



Safety of herbal galactagogues: A systematic review of preclinical and clinical evidence

[Seguridad de los galactagogos a base de hierbas: una revisión sistemática de la evidencia preclínica y clínica]

Sara Nurmala^{1,3}, Neng F. Kurniati², Kusnandar Anggadiredja^{2*}

¹Doctoral Program, School of Pharmacy, Bandung Institute of Technology, Bandung, Indonesia.

²Department of Pharmacology and Clinical Pharmacy, School of Pharmacy, Bandung Institute of Technology, Bandung, Indonesia.

³Department of Pharmacy, Faculty of Mathematics and Natural Sciences, Pakuan University, Bogor, Indonesia.

*E-mail: kusnandar_a@itb.ac.id

Abstract

Context: Herbal galactagogues are commonly used to promote lactation. Despite their increasing use, concerns remain regarding their safety because evidence from preclinical and clinical studies is limited and heterogeneous. Therefore, an updated systematic review is needed to synthesize the current evidence and inform clinical practice and future research.

Aims: To provide a systematic and integrated assessment of the available preclinical and clinical evidence regarding the safety of herbal galactagogues.

Methods: This systematic review was conducted in accordance with the PRISMA 2020 Statement. Eligible studies were identified through systematic searches of PubMed, ScienceDirect, Springer Nature Link, and SAGE, including all records indexed from database inception to July 31, 2026. Study selection and data extraction were performed independently by two reviewers. Thirteen studies met the prespecified selection criteria after full-text review. Quality appraisal was undertaken using instruments appropriate to the study design, with the SYRCL Risk of Bias tool and the Joanna Briggs Institute (JBI) Critical Appraisal Checklists.

Results: The review ultimately included 13 eligible studies. Preclinical studies generally reported no treatment-related toxicity, while clinical studies reported no serious treatment-related adverse events, although safety reporting varied across study designs. Heterogeneous interventions and inconsistent safety reporting limited the interpretation of the findings.

Conclusions: Current evidence did not identify major short-term treatment-related safety concerns. However, heterogeneous methods, inconsistent safety reporting, and limited long-term data warrant further clinical studies using standardized herbal preparations and integrated maternal–infant safety monitoring.

Keywords: adverse effects; animal models; breastfeeding; phytotherapy; postpartum period.

Resumen

Contexto: Los galactagogos a base de hierbas se utilizan habitualmente para fomentar la lactancia. A pesar de su creciente uso, persisten dudas sobre su seguridad, ya que la evidencia procedente de estudios preclínicos y clínicos es limitada y heterogénea. Por ello, es necesaria una revisión sistemática actualizada que sintetice la evidencia actual y oriente la práctica clínica y las investigaciones futuras.

Objetivos: Ofrecer una evaluación integrada y sistemática de la evidencia preclínica y clínica disponible sobre la seguridad de los galactagogos a base de hierbas.

Métodos: La metodología y la elaboración de esta revisión se ajustaron a las directrices PRISMA 2020. Se identificaron los estudios elegibles mediante búsquedas sistemáticas en PubMed, ScienceDirect, Springer Nature Link y SAGE, incluyendo todos los registros indexados desde la creación de las bases de datos hasta el 31 de julio de 2026. La selección de estudios y la extracción de datos fueron realizadas de forma independiente por dos revisores. Un total de 13 estudios cumplieron los criterios de selección preestablecidos tras la revisión del texto completo. La evaluación de la calidad se realizó utilizando instrumentos adecuados al diseño de cada estudio: la herramienta SYRCL para evaluar el riesgo de sesgo y las listas de verificación de evaluación crítica del Joanna Briggs Institute (JBI).

Resultados: En última instancia, la revisión incluyó 13 estudios elegibles. Por lo general, los estudios preclínicos no notificaron toxicidad relacionada con el tratamiento, mientras que los estudios clínicos no registraron acontecimientos adversos graves asociados al mismo, si bien la notificación de datos de seguridad varió según el diseño de los estudios. La heterogeneidad de las intervenciones y la inconsistencia en la notificación de la seguridad limitaron la interpretación de los hallazgos.

Conclusiones: La evidencia actual no identificó problemas de seguridad importantes a corto plazo. Sin embargo, la heterogeneidad de los métodos, la inconsistencia en la notificación de seguridad y la escasez de datos a largo plazo justifican la realización de nuevos estudios clínicos que utilicen preparados herbales estandarizados y un seguimiento integrado de la seguridad materno-infantil.

Palabras Clave: efectos adversos; fitoterapia; lactancia materna; modelos animales; período posparto.

ARTICLE INFO

Received: March 26, 2026.

Accepted: September 17, 2026.

Available Online: September 25, 2026.

AUTHOR INFO

ORCID:

[0000-0001-9879-6112](https://orcid.org/0000-0001-9879-6112) (KA)

[0000-0002-3313-6612](https://orcid.org/0000-0002-3313-6612) (NFK)

[0000-0003-1102-2929](https://orcid.org/0000-0003-1102-2929) (SN)

Abbreviations: AE: Adverse Event; ALP: Alkaline Phosphatase; ALT: Alanine Aminotransferase; AST: Aspartate Aminotransferase; CBC: Complete Blood Count; JBI: Joanna Briggs Institute; MeSH: Medical Subject Headings; PICOS: Population, Intervention, Comparison, Outcomes, and Study Design; PRISMA: Preferred Reporting Items for Systematic Reviews and Meta-Analyses; RCT: Randomized Controlled Trial; SYRCLE: Systematic Review Centre for Laboratory Animal Experimentation.

INTRODUCTION

Breastfeeding is recognized worldwide as an essential public health measure that enhances infant survival, immune development, and maternal health; however, inadequate milk production remains a prevalent obstacle, prompting mothers to seek supplementary treatments to facilitate lactation (Balkam, 2022; Foong et al., 2020; Nurhayati et al., 2024). In response to these challenges, galactagogue substances that stimulate or increase milk production have been increasingly utilized, encompassing both pharmaceutical and herbal approaches (Gabay, 2002; Mortel & Mehta, 2013).

Preclinical research has provided important mechanistic insights into the biological effects and safety profiles of herbal galactagogues. Experimental studies indicate that several plant-based compounds may promote lactation through endocrine modulation, including prolactin stimulation and phytoestrogenic activity. For instance, fenugreek (*Trigonella foenum-graecum*) contains bioactive constituents associated with lactogenic effects (Basch et al., 2003). Additionally, emerging evidence highlights the role of hormonal regulation in lactation physiology, suggesting that plant-derived compounds may influence endocrine pathways relevant to milk production (Jin et al., 2024). Traditional plant-based foods and herbal preparations have also been investigated in experimental and ethnopharmacological contexts, supporting their potential role in enhancing milk production (Buntuchai et al., 2017). Recent experimental studies have further demonstrated that standardized herbal galactagogue formulations may enhance lactation without apparent short-term toxicity under controlled experimental conditions, although comprehensive toxicological evaluation remains necessary (Chotitham et al., 2025).

More recently, combination herbal extracts containing *Sauropus androgynus*, *Moringa oleifera*, and *Coleus amboinicus* have also demonstrated promising lactation-supporting activity in experimental models (Intan et al., 2024). Despite these promising mechanistic findings, the translation of preclinical evidence into clinical practice remains complex. Variability in experimental models, dosing regimens, and reporting of toxicological endpoints limits the generalizability of preclinical findings. Moreover, safety data in preclinical studies are often inconsistently reported, raising concerns regarding the completeness of toxicological evaluation. Ethnobotanical investigations have also documented

the widespread traditional use of diverse plant species to improve breast milk quantity and quality across different cultures, further highlighting the longstanding role of herbal galactagogues in maternal healthcare (Jendras et al., 2020).

In clinical settings, the use of herbal galactagogues has increased globally, reflecting broader trends in the adoption of complementary and traditional medicine across both high-income and low- to middle-income countries (LMICs) (Zapantis et al., 2012). Herbal agents such as *Pimpinella anisum* and *Moringa oleifera* are widely used due to cultural acceptance, accessibility, and the perception that natural products are safer than pharmaceutical alternatives (Khalili et al., 2023; Sim et al., 2015). Clinical and observational studies have reported predominantly mild short-term adverse events; however, safety evidence remains heterogeneous and incompletely reported.

The growing use of herbal medicine aligns with global health initiatives to integrate traditional medicine into healthcare systems, but it also presents important safety and regulatory challenges (Dubale et al., 2025; Sethi et al., 2025; Usure et al., 2024). Herbal products are frequently marketed with limited clinical evaluation, leading to variability in composition, unclear dosing, and inconsistent quality standards (Heinrich, 2015; Sanghvi et al., 2023). Pharmacovigilance studies have identified risks including contamination, adulteration, and herb-drug interactions, all of which may have implications for breastfeeding populations (Alharbi et al., 2024).

Additionally, the use of herbal medicines during breastfeeding is often underreported to healthcare providers, limiting clinical oversight and safety monitoring (Gossler, 2010; Khan et al., 2025). Although traditional use provides valuable insights, it does not guarantee safety in contemporary clinical practice, and evidence from recent clinical studies remains limited and inconsistently reported (Posadzki et al., 2013; Zulkarnain et al., 2024).

Although both preclinical and clinical studies have investigated herbal galactagogues, most have focused primarily on efficacy rather than comprehensive safety assessment. Preclinical studies mainly provide mechanistic and toxicological evidence, whereas clinical studies evaluate maternal and infant outcomes using heterogeneous designs and safety measures, limiting direct comparison across studies (Khan et al., 2018; Rouhi et al., 2025).

Therefore, an up-to-date systematic review integrating preclinical and clinical evidence is required to critically determine the safety of herbal galactagogues and identify gaps for future research and clinical practice.

MATERIAL AND METHODS

Study design and reporting guidelines

This systematic review was conducted in accordance with the Preferred Reporting Items for Systematic Reviews and Meta-Analyses (PRISMA 2020) Statement to ensure transparent and reproducible reporting (Page et al., 2021). The review synthesized evidence from both preclinical and clinical studies evaluating the safety of herbal galactagogues. A review protocol was developed before study selection to guide the review process but was not prospectively registered (Supplementary Table S5).

Research question and conceptual framework

To ensure a structured review process, the Population-Intervention-Comparison-Outcomes-Study Design (PICOS) framework was applied to formulate the review question, specify the eligibility criteria, and develop the literature search strategy.

The PICOS components were delineated as follows:

Population: Lactating animal models or lactating mothers.

Intervention: Single-herb and polyherbal preparations used as a herbal galactagogue.

Comparison: Placebo, usual treatment, or untreated control groups.

Outcomes: Safety-related parameters encompassing adverse events, biochemical indicators, endocrine alterations, histopathological findings, and maternal-infant outcomes.

Study design: Original preclinical animal studies and clinical studies, including randomized controlled trials, observational, cross-sectional, and qualitative studies evaluating the safety of herbal galactagogues.

Eligibility criteria

Original preclinical and clinical studies evaluating the safety of herbal galactagogues used to support lactation were eligible for inclusion. The eligibility criteria allowed the inclusion of experimental animal studies together with clinical investigations employing randomized controlled, cross-sectional, or observational study designs. Studies were required to report at least one safety-related outcome, including adverse events, biochemical or hematological parameters, endocrine

markers, toxicological findings, or maternal and infant safety outcomes. The original search period was subsequently expanded during the revision process to include records from database inception through July 31, 2026, to capture recent evidence relevant to the safety of herbal galactagogues. This amendment was made during revision and was not part of the original search period. The review was restricted to full-text articles published in English. Review articles, editorials, conference abstracts, letters, case reports, studies evaluating non-herbal galactagogues, and studies that did not report safety-related outcomes were omitted. The complete review protocol is provided in Supplementary Table S5.

Information sources

Relevant publications were identified by systematically searching PubMed, ScienceDirect, Springer Nature Link, and SAGE to identify original preclinical and clinical studies evaluating the safety of herbal galactagogues. All databases were searched from database inception to July 2026, and the search was restricted to English-language, full-text, peer-reviewed original research articles.

To maximize study identification, the reference lists of all included articles were manually screened to identify additional eligible studies. Only peer-reviewed original research articles were considered eligible. Grey literature, conference proceedings, clinical trial registries, regulatory databases, and review articles were not systematically searched or included in the qualitative synthesis.

Search strategy

Development of the review question and eligibility criteria was informed by the PICOS framework for development of the literature search strategy, enabling systematic identification of potentially relevant studies, while maintaining relevance to the review question. Search terms included concepts related to breastfeeding or lactation (Population), herbal galactagogues (Intervention), and safety outcomes (Outcome).

Database-specific search strategies were developed for PubMed, ScienceDirect, Springer Nature Link, and SAGE, using controlled vocabulary where appropriate (e.g., Medical Subject Headings [MeSH] in PubMed) together with free-text terms and Boolean operators adapted to the search functionality of each database. For PubMed, three complementary searches (A, B, and C) were conducted separately, and the records retrieved from these searches were subsequently pooled before being combined with records from the other databases for duplicate removal. The complete search strategies are provided in Supplementary Table S1.

