharmacology of *Asparagus racemosus* (*Shatavari*): a review. Pharmacogn Rev. 2018;12(24):46-52.

[30] Krishnaveni M, Mirunalini S. Therapeutic potential of *Emblica officinalis* (*Amalaki*): an overview. J Basic Clin Physiol Pharmacol. 2010;21(1):93-105.

[31] Sharma U, Bala M, Kumar N, Singh B, Munshi RK, Bhalerao S. Immunomodulatory active compounds from *Tinospora cordifolia*. J Ethnopharmacol. 2012;141(3):918-926.

[32] Pastorino G, Cornara L, Soares S, Rodrigues F, Oliveira MBPP. Liquorice (*Glycyrrhiza glabra*): a phytochemical and pharmacological review. Phytother Res. 2018;32(12):2323-2339.

[33] Wallace WHB, Kelsey TW. Human ovarian reserve from conception to menopause. PLoS One. 2010;5:e8772.

[34] te Velde ER, Pearson PL. The variability of female reproductive ageing. Hum Reprod Update. 2002;8(2):141-154.

[35] Baker TG. A quantitative and cytological study of germ cells in human ovaries. Proc R Soc Lond B Biol Sci. 1963;158:417-433.

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