The final electronic searches of all databases were conducted on July 31, 2026, and the review considered only English-language original research with accessible full-text versions that had undergone peer review. Search terms included keywords and synonyms related to breastfeeding, lactation, herbal medicine, medicinal plants, galactagogues, and safety outcomes.

Selection process

Search results were managed in Mendeley Reference Manager, and duplicate records were eliminated before the screening process. Study selection was performed in accordance with the PRISMA 2020 Statement (Page et al., 2021). Two reviewers independently screened titles and abstracts against the prespecified eligibility criteria. Potentially eligible articles subsequently underwent full-text assessment to determine their inclusion in the review.

Disagreements during study selection were resolved through discussion. Studies that did not meet the prespecified eligibility criteria were excluded. The final set of eligible studies was retained for qualitative synthesis.

Data collection process

A standardized data extraction form was developed before data extraction to ensure that all information from the studies was consistent and thorough. Two reviewers independently extracted data from each included publication, and any inconsistencies were resolved through discussion and consensus among the research team. When needed, the extracted data were validated against the source publications to ensure their accuracy.

The extracted data included study characteristics (author, year, country, and study design), intervention details (herbal galactagogue, dosage, and treatment duration), study population or animal model, safety outcomes (adverse events, biochemical and hematological parameters, endocrine markers, toxicological findings, and maternal and infant safety outcomes), and the main findings relevant to the review objectives.

Data items

Prior to data extraction, a standardized set of data elements was established to support consistent and reproducible data collection across the included studies.

For preclinical studies, the extracted variables included animal species or experimental model, sample size, herbal galactagogue or plant extract, formulation, dosage, route of administration, treatment duration, and safety outcomes, including adverse events, biochemical and hematological parameters, endocrine

markers, toxicological findings, organ weights, and histopathological findings.

For clinical studies, information collected included study design, participant characteristics, and details of the intervention (plant species, formulation, dosage, and treatment duration), comparator, and reported safety outcomes, including adverse events, maternal safety indicators, and infant-related outcomes when available. General study characteristics (author, publication year, country, and outcome assessment methods) were also extracted to facilitate qualitative evidence synthesis.

Risk-of-bias assessment

Assessment of methodological quality and risk of bias was performed using study design-specific appraisal instruments. The SYRCLE Risk of Bias tool was applied to preclinical animal studies (Hooijmans et al., 2014), evaluating ten domains related to selection, performance, detection, attrition, reporting, and other potential sources of bias.

The methodological quality of the included clinical studies was evaluated using the Joanna Briggs Institute (JBI) Critical Appraisal Checklists, with the selection of the appraisal tool based on the design of each included study. The corresponding JBI checklists for Randomized Controlled Trials, Analytical Cross-Sectional Studies, and Qualitative Research were applied to assess the risk of methodological bias and overall study quality. Risk of bias assessments are provided in Supplementary Table S4.

Effect measures

The principal effect measures focused on safety-related outcomes reported in both preclinical and clinical studies. In preclinical investigations, effect measures included changes in biochemical parameters, endocrine responses, organ weights, histopathological findings, and indicators of toxicity or physiological alterations following exposure to herbal galactagogues, which are commonly used to assess toxicological profiles in experimental models (Asare et al., 2012; Sahoo et al., 2016).

In clinical investigations, effect measures comprised reported adverse events, tolerability, maternal health indicators, and, when available, infant-related safety outcomes. These outcomes are consistent with previous clinical evaluations of galactagogues and lactation-support interventions (Foong et al., 2020). Quantitative meta-analysis was not conducted due to substantial heterogeneity in study designs, intervention characteristics, and reported safety outcomes across preclinical and clinical evidence, which limited the feasibility of statistical pooling (Dwan et al., 2013).

Synthesis methods

A narrative qualitative synthesis was conducted because substantial methodological heterogeneity precluded quantitative pooling of the results. Evidence from preclinical and clinical studies was synthesized separately and subsequently integrated to provide an overall assessment of the safety of herbal galactagogues during lactation (Van der Worp et al., 2010; Van Norman, 2019).

Studies were grouped according to study design, herbal galactagogue, and reported safety outcomes. The findings were summarized descriptively, with emphasis on adverse events, toxicological findings, maternal safety indicators, infant-related safety outcomes, and methodological quality. Similarities and differences across studies were identified to facilitate interpretation of the available evidence.

Ethics statement

Ethical approval was not required for this study because it is a systematic review based on previously published studies and did not involve direct participation of human subjects or experimental animals.

RESULTS

Study selection

The database search identified 862 records from four electronic databases, including PubMed (n = 274), ScienceDirect (n = 275), Springer Nature (n = 265), and SAGE (n = 48). Before screening, 595 records were removed using database filters (original articles and free full-text availability), and 45 duplicate records were removed using Mendeley Reference Manager. This process resulted in 222 records remaining for title and abstract screening.

After title and abstract screening, 183 records were excluded for failing to meet the prespecified eligibility criteria. Subsequently, the full texts of the remaining 39 articles were retrieved and assessed for eligibility. Of these, 26 articles were excluded, including one article for which the full text could not be retrieved and 25 articles that did not meet the prespecified eligibility criteria (population, intervention, outcomes, or study design).

In total, 13 studies fulfilled the eligibility criteria and were included in the qualitative synthesis, consisting of five preclinical studies and eight clinical studies. The complete study-selection process is presented in the PRISMA 2020 flow diagram (Fig. 1).

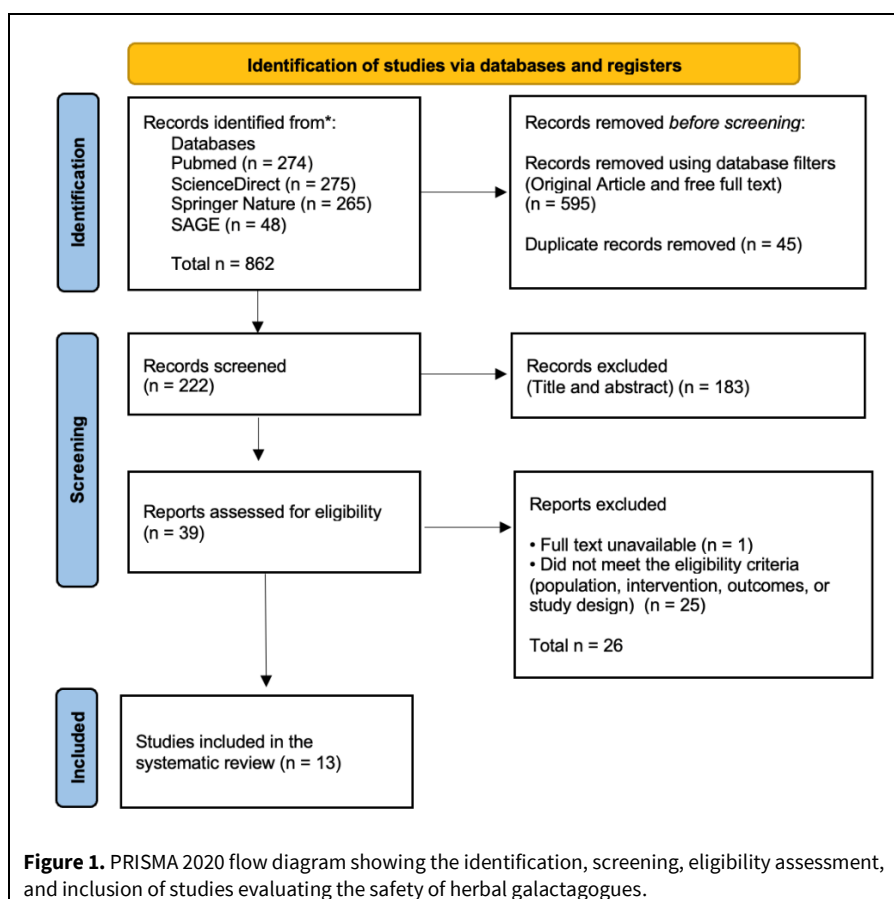


Table 1. Characteristics and reported safety findings of included studies on herbal galactagogues in preclinical studies.

Study	Intervention	Outcomes	Safety Findings
Sahoo et al. (2016)	<i>Teramnus labialis</i>	Milk yield, prolactin	No mortality or signs of acute toxicity were observed following oral administration of 2,000 mg/kg in albino rats.
Mahmood et al. (2012)	<i>Musa × paradisiaca</i> flower extract	Milk production, pup weight gain	No mortality, clinical signs of toxicity, or treatment-related adverse effects were reported during the experimental period. However, no dedicated biochemical, hematological, or histopathological toxicity assessment was performed.
(Simelane et al., 2012)	<i>Gunnera perpensa</i> aqueous rhizome extract	Milk production, pup weight gain, mammary gland histology	No significant alterations in serum ALT, AST, albumin, prolactin, growth hormone, or cortisol. Cytotoxicity testing and mammary histology showed no evidence of treatment-related toxicity.
Dhumal et al. (2014)	Maa-Lact polyherbal granules	Milk production, pup growth, prolactin, mammary histology	Normal clinical observations with no maternal mortality. Hematological and biochemical parameters remained largely within normal ranges, and mammary histopathology showed no treatment-related toxicity.
Chotitham et al. (2025)	Prasanamnom Formula (PNF)	Milk production, serum prolactin, maternal and pup liver/kidney biochemical markers	No clinically significant maternal or pup renal or hepatic toxicity was observed. Liver and kidney biochemical parameters remained within normal ranges, and no abnormal clinical signs or behavioral changes were reported.

After evaluation of titles and abstracts, 183 records were deemed ineligible and were removed from further consideration because they did not fulfill the prespecified inclusion criteria. The majority were excluded due to publication type, lack of relevance to herbal galactagogues, failure to report the prespecified safety endpoints, or the use of ineligible methodological approaches or interventions.

Following full-text evaluation, 26 of the 39 articles were found not to meet the eligibility criteria and were therefore excluded from the review. One article could not be evaluated because the full text was inaccessible. The remaining studies were considered ineligible because they did not fulfill the prespecified PICOS eligibility criteria. The rationale for each full-text exclusion is summarized in Supplementary Table S2.

Study characteristics

A total of 13 studies met the eligibility criteria and were included in the qualitative synthesis, comprising 5 preclinical studies and 8 clinical studies. The included studies evaluated a variety of herbal galactagogues, study populations, experimental models, intervention regimens, and safety outcomes. Considerable methodological heterogeneity was observed across studies with respect to study design, herbal preparations, treatment duration, and outcome assessment, precluding quantitative meta-analysis.

The key characteristics of the included preclinical and clinical studies are presented in Tables 1 and 2, respectively. Comprehensive information for each included study, including the study design, interventions, comparators, treatment duration, primary

outcomes, and safety assessments, is available in Supplementary Table S3.

Preclinical study characteristics

The qualitative synthesis included five preclinical studies evaluating the safety of herbal galactagogues using experimental animal models. The investigated herbal interventions included *Musa × paradisiaca* flower extract, *Gunnera perpensa* aqueous extract, the Maa-Lact herbal formulation, *Teramnus labialis* fruit extract, and the Prasanamnom Formula (PNF). Considerable heterogeneity was observed in the herbal preparations, experimental animal models, treatment duration, comparator groups, and safety assessment methods across the included studies. The reported safety outcomes included clinical observations, biochemical and hematological parameters, liver and kidney function markers, endocrine markers, histopathological findings, cytotoxicity, and indicators of milk production and pup growth. Four of the five preclinical studies incorporated specific biochemical, hematological, histopathological, or toxicity-related safety assessments and reported no evidence of treatment-related toxicity within the investigated experimental conditions. Chotitham et al. (2025), which evaluated the Prasanamnom Formula, specifically assessed maternal and pup renal and hepatic biochemical parameters and reported no clinically significant renal or hepatic toxicity, with biochemical parameters remaining within normal ranges. In contrast, Mahmood et al. (2012) primarily evaluated lactogenic efficacy and did not include dedicated biochemical, hematological, or histopathological toxicity assessments, although no mortality, clinical signs of toxicity, or treatment-related adverse effects were reported during the experimental

period. The characteristics and safety findings of the included preclinical studies are summarized in Table 1.

The reported safety findings included clinical observations, biochemical and hematological parameters, liver function markers (ALT and AST), endocrine markers, histopathological findings, cytotoxicity, and indicators of milk production and pup growth. Four of the five preclinical studies incorporated specific biochemical, hematological, histopathological, or toxicity-related safety assessments and reported no evidence of treatment-related toxicity within the investigated experimental conditions. In contrast, one study primarily evaluated lactogenic efficacy and did not include dedicated biochemical, hematological, or histopathological toxicity assessments, although no mortality, clinical signs of toxicity, or treatment-related adverse effects were reported during the experimental period.

Clinical study characteristics

Clinical investigations included randomized controlled trials, a qualitative study, and observational studies evaluating the safety of herbal galactagogues among breastfeeding women. Considerable heterogeneity was observed with respect to participant characteristics, herbal interventions, treatment duration,

comparator groups, and safety monitoring approaches, reflecting the diversity of clinical research in this field. The included studies evaluated a range of herbal interventions, including *Pimpinella anisum* herbal tea, barley malt-based galactagogue, Ayush-SS granules, the Plook-Fire-Thatu formulation, and various herbal galactagogues used in routine practice.

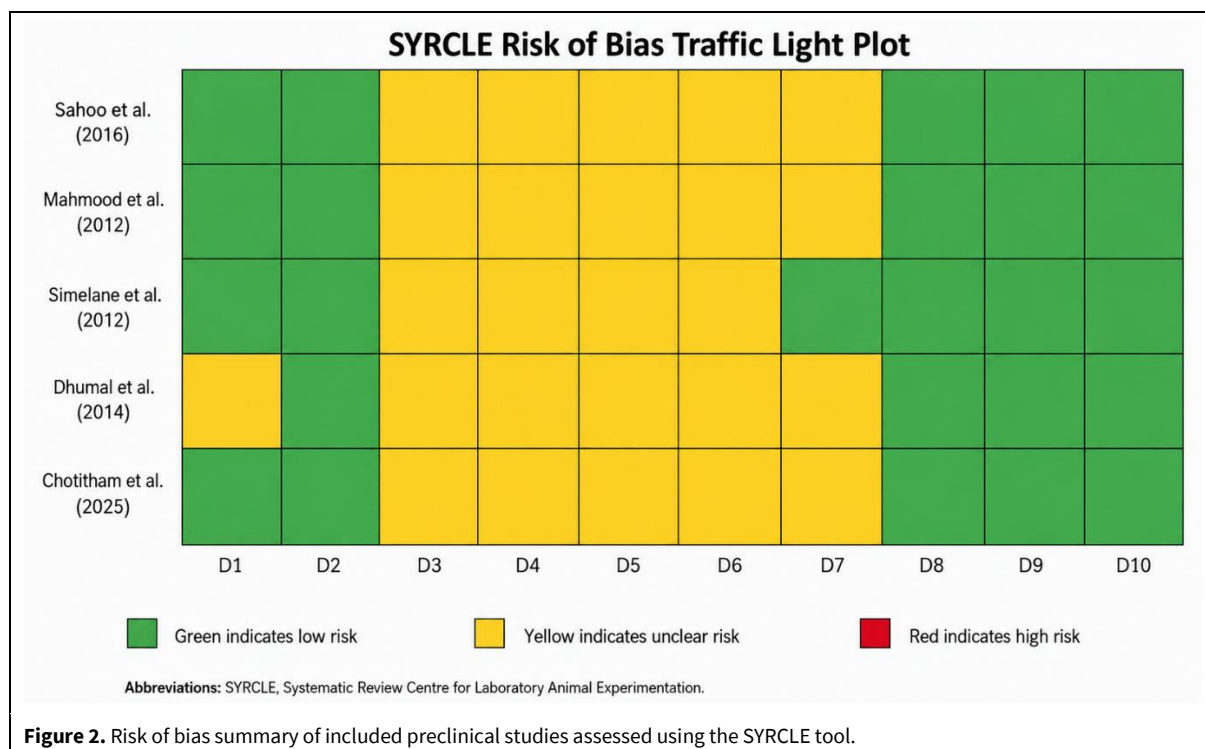
Reported outcomes primarily focused on adverse events, treatment tolerability, maternal safety indicators, and, where available, infant-related safety outcomes. Randomized controlled trials generally reported no serious treatment-related adverse events during the intervention period, with reported adverse events being predominantly mild and self-limiting. In contrast, observational and qualitative studies mainly described patterns of herbal galactagogue use, perceived safety, and self-reported adverse effects rather than prospectively monitored safety outcomes.

Overall, the included clinical studies demonstrated substantial heterogeneity in study design, participant characteristics, herbal interventions, outcome reporting, and methodological quality, limiting direct comparison across studies. The characteristics and reported safety findings of the included clinical studies are summarized in Table 2.

Table 2. Characteristics and reported safety findings of included clinical studies on herbal galactagogues.

Study (design)	Population	Intervention	Safety findings
(Ajgaonkar et al., 2025) (RCT)	120 postpartum women; 20–40 years; ≥37 weeks' gestation; uncomplicated vaginal/caesarean delivery; breastfeeding intention	<i>A. racemosus</i> root extract 300 mg/day for 72 h; standardized to >10% total shatavarin	No adverse events were reported during the 72-hour intervention period
(Khalili et al., 2023) (RCT)	Mothers of preterm infants	<i>Pimpinella anisum</i> tea	No treatment-related adverse events were reported
(Wesolowska et al., 2021) (RCT)	Preterm mothers	Barley malt formulation	No treatment-related adverse events were reported
(Saxena et al., 2025) (RCT)	Lactating mothers	Ayush-SS granules	No serious adverse events observed
(Sintupattanapun et al., 2025) (RCT)	Healthy postpartum women	Plook-Fire-Thatu herbal recipe	No serious adverse events were reported during the intervention, and no clinically significant changes in breast milk macronutrient composition or maternal safety outcomes were observed
(McBride et al., 2021) (Survey)	Australian mothers	Various galactagogues	Self-reported adverse events were reported by a minority of herbal users
(James et al., 2019) (Cross-sectional)	Breastfeeding mothers	Herbal medicine use	Potential safety concerns, herb–drug interactions and limited safety awareness
(Sim et al., 2015) (Qualitative)	Breastfeeding women	Herbal galactagogues	Safety findings were based on maternal perceptions and experiences

Notes: Overall safety interpretation was based on reported adverse events, safety outcomes, and study design.



Risk of bias in studies

The methodological quality of the included studies varied between preclinical and clinical investigations. The preclinical studies, assessed using the SYRCLE Risk of Bias tool, demonstrated an overall moderate risk of bias, primarily because of incomplete reporting of methodological procedures. The most frequently identified methodological limitations were inadequate reporting of sequence generation, allocation concealment, random housing, blinding of caregivers and outcome assessors, and random outcome assessment. Consequently, several domains were judged as having an unclear risk of bias.

The clinical studies were assessed using the Joanna Briggs Institute (JBI) Critical Appraisal Checklists appropriate for each study design. Overall, randomized controlled trials demonstrated higher methodological quality than observational and qualitative studies, fulfilling most appraisal criteria related to participant selection, intervention delivery, outcome measurement, and data analysis. However, incomplete reporting of several methodological aspects, including allocation procedures, follow-up, and reporting transparency, resulted in some appraisal items being rated as unclear or not applicable. Observational and qualitative studies showed greater methodological limitations, particularly with respect to participant recruitment, confounding, reliance on self-reported outcomes, and variability in safety outcome reporting.

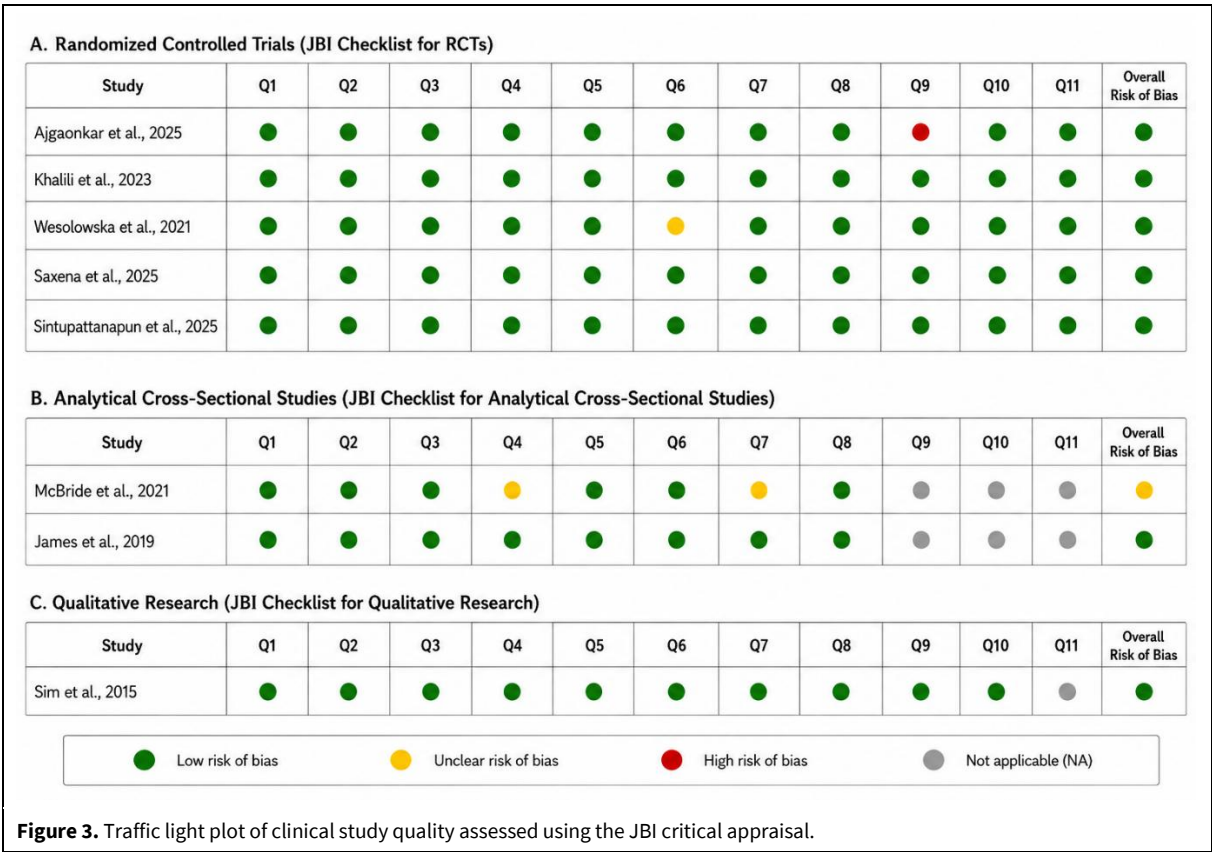
Overall, the methodological limitations identified across both preclinical and clinical studies should be

considered when interpreting the available evidence on the safety of herbal galactagogues. Figs. 2 and 3 provide an overview of the risk-of-bias assessment and the methodological quality evaluation of the included clinical studies. A detailed breakdown of the appraisal for each assessment item is reported in Supplementary Table S4.

Results of individual studies

Most included studies did not report major treatment-related safety concerns; however, the completeness and quality of safety reporting varied substantially across study designs.

Preclinical studies generally reported no evidence of treatment-related toxicity under the evaluated experimental conditions. Mahmood et al. (2012) reported no mortality, clinical signs of toxicity, or treatment-related adverse effects during the experimental period, although comprehensive toxicity assessments were not performed. Sahoo et al. (2016) observed no mortality or signs of acute toxicity at an oral dose of 2,000 mg/kg. Simelane et al. (2012) found no significant alterations in biochemical or endocrine parameters and no evidence of cytotoxicity or mammary histopathological abnormalities. Similarly, Dhumal et al. (2014) reported normal clinical observations, hematological and biochemical parameters, and mammary histopathology, with no evidence of treatment-related toxicity. These findings did not identify major treatment-related short-term safety concerns under the evaluated experimental conditions, although the extent of toxicity assessment varied among studies.



Randomized controlled trials generally reported no serious treatment-related adverse events during the intervention periods. Across the five randomized controlled trials evaluating Shatavari (*Asparagus racemosus*) root extract (Ajgaonkar et al., 2025), *Pimpinella anisum* herbal tea (Khalili et al., 2023), a barley malt-based formulation (Wesolowska et al., 2021), Ayush-SS granules (Saxena et al., 2025), and the Plook-Fire-Thatu herbal formulation (Sintupattanapun et al., 2025), no serious treatment-related adverse events were reported.

In contrast, observational and qualitative studies provided more variable safety information. These studies primarily described patterns of herbal medicine use, maternal experiences, and perceived safety rather than objectively evaluating treatment-related adverse events (James et al., 2019; McBride et al., 2021; Sim et al., 2015). They also highlighted potential real-world safety considerations, including limited disclosure of herbal medicine use to healthcare professionals, possible herb–drug interactions, variability in herbal products, and reliance on self-reported outcomes, indicating the need for more consistent and standardized safety monitoring in future clinical investigations.

Overall, the available evidence suggests that herbal galactagogues were not associated with major treatment-related safety concerns under the investigated study conditions. Preclinical studies did not identify

treatment-related toxicity within the evaluated dose ranges, whereas randomized controlled trials generally reported no serious treatment-related adverse events. Nevertheless, substantial differences in herbal formulations, study designs, experimental protocols, safety outcome assessment, and the completeness of safety reporting limited direct comparison across studies. Nevertheless, the strength of the available evidence remains limited because of methodological heterogeneity, inconsistent safety reporting, and the paucity of standardized long-term safety data.

Synthesis of findings

The synthesis of available evidence indicates that most included studies did not report major short-term treatment-related adverse events; however, the available safety evidence remains limited.

In preclinical studies, the included herbal interventions generally did not demonstrate treatment-related toxicity under the evaluated experimental conditions. Acute toxicity testing, biochemical and hematological analyses, clinical observations, and histopathological evaluations, where performed, showed no evidence of significant toxicity associated with *Teramnus labialis*, *Musa × paradisiaca* flower extract, *Gunnera perperna* aqueous extract, Maa-Lact polyherbal granules, or the Prasanamnom formula (Chotitham et al., 2025; Dhupal et al., 2014; Mahmood et al., 2012; Sahoo et al.,

2016; Simelane et al., 2012). Notably, Chotitham et al. (2025) incorporated maternal and pup liver and kidney biochemical assessments and reported no clinically significant renal or hepatic toxicity. Nevertheless, safety endpoints were not consistently evaluated across all studies, and comprehensive toxicological assessments were unavailable for some interventions, limiting the strength of the preclinical evidence.

Variability in safety reporting

Assessment of reporting bias revealed substantial limitations in the transparency and completeness of safety data across the included studies.

The preclinical evidence demonstrated considerable variability in the methods used to assess and report safety outcomes. Chotitham et al. (2025), Dhumal et al. (2014), Sahoo et al. (2016), and Simelane et al. (2012) incorporated biochemical, histopathological, or toxicity-related assessments, whereas Mahmood et al. (2012) primarily focused on lactogenic efficacy and provided only limited safety information. Consequently, direct comparison of toxicity outcomes across preclinical studies was constrained by differences in reported safety endpoints and the lack of standardized toxicity assessment.

Similarly, reporting varied across the clinical studies. Randomized controlled trials generally provided structured reporting of adverse events and maternal safety outcomes (Ajgaonkar et al., 2025; Khalili et al., 2023; Saxena et al., 2025; Sintupattanapun et al., 2025; Wesolowska et al., 2021), whereas observational and qualitative studies primarily relied on participant-reported experiences and descriptions of herbal medicine use (James et al., 2019; McBride et al., 2021; Sim et al., 2015). The extent and format of adverse-event reporting differed substantially among studies, limiting direct comparison of safety outcomes.

Overall, inconsistent reporting of safety outcomes, heterogeneity in assessment methods, and incomplete descriptions of adverse events limited the comparability and comprehensive evaluation of the reported safety outcomes of herbal galactagogues.

DISCUSSION

Overall interpretation of the evidence

This systematic review synthesized preclinical and clinical evidence regarding the safety of herbal galactagogues. Overall, the available evidence did not identify major short-term treatment-related safety concerns under the investigated study conditions. Across the included randomized controlled trials, herbal interventions, including Shatavari (*Asparagus racemosus*) root extract, *Pimpinella anisum* herbal tea, barley malt-based

formulations, Ayush-SS granules, and the Plook-Fire-Thatu herbal formulation, were generally well tolerated, with no serious treatment-related adverse events reported (Ajgaonkar et al., 2025; Khalili et al., 2023; Saxena et al., 2025; Sintupattanapun et al., 2025; Wesolowska et al., 2021).

The preclinical evidence was broadly consistent with the clinical findings, although the extent of safety assessment varied among studies. The five preclinical investigations evaluated different safety domains, including clinical observations, acute toxicity, biochemical and hematological parameters, endocrine markers, cytotoxicity, and histopathological findings. Chotitham et al. (2025) additionally assessed maternal and pup renal and hepatic biochemical parameters and reported no clinically significant toxicity, whereas other studies reported no mortality or treatment-related clinical signs under the investigated experimental conditions (Chotitham et al., 2025; Dhumal et al., 2014; Mahmood et al., 2012; Sahoo et al., 2016; Simelane et al., 2012).

Nevertheless, these findings should not be interpreted as establishing the overall safety of herbal galactagogues. Differences in herbal formulations, doses, treatment durations, study designs, and safety assessment methods limit direct comparison and generalizability. In particular, the absence of reported adverse events does not necessarily indicate the absence of uncommon, delayed, or cumulative effects.

Preclinical safety evidence

The five included preclinical studies generally reported no evidence of treatment-related toxicity within the evaluated experimental conditions. Mahmood et al. (2012) reported no mortality, clinical signs of toxicity, or treatment-related adverse effects, although dedicated biochemical, hematological, and histopathological assessments were not performed. Sahoo et al. (2016) reported no mortality or signs of acute toxicity following oral administration of 2,000 mg/kg, while Simelane et al. (2012) found no significant alterations in biochemical or endocrine parameters and no evidence of cytotoxicity or mammary histopathological abnormalities. Dhumal et al. (2014) similarly reported normal clinical, hematological, biochemical, and mammary histopathological findings.

Chotitham et al. (2025) strengthened the available preclinical evidence by incorporating maternal and pup liver and kidney biochemical assessments. No clinically significant renal or hepatic toxicity was observed, and the measured biochemical parameters remained within normal ranges. However, the safety domains evaluated across the five studies were not uniform, and one study primarily focused on lactogenic

efficacy rather than comprehensive toxicity assessment. Consequently, the preclinical findings provide supportive evidence of short-term tolerability but do not establish comprehensive toxicological safety across different doses, durations, or populations.

The methodological quality of the animal studies also needs to be considered. The SYRCLE assessment indicated moderate methodological concerns, particularly related to incomplete reporting of sequence generation, allocation concealment, random housing, and blinding. These limitations may reduce confidence in the reproducibility and internal validity of the reported safety findings (Hooijmans et al., 2014; Kilkenney et al., 2010).

Clinical safety evidence

The clinical evidence generally indicated reassuring short-term tolerability, particularly among randomized controlled trials. Five randomized controlled trials evaluating Shatavari (*Asparagus racemosus*) root extract, *Pimpinella anisum* herbal tea, a barley malt-based formulation, Ayush-SS granules, and Plook-Fire-Thatu reported no serious treatment-related adverse events during the respective intervention periods (Ajgaonkar et al., 2025; Khalili et al., 2023; Saxena et al., 2025; Sintupattanapun et al., 2025; Wesolowska et al., 2021). However, these findings primarily reflect short-term intervention periods and should not be interpreted as evidence of long-term maternal or infant safety.

Additional safety information was reported in the abstract of Zulkarnain et al. (2024), which evaluated an Indonesian polyherbal galactagogue in breastfeeding mothers. Mean ALT, AST, urea, and creatinine levels remained within normal ranges across the three assessment points; however, approximately 3–5% of mothers experienced elevated ALT or AST levels and nausea, which were reported as tolerable, while no adverse effects were reported in infants. Because the full text could not be retrieved, these findings were not included in the formal qualitative synthesis and should therefore be interpreted cautiously.

In contrast, observational and qualitative studies provided more variable safety information. James et al. (2019), McBride et al. (2021), and Sim et al. (2015) primarily described herbal medicine use, maternal experiences, perceived safety, and self-reported adverse effects rather than prospectively monitored treatment-related outcomes. Although these studies provide valuable real-world information, their reliance on self-reporting and differences in exposure and product use limit objective assessment of causality and safety.

The methodological quality of the clinical evidence also varied. Randomized controlled trials generally demonstrated higher methodological quality, whereas

observational and qualitative studies showed greater limitations related to participant recruitment, confounding, self-reported outcomes, and variability in safety reporting. These differences should therefore be considered when integrating clinical evidence across study designs.

Safety considerations beyond controlled studies

Safety in routine use may be influenced by factors that are not fully captured in controlled clinical trials. Observational and qualitative studies highlighted variability in herbal medicine use, including differences in product composition, dosing, duration of use, and patterns of self-medication. Limited disclosure of herbal medicine use to healthcare professionals may further complicate assessment of treatment-related adverse events and potential herb–drug interactions (James et al., 2019; McBride et al., 2021; Sim et al., 2015). These findings emphasize the importance of obtaining a complete history of herbal medicine use and concomitant medications when evaluating the safety of herbal galactagogues during breastfeeding.

Product quality is another important consideration beyond the controlled study setting. Variability in herbal preparations, together with potential contamination or adulteration, may introduce safety risks that are not necessarily detected in clinical trials. Previous reports have described contamination with heavy metals and the presence of undeclared compounds in some herbal medicinal products (Alharbi et al., 2024; Bent, 2008; Ekor, 2014; Ernst, 2002; Posadzki et al., 2013; Saper et al., 2008). In addition, potential herb–drug interactions remain insufficiently characterized, particularly in postpartum women who may use herbal products concomitantly with conventional medicines (Cheng et al., 2023; Fasinu et al., 2012). Therefore, product standardization, quality control, pharmacovigilance, and improved communication between breastfeeding women and healthcare professionals are important components of safety assessment beyond controlled research settings.

Limitations of evidence

Several limitations should be considered when interpreting the clinical evidence. Although the inclusion of the recent randomized controlled trial by Ajgaonkar et al. (2025) strengthens the available clinical evidence on herbal galactagogues, it does not eliminate the substantial heterogeneity among the included studies. The studies differed considerably in terms of the herbal species and formulations investigated, plant parts and preparation methods, dosage and treatment regimens, study populations, outcome measures, and duration of follow-up. Such variability limits direct comparison across studies and may contribute to differences in the

observed efficacy and safety outcomes. In particular, Ajgaonkar et al. (2025) evaluated *Asparagus racemosus* root extract for only 72 hours postpartum; therefore, the absence of reported adverse events primarily provides evidence of short-term tolerability and should not be interpreted as evidence of long-term maternal or infant safety.

Furthermore, adverse-event definitions, monitoring procedures, and reporting practices were not uniform across the included clinical studies, which may limit the comparability of safety findings and potentially result in underrecognition or underreporting of adverse events. The limited duration of follow-up across several studies also restricts the assessment of delayed or cumulative adverse effects, particularly in breastfeeding infants who may be exposed through breast milk. Therefore, the current clinical evidence remains insufficient to establish the long-term safety profile of herbal galactagogues. Future clinical studies should incorporate standardized characterization of herbal preparations, clearly defined dosing regimens, longer follow-up periods, systematic and standardized adverse-event monitoring, and dedicated assessment of both maternal and infant safety outcomes.

Limitations of the review process

This review has several methodological limitations. Restriction to English-language publications may have resulted in the exclusion of relevant evidence published in other languages, introducing the possibility of language bias (Ekor, 2014). In addition, grey literature, conference proceedings, dissertations, theses, and clinical trial registries were not systematically searched, which may have contributed to publication bias, particularly if studies with negative or inconclusive safety findings were less likely to be published in peer-reviewed journals (Dwan et al., 2013). The ScienceDirect search was subject to a platform-specific query constraint that required a narrower search string, which may have reduced sensitivity to eligible records using alternative terms such as breastfeeding, lactation, toxicity, adverse events, or specific plant names.

A narrative synthesis was used because substantial clinical, methodological, and outcome heterogeneity prevented appropriate quantitative pooling. The included studies differed considerably in populations, herbal formulations, intervention regimens, comparator groups, study designs, and safety endpoints, including biochemical and hematological parameters, histopathological findings, endocrine markers, adverse events, and maternal–infant outcomes.

Despite these limitations, several methodological measures strengthened the review, including

comprehensive database searching, duplicate study selection, independent data extraction, prespecified eligibility criteria, and design-specific methodological appraisal. The complete review protocol was also developed before study selection and is provided as Supplementary Table S5, supporting transparency and reproducibility of the review process.

Clinical and research implications

The findings of this systematic review suggest that current evidence did not identify major short-term treatment-related safety concerns under the evaluated study conditions. However, their use should remain cautious because the current evidence is limited by methodological heterogeneity, incomplete safety reporting, and insufficient long-term follow-up. Healthcare professionals should routinely inquire about herbal medicine use during breastfeeding, including product type, dosage, duration, and concomitant medications, and provide evidence-based counseling to minimize potential risks and identify possible herb–drug interactions (James et al., 2019; McBride et al., 2021; Sim et al., 2015).

From a regulatory perspective, greater emphasis should be placed on the standardization of herbal preparations, quality control throughout manufacturing, and strengthened pharmacovigilance systems to improve product consistency and post-marketing safety surveillance (Choudhury et al., 2023; Ekor, 2014; Heinrich, 2015). Standardized reporting of adverse events would also improve the comparability of future clinical studies.

These findings support cautious clinical use accompanied by appropriate safety monitoring and highlight the need for standardized reporting and pharmacovigilance. In addition, observational studies with rigorous adverse-event reporting and pharmacovigilance data are needed to better characterize the long-term safety profile of herbal galactagogues under routine clinical practice. Such evidence will enhance clinical decision-making and facilitate the development of evidence-informed recommendations for the integration of herbal galactagogues while breastfeeding.

Future research directions

Future investigations should use rigorous, standardized preclinical study designs to establish the safety of herbal galactagogues. To determine dose–response relationships, safety margins, and target organ toxicity, well-designed *in vivo* studies are required. Comprehensive toxicological evaluations, including detailed histopathological analysis, should be performed using validated models. Future animal studies should also adhere to reporting guidelines such as ARRIVE to

improve methodological quality, transparency, and reproducibility.

Subsequent clinical investigations should evaluate not only lactogenic efficacy but also safety-related outcomes in both breastfeeding mothers and infants. As herbal galactagogues are consumed during breastfeeding, future investigations should adopt a mother–infant safety framework, integrating maternal safety with infant health outcomes. In addition to using chemically standardized herbal preparations, prespecified adverse-event monitoring, liver and renal function assessments, endocrine biomarker evaluation, breast milk transfer studies, and herb–drug interaction assessment, future trials should include longitudinal monitoring of infant weight gain, growth and developmental parameters, feeding tolerance, and clinically relevant adverse events. Such an integrated approach is essential to establish the overall benefit–risk profile and support safe clinical use.

Mechanistic studies should clarify how herbal constituents influence endocrine and immune pathways and interact with concomitant medicines. Considering the prevalent application of polyherbal formulations, subsequent research ought to explore potential synergistic and antagonistic interactions among plant constituents. Pharmacovigilance systems, cohort studies, and registry-based research should be strengthened to detect rare or delayed adverse events, providing a stronger evidence base for clinical and regulatory decision-making.

CONCLUSION

The current evidence did not identify major short-term treatment-related safety concerns for the evaluated herbal galactagogues under the investigated study conditions. Interpretation of the available evidence is limited by methodological heterogeneity, formulation-related variability, inconsistent documentation of safety outcomes, and insufficient long-term maternal and infant safety data. Therefore, these findings should not be generalized to all herbal galactagogues or commercial herbal products. Future well-designed randomized controlled trials using standardized herbal preparations, prespecified safety endpoints, comprehensive maternal–infant safety monitoring, and longer follow-up periods are required to strengthen the evidence regarding the safety of herbal galactagogues during breastfeeding.

CONFLICT OF INTEREST

The authors declare that there are no conflicts of interest regarding the publication of this paper. The authors have no financial, personal, or institutional relationships that could

inappropriately influence or bias the work reported in this study.

ACKNOWLEDGMENTS

The authors extend their sincere appreciation to Institut Teknologi Bandung for enabling access to a comprehensive collection of internationally recognized scientific journals, which provided essential scholarly resources throughout this research. This research did not receive any specific grant from funding agencies in the public, commercial, or not-for-profit sectors.

GENERATIVE ARTIFICIAL INTELLIGENCE (AI)

The authors used Grammarly (Grammarly Inc.) and QuillBot (Learneo, Inc.) to improve the language and readability of the manuscript. The authors reviewed and edited the content and take full responsibility for its accuracy. No images were generated or manipulated using AI tools.

REFERENCES

- Ajgaonkar A, Debnath T, Bhatnagar S, Debnath K, Langade J (2025) Shatavari (*Asparagus racemosus* Willd) root extract for postpartum lactation: A randomised, double-blind, placebo-controlled study. *J Obstet Gynaecol* 45(1): 2564168. <https://doi.org/10.1080/01443615.2025.2564168>
- Alharbi SF, Althbah AI, Mohammed AH, Alrasheed MA, Ismail M, Allemailem KS, Alnuqaydan AM, Baabdullah AM, Alkhalifah A (2024) Microbial and heavy metal contamination in herbal medicine: a prospective study in the central region of Saudi Arabia. *BMC Complement Med Ther* 24: 2. <https://doi.org/10.1186/s12906-023-04307-y>
- Asare GA, Gyan B, Bugyei K, Adjei S, Mahama R, Addo P, Otu-Nyarko L, Wiredu EK, Nyarko A (2012) Toxicity potentials of the nutraceutical *Moringa oleifera* at supra-supplementation levels. *J Ethnopharmacol* 139(1): 265–272. <https://doi.org/10.1016/j.jep.2011.11.009>
- Balkam JJ (2022) Galactagogues and lactation: considerations for counseling breastfeeding mothers. *MCN Am J Matern Child Nurs* 47(3): 130–137. <https://doi.org/10.1097/NMC.0000000000000810>
- Basch E, Ulbricht C, Kuo G, Szapary P, Smith M (2003) Therapeutic applications of fenugreek. *Altern Med Rev* 8(1): 20–27.
- Bent S (2008) Herbal medicine in the United States: Review of efficacy, safety, and regulation. *J Gen Intern Med* 23: 854–859. <https://doi.org/10.1007/s11606-008-0632-y>
- Buntuchai G, Pavadhgul P, Kittipichai W, Satheannoppakao W (2017) Traditional galactagogue foods and their connection to human milk volume in Thai breastfeeding mothers. *J Hum Lact* 33(3): 552–559. <https://doi.org/10.1177/0890334417709432>
- Cheng W, Xia K, Wu S, Li Y (2023) Herb–drug interactions and their impact on pharmacokinetics: An update. *Curr Drug Metab* 24(1): 28–69. <https://doi.org/10.2174/1389200224666230116113240>
- Chothitham P, Booranasubkajorn S, Pattanapholkornsakul S, Akarasereenont P, Tripatara P (2025) Efficacy and safety of an herbal galactagogue decoction versus powdered formulation in lactating rats. *Phytomedicine Plus* 5(1): 100745. <https://doi.org/10.1016/j.phyplu.2025.100745>
- Choudhury A, Singh PA, Bajwa N, Dash S, Bisht P (2023) Pharmacovigilance of herbal medicines: Concerns and future prospects. *J Ethnopharmacol* 309: 116383. <https://doi.org/10.1016/j.jep.2023.116383>

- Dhumal R, Selkar NA, Chawda MB, Thakur KS, Vahalia MK, Gopal VJ, Vanage G (2014) Evaluation of safety and efficacy of Maa-Lact in lactating Holtzman rats. *Asian Pac J Reprod* 3(1): 8–12. [https://doi.org/10.1016/S2305-0500\(13\)60177-3](https://doi.org/10.1016/S2305-0500(13)60177-3)
- Dubale S, Usure RE, Mekasha YT, Hasen G, Hafiz F, Kebebe D, Suleman S (2025) Traditional herbal medicine legislative and regulatory framework: A cross-sectional quantitative study and archival review perspectives. *Front Pharmacol* 16: 1475297. <https://doi.org/10.3389/fphar.2025.1475297>
- Dwan K, Gamble C, Williamson PR, Kirkham JJ (2013) Systematic review of the empirical evidence of study publication bias and outcome reporting bias – An updated review. *PLoS ONE* 8: e66844. <https://doi.org/10.1371/journal.pone.0066844>
- Ekor M (2014) The growing use of herbal medicines and safety concerns. *Front Pharmacol* 4: 177. <https://doi.org/10.3389/fphar.2013.00177>
- Ernst E (2002) Toxic heavy metals and undeclared drugs in Asian herbal medicines. *Trends Pharmacol Sci* 23(3): 136–139. [https://doi.org/10.1016/S0165-6147\(00\)01972-6](https://doi.org/10.1016/S0165-6147(00)01972-6)
- Fasinu PS, Bouic PJ, Rosenkranz B (2012) An overview of the evidence and mechanisms of herb–drug interactions. *Front Pharmacol* 3: 69. <https://doi.org/10.3389/fphar.2012.00069>
- Foong SC, Tan ML, Foong WC, Marasco LA, Ho JJ, Ong JH (2020) Oral galactagogues (natural therapies or drugs) for increasing breast milk production in mothers of non-hospitalised term infants. *Cochrane Database Syst Rev* 5: CD011505. <https://doi.org/10.1002/14651858.CD011505.pub2>
- Gabay MP (2002) Galactagogues: Medications that induce lactation. *J Hum Lact* 18(3): 274–279. <https://doi.org/10.1177/089033440201800311>
- Gossler SM (2010) Use of complementary and alternative therapies during pregnancy, postpartum, and lactation. *J Psychosoc Nurs Ment Health Serv* 48(11): 30–36. <https://doi.org/10.3928/02793695-20100930-02>
- Heinrich M (2015) Quality and safety of herbal medical products: Regulation and the need for quality assurance along the value chains. *Br J Clin Pharmacol* 80(1): 62–66. <https://doi.org/10.1111/bcp.12586>
- Hooijmans CR, Rovers MM, de Vries RBM, Leenaars M, Ritskes-Hoitinga M, Langendam MW (2014) SYRCLE's risk of bias tool for animal studies. *BMC Med Res Methodol* 14: 43. <https://doi.org/10.1186/1471-2288-14-43>
- Intan PR, Alegantina S, Isnawati A, Yunarto N, Ekawasti F, Rinendyaputri R, Sunarno S, Sani Y, Mariya SS, Handharyani E (2024) Effects of a blend extract of *Sauropus androgynus*, *Moringa oleifera*, and *Coleus amboinicus* on milk production in lactating rats. *Open Vet J* 14(12): 3630–3639. <https://doi.org/10.5455/OVJ.2024.v14.i12.44>
- James PB, Kaikai AI, Bah AJ, Steel A, Wardle J (2019) Herbal medicine use during breastfeeding: a cross-sectional study among mothers visiting public health facilities in the Western area of Sierra Leone. *BMC Complement Altern Med* 19: 66. <https://doi.org/10.1186/s12906-019-2479-7>
- Jendras G, Monizi M, Neinhuis C, Lautenschläger T (2020) Plants, food and treatments used by BaKongo tribes in Uíge (northern Angola) to affect the quality and quantity of human breast milk. *Int Breastfeed J* 15: 88. <https://doi.org/10.1186/s13006-020-00329-1>
- Jin X, Perrella SL, Lai CT, Taylor NL, Geddes DT (2024) Causes of low milk supply: The roles of estrogens, progesterone, and related external factors. *Adv Nutr* 15(1): 100129. <https://doi.org/10.1016/j.advnut.2023.10.002>
- Khalili S, Amiri-Farahani L, Haghani S, Bordbar A, Shojaii A, Pezaro S (2023) The effect of *Pimpinella anisum* herbal tea on human milk volume and weight gain in the preterm infant: a Randomised controlled clinical trial. *BMC Complement Med Ther* 23: 19. <https://doi.org/10.1186/s12906-023-03848-6>
- Khan MAA, Khalid M, Malik O (2025) The safety of herbal medicines in low- and middle-income countries (LMICs): current landscape and promoting the pharmacovigilance practices. *J Pharm Policy Pract* 18(1): 2574651. <https://doi.org/10.1080/20523211.2025.2574651>
- Khan TM, Wu DB, Dolzhenko AV (2018) Effectiveness of fenugreek as a galactagogue: A network meta-analysis. *Phytother Res* 32(3): 402–412. <https://doi.org/10.1002/ptr.5972>
- Kilkenny C, Browne WJ, Cuthill IC, Emerson M, Altman DG (2010) Improving bioscience research reporting: The ARRIVE guidelines for reporting animal research. *PLoS Biol* 8(6): e1000412. <https://doi.org/10.1371/journal.pbio.1000412>
- Mahmood A, Omar MN, Ngah N (2012) Galactagogue effects of *Musa × paradisiaca* flower extract on lactating rats. *Asian Pac J Trop Med* 5(11): 882–886. [https://doi.org/10.1016/S1995-7645\(12\)60164-3](https://doi.org/10.1016/S1995-7645(12)60164-3)
- McBride GM, Stevenson R, Zizzo G, Rumbold AR, Amir LH, Keir AK, Grzeskowiak LE (2021) Use and experiences of galactagogues while breastfeeding among Australian women. *PLoS ONE* 16(7): e0254049. <https://doi.org/10.1371/journal.pone.0254049>
- Mortel M, Mehta SD (2013) Systematic review of herbal galactagogues. *J Hum Lact* 29(2): 154–162. <https://doi.org/10.1177/0890334413477243>
- Nurhayati, Rompegading AB, Rahma BN, Yanti R (2024) The effect of katuk leaf (*Sauropus androgynus*) on increased milk production in breastfeeding mothers. *Hayyan Journal* 1(3): 13–16. <https://doi.org/10.51574/hayyan.v1i3.1739>
- Page MJ, McKenzie JE, Bossuyt PM, Boutron I, Hoffmann TC, Mulrow CD, Shamseer L, Tetzlaff JM, Akl EA, Brennan SE, Chou R, Glanville J, Grimshaw JM, Hróbjartsson A, Lalu MM, Li T, Loder EW, Mayo-Wilson E, McDonald S, McGuinness LA, Stewart LA, Thomas J, Tricco AC, Welch VA, Whiting P, Moher D (2021) The PRISMA 2020 statement: an updated guideline for reporting systematic reviews. *BMJ* 372: n71. <https://doi.org/10.1136/bmj.n71>
- Posadzki P, Watson L, Ernst E (2013) Contamination and adulteration of herbal medicinal products (HMPs): an overview of systematic reviews. *Eur J Clin Pharmacol* 69: 295–307. <https://doi.org/10.1007/s00228-012-1353-z>
- Rouhi M, Hossieni MB, Khodaie L, Mohammad-Alizadeh-Charandabi S, Mirghafourvand M (2025) Investigating the effectiveness of fenugreek on the quantity of breast milk and the level of prolactin in mothers of preterm newborns: A randomised controlled clinical trial. *Curr Drug Res Rev* 17(3): 471–480. <https://doi.org/10.2174/0125899775313919240822102906>
- Sahoo HB, Bhajji A, Santani DD (2016) Lactogenic activity of *Teramnus labialis* (Linn.) fruit with special reference to the estimation of serum prolactin and cortisol level in nursing rats. *Indian J Pharmacol* 48(6): 715–719. <https://doi.org/10.4103/0253-7613.194856>
- Sanghvi K, Subraya CK, Pai V, Nanjundaiah ARHH, Kunhikatta V (2023) Pharmacovigilance in herbal drugs: A challenge. *Curr Drug Saf* 18(2): e280422204219. <https://doi.org/10.2174/1574886317666220428125943>
- Saper RB, Phillips RS, Sehgal A, Khouri N, Davis RB, Paquin J, Thuppil V, Kales SN (2008) Lead, mercury, and arsenic in US- and Indian-manufactured Ayurvedic medicines sold via the Internet. *JAMA* 300(8): 915–923. <https://doi.org/10.1001/jama.300.8.915>
- Saxena U, Ota S, Rajput S, Anand B, Tripathi A, Singhal R, Kumar A, Lachyan A (2025) Clinical evaluation of Ayush-SS granules in exclusively breastfeeding mothers with insufficient lactation: a

randomized, double-blind, placebo-controlled trial. *Int Breastfeed J* 20: 26. <https://doi.org/10.1186/s13006-025-00721-9>

Sethi SS, Bhardwaj T, Sethi SK, Kaur S, Rimpi, Baldi A (2025) Advancing herbal medicine safety: the need for a global pharmacovigilance approach. *Naunyn Schmiedebergs Arch Pharmacol* 398: 13499–13514. <https://doi.org/10.1007/s00210-025-04066-2>

Sim TF, Hattingh HL, Sherriff J, Tee LB (2015) The use, perceived effectiveness and safety of herbal galactagogues during breastfeeding: A qualitative study. *Int J Environ Res Public Health* 12(9): 11050–11071. <https://doi.org/10.3390/ijerph120911050>

Simelane MBC, Lawal OA, Djarova TG, Musabayane CT, Singh M, Opoku AR (2012) Lactogenic activity of rats stimulated by *Gunnera perpensa* L. (Gunneraceae) from South Africa. *Afr J Tradit Complement Altern Med* 9(4): 561–573. <https://doi.org/10.4314/ajtcam.v9i4.14>

Sintupattanapun P, Namvichaisirikul N, Tongdee P, Suwannobol N, Thueng-in K, Chueadet A, Tastub S (2025) Efficacy and safety of the Plook-Fire-Thatu recipe on breast milk volume and breast milk macronutrient composition in postpartum women: A randomised controlled trial. *Complement Ther Med* 94: 103255. <https://doi.org/10.1016/j.ctim.2025.103255>

Usure RE, Kebebe D, Mekasha YT, Hasen G, Chura Waritu N, Dubale S, Suleman S (2024) Traditional herbal medicine regulatory implementation in Ethiopia: A qualitative study. *Front Pharmacol* 15: 1392330. <https://doi.org/10.3389/fphar.2024.1392330>

Van der Worp HB, Howells DW, Sena ES, Porritt MJ, Rewell S, O'Collins V, Macleod MR. (2010) Can animal models of disease reliably inform human studies? *PLoS Med* 7(3): e1000245. <https://doi.org/10.1371/journal.pmed.1000245>

Van Norman GA (2019) Limitations of animal studies for predicting toxicity in clinical trials: Is it time to rethink our current approach? *JACC Basic Transl Sci* 4(7): 845–854. <https://doi.org/10.1016/j.jacbts.2019.10.008>

Wesolowska A, Pietrzak B, Kociszewska-Najman B, Wielgos M, Czajkowski K, Wietrak E, Karzel K, Borszewska-Kornacka MK (2021) Barley malt-based composition as a galactagogue - A randomised, controlled trial in preterm mothers. *Ginekol Pol* 92(2): 118–125. <https://doi.org/10.5603/GP.a2020.0107>

Zapantis A, Steinberg JG, Schilit L (2012) Use of herbals as galactagogues. *J Pharm Pract* 25(2): 222–231. <https://doi.org/10.1177/0897190011431636>

Zulkarnain Z, Fitriani U, Ardiyanto D, Saryanto, Wijayanti E, Triyono A, Novianto F (2024) Galactagogue activity of poly-herbal decoction from Indonesia: A randomised open label controlled trial. *J Complement Integr Med* 21(4): 532–539. <https://doi.org/10.1515/jcim-2020-0246>

AUTHOR CONTRIBUTION:

Contribution	Nurmala S	Kurniati NF	Anggadiredja K
Concepts or ideas	x	x	x
Design	x	x	
Definition of intellectual content	x		x
Literature search	x	x	x
Experimental studies			
Data acquisition	x	x	
Data analysis	x		x
Statistical analysis	x		
Manuscript preparation	x		
Manuscript editing	x	x	x
Manuscript review	x	x	x

Citation Format: Nurmala S, Kurniati NF, Anggadiredja K (2026) Safety of herbal galactagogues: A systematic review of preclinical and clinical evidence. *J Pharm Pharmacogn Res* 14(5): 2828. https://doi.org/10.56499/jppres_14.5.2828

Publisher’s Note: All claims expressed in this article are solely those of the authors and do not necessarily represent those of their affiliated organizations, or those of the publisher, the editors and the reviewers. Any product that may be evaluated in this article, or claim that may be made by its manufacturer, is not guaranteed or endorsed by the publisher.

Open Access: This article is distributed under the terms of the Creative Commons Attribution 4.0 International License (<http://creativecommons.org/licenses/by/4.0/>), which permits use, duplication, adaptation, distribution and reproduction in any medium or format, as long as you give appropriate credit to the original author(s) and the source, provide a link to the Creative Commons license and indicate if changes were made.

Supplementary data

Annex 1. PRISMA 2020 item checklist.

Safety of Herbal Galactagogues: A Systematic Review of Preclinical and Clinical Evidence			
Section and topic	Item #	Checklist item	Location where item is reported
Title	1	Identify the report as a systematic review.	Title page, p. 1
Abstract	2	See the PRISMA 2020 for Abstracts checklist.	Abstract, p. 1
Introduction	3	Describe the rationale for the review in the context of existing knowledge.	Introduction, p. 2
Introduction	4	Provide an explicit statement of the objective(s) or question(s) the review addresses.	Introduction, final paragraph, p. 2
Methods	5	Specify the inclusion and exclusion criteria and how studies were grouped for syntheses.	Methods – Eligibility criteria; PICOS, p. 3
Methods	6	Specify all databases/sources searched and the date last searched.	Methods – Information sources; Search strategy, p. 3
Methods	7	Present the full search strategies for all databases/websites, including filters and limits.	Methods – Search strategy; Supplementary Table S1, p. 7
Methods	8	Specify methods for study selection, number of reviewers, independence, and conflict resolution.	Methods – Selection process, p. 4
Methods	9	Specify methods for data collection, number of reviewers, independence, and discrepancy resolution.	Methods – Data collection process, p. 4
Methods	10a	List and define all outcomes for which data were sought.	Methods – Data items, p. 4
Methods	10b	List and define other variables for which data were sought and assumptions about missing/unclear information.	Methods – Data items, p. 4
Methods	11	Specify risk-of-bias methods, tools, number of assessors and independence.	Methods – Risk-of-bias assessment; Supplementary Table S4, p. 4
Methods	12	Specify effect measures for each outcome used in synthesis/presentation.	Methods – Effect measures, p. 4
Methods	13a	Describe how studies were selected for each synthesis.	Supplementary Table S3
Methods	13b	Describe data preparation/conversions, if any.	Supplementary Table S1
Methods	13c	Describe methods for tabulating or visually displaying results.	Methods – Synthesis methods; p. 5
Methods	13d	Describe synthesis methods and rationale; meta-analysis details if performed.	Methods – Synthesis methods; p. 5
Methods	13e	Describe methods to explore causes of heterogeneity.	Not applicable; no formal subgroup analysis/meta-regression performed.
Methods	13f	Describe sensitivity analyses.	Not applicable; no sensitivity analyses performed.
Methods	14	Describe methods to assess reporting bias due to missing results.	Not formally assessed in this review.
Methods	15	Describe methods to assess certainty/confidence in the body of evidence.	Not formally assessed in this review.
Results	16a	Describe search and selection results, ideally with a flow diagram.	Results – Study selection + Fig. 1, p. 5
Results	16b	Cite potentially eligible excluded studies and explain why they were excluded.	Results – Excluded studies; Supplementary Table S2
Results	17	Cite each included study and present characteristics.	Study characteristics; p. 7
Results	18	Present risk-of-bias assessments for each included study.	Results – Risk of bias; p. 8
Results	19	Present results for each study for all outcomes,	Results of individual studies; Table 1 p. 6;

		with summary statistics/effect estimates where appropriate.	Table 2 p. 7
Results	20a	Summarise characteristics and risk of bias among studies contributing to each synthesis.	Results of syntheses, p. 9
Results	20b	Present results of statistical syntheses, if performed.	Not applicable; no meta-analysis/statistical synthesis performed.
Results	20c	Present results of investigations of causes of heterogeneity.	Not applicable; no formal heterogeneity investigation performed.
Results	20d	Present sensitivity analyses, if conducted.	Not applicable; no sensitivity analyses performed.
Results	21	Present assessments of reporting bias for each synthesis assessed.	Not formally assessed in this review.
Results	22	Present certainty/confidence assessments for each outcome assessed.	Not formally assessed in this review.
Discussion	23a	Provide general interpretation in context of other evidence.	Discussion – Overall interpretation of the evidence, p. 10
Discussion	23b	Discuss limitations of the evidence included in the review.	Discussion – Limitations of evidence, p. 11
Discussion	23c	Discuss limitations of the review processes.	Discussion – Limitations of the Review Process, p. 12
Discussion	23d	Discuss implications for practice, policy and future research.	Discussion – Clinical and research implications; Future Research Directions, p. 12
Other information	24a	Provide registration information or state that the review was not registered.	Methods – Study design and reporting guidelines: protocol not prospectively registered
Other information	24b	Indicate where the protocol can be accessed or state that none was prepared.	Methods – Study design and reporting guidelines; Supplementary Table S5
Other information	24c	Describe and explain amendments to registration/protocol information.	Methods – Eligibility criteria: date range expanded during revision
Other information	25	Describe sources of financial or non-financial support for the review, and the role of funders.	Funding: The authors received no specific funding for this work, p. 13.
Other information	26	Declare competing interests.	Conflict of Interest, p. 13
Other information	27	Report availability of data, code and other materials.	Supplementary Tables S1–S5.

Funding statement: The authors received no specific funding for this work.

Annex 2. PRISMA 2020 for abstracts checklist.

A Systematic Review of Preclinical and Clinical Evidence			
Section and topic	Item #	Checklist item	Location where item is reported
Title	1	Identify the report as a systematic review.	Title page
Background – Objectives	2	Provide an explicit statement of the main objective(s) or question(s) addressed.	Abstract – Aims
Methods – Eligibility criteria	3	Specify the inclusion and exclusion criteria for the review.	Abstract – Methods; detailed criteria in Methods
Methods – Information sources	4	Specify the information sources and the date when each was last searched.	Abstract – Methods: PubMed, ScienceDirect, Springer Nature Link, and SAGE; searched through July 31, 2026
Methods – Risk of bias	5	Specify the methods used to assess risk of bias in the included studies.	Abstract – Methods: SYRCLE Risk of Bias tool and JBI Critical Appraisal Checklists
Methods – Synthesis of results	6	Specify the methods used to present and synthesise results.	Abstract – Methods: systematic review with qualitative/narrative synthesis; no meta-analysis
Results – Included studies	7	Give the total number of included studies and participants and summarise relevant characteristics.	Abstract – Results: 13 studies (5 preclinical and 8 clinical). Participant/animal totals are not aggregated in the abstract.
Results – Synthesis of results	8	Present results for the main outcomes, preferably indicating the number of included studies/participants for each; report meta-analysis estimates if applicable.	Abstract – Results: safety findings summarized; no meta-analysis conducted
Discussion – Limitations of evidence	9	Provide a brief summary of limitations of the evidence included in the review.	Abstract – Results/Conclusions: methodological heterogeneity, formulation variability, inconsistent safety reporting, and insufficient long-term maternal and infant safety data
Discussion – Interpretation	10	Provide a general interpretation of the results and important implications.	Abstract – Conclusions
Other – Funding	11	Specify the primary source of funding for the review.	Funding: The authors received no specific funding for this work.
Other – Registration	12	Provide the register name and registration number.	Methods: the systematic review was not prospectively registered; review protocol was developed but not registered.

Funding statement: The authors received no specific funding for this work.

Supplementary Table S1. Literature search strategies and study selection process

A. Database search strategies

Database	Search period	Search	Search strategy	Records identified	Total
PubMed	Database inception–through July 31, 2026	Search A	(galactagogue* OR lactagogue*) AND (Moringa oleifera OR Musa paradisiaca OR Teramnus labialis OR Pimpinella anisum OR Foeniculum vulgare OR Trigonella foenum-graecum OR Asparagus racemosus OR Galega officinalis OR Silybum marianum OR Lepidium sativum OR Lactuca sativa OR Cnicus benedictus OR Allium sativum OR Sauropus androgynus OR Kaempferia galanga OR barley OR malt OR fenugreek OR fennel OR shatavari OR moringa OR goat's rue OR milk thistle OR anise OR herbal OR medicinal plant)	122	274
		Search B	(galactagogue*[Title/Abstract] OR lactagogue*[Title/Abstract] OR "milk production"[Title/Abstract] OR prolactin[Title/Abstract]) AND ("Moringa oleifera"[Title/Abstract] OR "Teramnus labialis"[Title/Abstract] OR herbal[Title/Abstract] OR "medicinal plant"[Title/Abstract]) AND (rat[Title/Abstract] OR rats[Title/Abstract] OR mice[Title/Abstract] OR mouse[Title/Abstract] OR animal*[Title/Abstract])	73	
		Search C	("herbal medicine") AND (breastfeeding OR lactation)	79	
ScienceDirect	Database inception–through July 31, 2026	-	(Herbal) AND (Galactagogue) AND (Safety)		275
Springer Nature	Database inception–through July 31, 2026	-	(breastmilk OR "human milk") AND (galactagogue OR "herbal medicine" OR "plant extract" OR "natural product") AND (safety OR toxicity OR "adverse effect")		265
SAGE	Database inception–through July 31, 2026	-	("breastmilk" OR "human milk") AND (galactagogue OR "plant extract" OR "natural product") AND (toxicity OR "adverse effect" OR "side effect")		48

Note: Search strategies were adapted according to the indexing system and search functionality of each database. PubMed searches combined Medical Subject Headings (MeSH) with free-text terms, whereas ScienceDirect, Springer Nature, and SAGE used database-specific free-text Boolean search strategies. The search syntax for each database was modified as appropriate to accommodate platform-specific search functionality while maintaining the predefined concepts related to herbal interventions, lactation, and safety. PubMed searches A, B, and C were conducted separately, and the retrieved records were subsequently pooled to obtain the total PubMed yield. The pooled PubMed records were then combined with records from the other databases and exported as a single dataset for duplicate removal using Mendeley Reference Manager. The resulting dataset was used for title/abstract screening, followed by full-text eligibility assessment.

B. Study selection process

Screening stage	Records retrieved (n)
Records identified from electronic databases	862
Duplicate records removed	45
Records removed using database filters	595
Records screened: PubMed (144), ScienceDirect (26), Springer Nature (44), SAGE (8)	222
Records excluded after title and abstract screening	183
Full-text articles assessed for eligibility	39
Full-text articles excluded	26
Studies included in the systematic review	13

The 13 included studies comprised 5 preclinical studies and 8 clinical studies.

Supplementary Table S2. Full-text articles excluded after eligibility assessment, with reasons for exclusion.

No	Study	DOI	Study design	Main reason for exclusion
1	Serrao F, Corsello M, Romagnoli C, D'Andrea V, Zecca E. (2020). <i>Correction to: The long-term efficacy of a galactagogue containing silymarin-phosphatidylserine and galega on milk production of mothers of preterm infants.</i>	https://doi.org/10.1089/bfm.2017.0169.correx	Publisher correction (Erratum)	Correction notice; not an original research article and contained no primary efficacy or safety data.
2	Sevrin T, Boquien CY, Gandon A, et al. (2020). Fenugreek stimulates the expression of genes involved in milk synthesis and milk flow through modulation of insulin/GH/IGF-1 axis and oxytocin secretion.	https://doi.org/10.3390/genes11101208	Animal mechanistic study	Did not report predefined safety-related outcomes (e.g., biochemical, histopathological, or toxicity assessments) required for this systematic review.
3	Saejueng K, Nopsopon T, Wuttikonsammakit P, et al. (2022). Efficacy of Wang Nam Yen Herbal Tea on human milk production: A randomized controlled trial.	https://doi.org/10.1371/journal.pone.0247637	Double-blind randomized controlled trial	Comparator did not meet the predefined eligibility criteria (no placebo, usual treatment, or untreated control group).
4	Intan PR, Alegantina S, Isnawati A, et al. (2024). Effects of a blend extract of <i>Sauropus androgynus</i> , <i>Moringa oleifera</i> , and <i>Coleus amboinicus</i> on milk production in lactating rats.	https://doi.org/10.5455/OVJ.2024.v14.i12.44	Animal experimental study	Investigated a blended extract of three herbal species but safety of herbal galactagogues could not be determined.
5	Sim TF, Hattingh HL, Sherriff J, Tee LBG. (2015). What do breastfeeding women taking herbal galactagogues perceive of community pharmacists' role in breastfeeding support? A qualitative study.	https://doi.org/10.3390/ijerph120911132	Qualitative study	Qualitative study; no evaluation of galactagogue efficacy or safety outcomes.
6	Ammar M, Russo GL, Altamimi A, et al. (2025). <i>Moringa oleifera</i> supplementation as a natural galactagogue: A systematic review on its role in supporting milk volume and prolactin levels.	https://doi.org/10.3390/foods14142487	Systematic review	Secondary literature (systematic review); only original primary studies were eligible for inclusion.
7	Foong SC, Tan ML, Foong WC, et al. (2020). Oral galactagogues (natural therapies or drugs) for increasing breast milk production in mothers of non-hospitalised term infants.	https://doi.org/10.1002/14651858.CD011505.pub2	Cochrane systematic review	Secondary literature (Cochrane systematic review); excluded because only primary studies were eligible.
8	Garbacz A, Juszczak P, Nowicki M, et al. (2024). Exploring galactagogue use among breastfeeding women: Insights from an observational study.	https://doi.org/10.1371/journal.pone.0310867	Cross-sectional observational study	Observational study; no intervention evaluating the efficacy or safety of herbal galactagogues was conducted.
9	Cragg A, Levene I, Darabi S, Willcox M. (2025). Herbal galactagogues to improve breastmilk production and lactation in mothers of preterm babies: A systematic review of clinical trials.	https://doi.org/10.1038/s41430-025-01679-x	Systematic review	Secondary literature (systematic review); original clinical or preclinical studies only were eligible.
10	Sani NA, Kawu MU, Bakob IG. (2019). Effects of <i>Launaea taraxacifolia</i> and resveratrol on milk yield and serum prolactin and oxytocin levels: A lactogenic study.	https://doi.org/10.1080/23144599.2019.1694307	Animal experimental study	Did not report predefined safety-related outcomes (e.g., biochemical, histopathological, or toxicity assessments) required for this systematic review.
11	Issuriya A, Wetchakul P, Kaewmanee T, et al. (2026). Microencapsulated extracts from banana flowers induce milk production in lactating rats through increased α -lactalbumin, aquaporin, and prolactin levels.	https://doi.org/10.1155/sci5/5148782	Animal experimental study	Did not report predefined safety-related outcomes (e.g., biochemical, histopathological, or toxicity assessments) required for this systematic review.
12	Maru S, Belemkar S. (2025). Acute and subacute oral toxicity study of a herbal formulation containing <i>Asparagus racemosus</i> , <i>Tinospora cordifolia</i> , and <i>Trigonella foenum-graecum</i> in Mice.	https://doi.org/10.1155/jt/8221552	Animal toxicity study	Evaluated toxicity and safety only; no galactagogue efficacy outcomes (e.g., milk production, prolactin, mammary gland function) were assessed.
13	Chonsut P, Wetchakul P, Naphthalung J, et al. (2023). Potential galactagogue effect of Tri-Than-Thip remedy on milk synthesis in lactating rats: Impact on milk production-related parameters.	https://doi.org/10.7150/ijms.83869	Animal experimental study	Did not report predefined safety-related outcomes (e.g., biochemical, histopathological, or toxicity assessments) required for this systematic review.
14	Bettiol A, Lombardi N, Marconi E, et al. (2018). The use of complementary and alternative medicines during breastfeeding: results from the herbal supplements in breastfeeding Investigation (HaBIT) study.	https://doi.org/10.1111/bcp.13639	Web-based survey	Observational survey evaluating complementary and alternative medicine (CAM) use during breastfeeding; no intervention assessing galactagogue efficacy or safety was conducted.

15	Millinga VP, Im HB, Hwang JH, et al. (2022). Use of herbal medicines among breastfeeding mothers in Tanzania: A cross-sectional study.	https://doi.org/10.3389/fphar.2022.751129	Cross-sectional study	Observational study; no intervention evaluating galactagogue efficacy or safety outcomes was conducted.
16	Agagündüz D. (2020). Determination of the total antioxidant and oxidant status of some galactagogue and herbal teas.	https://doi.org/10.1016/j.fshw.2020.06.002	Laboratory analytical study	Laboratory analytical study; no biological, efficacy, or safety outcomes relevant to lactation were evaluated.
17	Othman N, Che Lamin RA, Othman CN. (2014). Exploring behavior on the herbal galactagogue usage among Malay lactating mothers in Malaysia.	https://doi.org/10.1016/j.sbspro.2014.10.054	Cross-sectional survey	Observational survey; no intervention evaluating galactagogue efficacy or safety outcomes was conducted.
18	Ryan RA, Hepworth AD, Lyndon A, et al. (2023). Use of galactagogues to increase milk production among breastfeeding mothers in the United States: A descriptive study.	https://doi.org/10.1016/j.jand.2023.05.019	Cross-sectional study	Observational study; No intervention evaluating galactagogue efficacy or safety was conducted.
19	Ryan RA, Hepworth AD, Bihuniak JD, et al. (2024). A qualitative study of breastfeeding experiences among mothers who used galactagogues to increase their milk supply.	https://doi.org/10.1016/j.jneb.2023.12.002	Qualitative study	Qualitative study; no evaluation of galactagogue efficacy or physiological lactation outcomes.
20	Liu H, Hua Y, Luo H, et al. (2015). An herbal galactagogue mixture increases milk production and aquaporin protein expression in the mammary glands of lactating rats.	https://doi.org/10.1155/2015/760585	Animal experimental study	Did not evaluate predefined safety outcomes (e.g., toxicity, biochemical parameters, or histopathological assessments) required by the review.
21	Simbar M, Nazarpour S, Mojab F, et al. (2022). A comparative study on the effects of honey and fenugreek with fenugreek on the breastfeeding success: A randomized trial.	https://doi.org/10.1155/2022/6048280	Triple-blind randomized controlled trial	Compared two active herbal interventions without a placebo, usual treatment, or untreated control group.
22	Giri KR, Palandurkar KM, Agrawal U, et al. (2024). In vivo Analysis of Puerarin from Pueraria tuberosa as a Promising Galactagogue.	https://doi.org/10.6026/9732063002001574	Animal experimental study	Evaluated an isolated bioactive compound (puerarin) in addition to the herbal extract rather than a herbal galactagogue intervention alone.
23	Zulkarnain Z, Fitriani U, Ardiyanto D, et al. (2024). Galactagogue activity of poly-herbal decoction from Indonesia: a randomized open-label controlled trial.	https://doi.org/10.1515/jcim-2020-0246	Randomized open-label controlled trial	Full text could not be retrieved; eligibility and complete safety outcomes could not therefore be assessed. Relevant abstract-level safety findings were acknowledged separately in the Discussion.
24	Chao J, Ko CY, Lin CY, et al. (2021). Ethnobotanical survey of natural galactagogues prescribed in Traditional Chinese Medicine Pharmacies in Taiwan.	https://doi.org/10.3389/fphar.2020.625869	Observational ethnobotanical survey	Observational ethnobotanical survey; no experimental evaluation of herbal galactagogue efficacy or safety was conducted.
25	Egbule MN, Oyelakin A, Anyasor GN, et al. (2026). Effect of <i>Pentadiplandra brazzeana</i> Baill root-supplemented diet on selected lactogenic biomarkers in postpartum Wistar rats.	https://doi.org/10.1016/j.phyplu.2026.101011	Animal experimental study	Evaluated lactogenic biomarkers only; did not assess predefined safety outcomes required by this review (e.g., toxicity, adverse events, biochemical safety markers, or histopathological safety evaluation).
26	Jendras G, Monizi M, Neinhuis C, et al. (2020). Plants, food and treatments used by BaKongo tribes in Uíge (northern Angola) to affect the quality and quantity of human breast milk.	https://doi.org/10.1186/s13006-020-00329-1	Ethnobotanical cross-sectional study	Ethnobotanical survey documenting the traditional use of plants and foods during breastfeeding; no experimental or clinical evaluation of galactagogue efficacy or safety was conducted.

Supplementary Table S3. Characteristics of the included studies.**Part A. Preclinical Studies**

Study	Country	Study design	Animal model	Herbal intervention	Comparator	Treatment duration	Primary outcomes	Safety assessment
Mahmood et al., 2012	Malaysia	Experimental animal study	Lactating Sprague-Dawley rats	<i>Musa × paradisiaca</i> flower extract	Distilled water	Days 5–14 postpartum	Milk yield, pup growth	No direct toxicity evaluation reported
Simelane et al., 2012	South Africa	Experimental animal study	Lactating rats	<i>Gunnera perpensa</i> aqueous extract	Vehicle control	As reported	Milk production, mammary development	ALT, AST, albumin, prolactin, cortisol, growth hormone, cytotoxicity
Dhumal et al., 2014	India	Experimental animal study	Lactating Holtzman rats	Maa-Lact herbal formulation	Control	21 days	Milk production, prolactin, pup growth	Clinical observations, hematology, biochemistry, histopathology
Sahoo et al., 2016	India	Experimental animal study	Lactating Wistar rats	<i>Teramnus labialis</i> fruit extract	Distilled water and domperidone	14 days	Milk yield, prolactin, cortisol, pup growth	No predefined toxicity assessment reported
Chotitham et al. (2025)	Thailand	Preclinical randomized controlled animal study	Lactating Wistar rats and pups	<i>Prasanamnom formula (PNF) decoction (300, 600, 1000 mg/kg) and PNF powder (100, 300, 1000 mg/kg)</i>	Vehicle control and domperidone (10 mg/kg)	PND 1–21	Milk production, serum prolactin levels	Maternal and pup safety assessed by renal and hepatic function (serum urea, creatinine, albumin, AST, ALT, ALP, total bilirubin), clinical observations, and physical appearance; no clinically significant renal or hepatic toxicity was observed.

Part B. Clinical studies

Study	Country	Study design	Participants	Herbal intervention	Comparator	Treatment duration	Primary outcomes	Safety assessment
Ajgaonkar et al., 2025	India	RCT, double-blind, placebo-controlled	120 postpartum women; PP: 57 SHT, 56 placebo	<i>A. racemosus</i> root extract 300 mg/day	Starch placebo	72 Hours	Breast fullness; expressed milk volume	Adverse events were monitored; no adverse events were reported during the 72-hour intervention period.
James et al., 2019	Sierra Leone	Cross-sectional study	378 breastfeeding mothers	Herbal medicine use during breastfeeding	N/A	N/A	Prevalence, utilization pattern	Maternal-reported herbal use and perceived safety
Sim et al., 2015	Australia	Qualitative study	Breastfeeding women using herbal galactagogues	Various herbal galactagogues	N/A	N/A	Perceived effectiveness	Participant-reported safety experiences
McBride et al., 2021	Australia	Cross-sectional survey	1,876 breastfeeding women	Herbal and pharmaceutical galactagogues	N/A	N/A	Utilization, effectiveness	Self-reported adverse effects
Wesolowska et al., 2021	Poland	Randomized controlled trial	Mothers of preterm infants	Barley malt-based galactagogue	Placebo	2 weeks	Milk volume	Product safety evaluated
Khalili et al., 2023	Iran	Randomized controlled trial	Mothers of preterm infants	<i>Pimpinella anisum</i> herbal tea	Placebo and control	7 days	Milk volume, infant weight	Adverse events monitored
Sintupattanapun et al., 2025	Thailand	Randomized controlled trial	60 postpartum women	Plook-Fire-Thatu formulation	Standard care	3 days	Milk volume, prolactin, milk composition	Hematology, blood chemistry, adverse events
Saxena et al., 2025	India	Double-blind randomized placebo-controlled trial	211 mothers with insufficient lactation	Ayush-SS granules	Placebo	12 weeks	Exclusive breastfeeding, infant weight gain	Safety monitoring, adverse events

Abbreviations: ALT: alanine aminotransferase; AST: aspartate aminotransferase; N/A: not applicable; RCT: randomized controlled trial.

Supplementary Table S4. Risk of Bias

A. SYRCLE Risk of Bias Assessment of the Included Preclinical Studies

SYRCLE Domain	Mahmood et al. (2012)	Simelane et al. (2012)	Dhumal et al. (2014)	Sahoo et al. (2016)	Chotitham et al. (2025)
1. Sequence generation	Low	Low	Unclear	Low	Low
2. Baseline characteristics	Low	Low	Low	Low	Low
3. Allocation concealment	Unclear	Unclear	Unclear	Unclear	Unclear
4. Random housing	Unclear	Unclear	Unclear	Unclear	Unclear
5. Blinding of caregivers/investigators	Unclear	Unclear	Unclear	Unclear	Unclear
6. Random outcome assessment	Unclear	Unclear	Unclear	Unclear	Unclear
7. Blinding of outcome assessment	Unclear	Low	Unclear	Unclear	Unclear
8. Incomplete outcome data	Low	Low	Low	Low	Low
9. Selective outcome reporting	Low	Low	Low	Low	Low
10. Other sources of bias	Low	Low	Low	Low	Low

Abbreviations: SYRCLE, Systematic Review Centre for Laboratory Animal Experimentation.

Legend: Low risk of bias; Unclear risk of bias; High risk of bias.

Justification for risk of bias assessment

Domain	Assessment criteria
Sequence generation	Rated Low when random allocation was explicitly reported; otherwise Unclear . Mahmood and Dhumal did not describe the randomization method, whereas Simelane and Sahoo explicitly reported random allocation.
Baseline characteristics	All studies reported comparable experimental animals and baseline conditions before treatment; therefore judged Low risk .
Allocation concealment	None of the studies described allocation concealment; therefore judged Unclear .
Random housing	Housing conditions were described, but no evidence that cage allocation was randomized; therefore Unclear .
Blinding of caregivers/investigators	None of the studies explicitly reported caregiver or investigator blinding; therefore Unclear .
Random outcome assessment	The order of outcome assessment was not reported in any study; therefore Unclear .
Blinding of outcome assessment	Simelane explicitly stated that mammary histology was evaluated by a pathologist blinded to treatment groups; therefore Low risk . The remaining studies did not report assessor blinding and were rated Unclear .
Incomplete outcome data	Outcome data were reported for all experimental groups without evidence of missing data or unexplained exclusions; therefore Low risk .
Selective outcome reporting	All prespecified outcomes described in the Methods were reported in the Results; therefore Low risk .
Other sources of bias	No obvious additional sources of bias were identified from the published reports; therefore Low risk .

B. JBI Risk of bias assessment of the included clinical studies

Randomized Controlled Trials (JBI Critical Appraisal Checklist for Randomized Controlled Trials)

Study	Q1	Q2	Q3	Q4	Q5	Q6	Q7	Q8	Q9	Q10	Q11	Overall risk of bias
Ajgaonkar et al. (2025)	Yes	Yes	Yes	Yes	Yes	Yes	Yes	Yes	No	Yes	Yes	Low
Khalili et al. (2023)	Yes	Yes	Yes	Yes	Yes	Yes	Yes	Yes	Yes	Yes	Yes	Low
Wesolowska et al. (2021)	Yes	Yes	Yes	Yes	Yes	Unclear	Yes	Yes	Yes	Yes	Yes	Low
Saxena et al. (2025)	Yes	Yes	Yes	Yes	Yes	Yes	Yes	Yes	Yes	Yes	Yes	Low
Sintupattanapun et al. (2025)	Yes	Yes	Yes	Yes	Yes	Yes	Yes	Yes	Yes	Yes	Yes	Low

Analytical cross-sectional studies (JBI Critical Appraisal Checklist for Analytical Cross-Sectional Studies)

Study	Q1	Q2	Q3	Q4	Q5	Q6	Q7	Q8	Overall risk of bias
McBride et al. (2021)	Yes	Yes	Yes	Unclear	Yes	Yes	Unclear	Yes	Moderate
James et al. (2019)	Yes	Yes	Yes	Yes	Yes	Yes	Yes	Yes	Low

Qualitative research (JBI Critical Appraisal Checklist for Qualitative Research)

Study	Q1	Q2	Q3	Q4	Q5	Q6	Q7	Q8	Q9	Q10	Overall risk of bias
Sim et al. (2015)	Yes	Yes	Yes	Yes	Yes	Yes	Yes	Yes	Yes	Yes	Low

Yes = criterion fulfilled; **No** = criterion not fulfilled; **Unclear** = insufficient information; **NA** = not applicable.

Abbreviations: JBI: Joanna Briggs Institute; RCT: randomized controlled trial.

Notes:

Q1–Q11 correspond to the items of the JBI Critical Appraisal Checklist for Randomized Controlled Trials.

Q1–Q8 correspond to the items of the JBI Critical Appraisal Checklist for Analytical Cross-Sectional Studies.

Q1–Q10 correspond to the items of the JBI Critical Appraisal Checklist for Qualitative Research.

Overall risk of bias was determined based on the overall appraisal of the relevant JBI Critical Appraisal Checklist.

Supplementary Table S5. Review protocol.

Title Safety of Herbal Galactagogues: A Systematic Review of Preclinical and Clinical Evidence 1. Review Objective The objective of this systematic review was to identify, critically appraise, and synthesize the available evidence on the safety of herbal galactagogues from preclinical animal studies and clinical studies involving breastfeeding women. 2. Review Question This review addressed the following research question: What is the current evidence regarding the safety of herbal galactagogues in preclinical animal models and breastfeeding women? 3. PICOS Framework Population - Lactating experimental animals - Breastfeeding women Intervention Herbal galactagogues, medicinal plants, plant extracts, herbal formulations, or phytogetic lactation-support therapies. Comparison - Placebo - Vehicle control - Standard care - Untreated controls - Positive controls (when applicable) Outcomes Primary safety outcomes included: - Adverse events - Clinical signs of toxicity - Liver function - Renal function - Hematological parameters - Biochemical parameters - Histopathological findings - Endocrine markers - Maternal safety outcomes and Infant-related safety outcomes
--

Study Design

Eligible study designs included:

- Experimental animal studies
- Randomized controlled trials
- Observational studies
- Cross-sectional studies
- Qualitative studies

4. Eligibility Criteria**Inclusion Criteria**

Studies were eligible if they:

- evaluated herbal galactagogues used during lactation;
- involved lactating animals or breastfeeding women;
- reported at least one predefined safety outcome;
- were original peer-reviewed research articles;
- were published in English;
- had accessible full-text articles.

Exclusion Criteria

The following studies were excluded:

- review articles;
- systematic reviews and meta-analyses;
- conference abstracts;
- editorials;
- letters;
- case reports;
- studies evaluating pharmaceutical galactagogues only;
- *in vitro* studies;
- *in silico* studies;
- studies without predefined safety outcomes.

5. Information Sources

Electronic literature searches were conducted in the following databases:

- PubMed
- ScienceDirect
- Springer Nature Link
- SAGE

Searches covered publications from **database inception through July 31, 2026**.

To maximize study identification, the reference lists of all included articles were manually screened for additional eligible studies.

6. Search Strategy

The search strategy was developed using the PICOS framework and combined controlled vocabulary (Medical Subject Headings [MeSH], where applicable) with free-text keywords related to:

- breastfeeding;
- lactation;
- herbal medicine;
- medicinal plants;
- galactagogues;
- safety;
- toxicity;
- adverse effects.

Search strategies were adapted according to the indexing system and search functionality of each database while maintaining the same predefined concepts. The complete database-specific search strategies are presented in **Supplementary Table S1**.

7. Study Selection

Study selection followed the **Preferred Reporting Items for Systematic Reviews and Meta-Analyses (PRISMA 2020)** Statement.

The selection process consisted of:

1. Database searching;
2. Duplicate removal using Mendeley Reference Manager;
3. Title and abstract screening;
4. Full-text eligibility assessment;
5. Final study inclusion.

Two reviewers independently screened all records and assessed full-text articles for eligibility. Any disagreements were resolved through discussion until consensus was reached.

8. Data Extraction

A standardized data extraction form was developed before study selection.

The following information was extracted from each eligible study:

- author;
- publication year;
- country;
- study design;
- study population or animal model;
- herbal intervention or formulation;
- dosage or treatment duration;
- comparator;
- safety outcomes and principal findings.

9. Methodological Quality Assessment

Methodological quality was assessed according to study design.

Preclinical animal studies were evaluated using the:

- **SYRCLE Risk of Bias Tool**

Clinical studies were evaluated using the:

- **Joanna Briggs Institute (JBI) Critical Appraisal Checklists**

Risk-of-bias assessments were conducted independently and disagreements were resolved through discussion.

10. Data Synthesis

A quantitative meta-analysis was not performed because of substantial heterogeneity among studies with respect to:

- herbal interventions;
- formulations;
- dosages;
- treatment duration;
- study populations;
- animal models;
- study designs;
- reported safety outcomes.

Therefore, a narrative qualitative synthesis was conducted. Evidence from preclinical and clinical studies was synthesized separately before integrating the overall findings regarding the safety of herbal galactagogues.

11. Reporting Guideline

This review was conducted and reported according to the **Preferred Reporting Items for Systematic Reviews and Meta-Analyses (PRISMA 2020)** Statement.

12. Protocol Registration

A review protocol was developed before the literature search and study selection to guide the review process.

The protocol was **not prospectively registered**.

13. Deviations and Methodological Amendments

The review protocol was developed before the literature search and study selection.

During the revision process, one methodological amendment was made:

The search period was expanded from 2015–2025 to database inception through July 31, 2026, following reviewer recommendations to improve the comprehensiveness of the literature search. This amendment resulted in the screening and inclusion of eligible studies published before 2015.

The core eligibility criteria regarding the population, intervention, comparator, study design, and predefined safety outcomes were otherwise maintained. No changes were made to the review objective or predefined safety outcomes.

14. Software Used

The following software and reporting tools were used during the review process:

- Mendeley Reference Manager (reference management and duplicate removal)
- Microsoft Excel (data extraction)
- PRISMA 2020 Flow Diagram
- SYRCLE Risk of Bias Tool
- Joanna Briggs Institute (JBI) Critical Appraisal Checklists