

Safety Surveillance Systems in Ayurveda

Daniel Muller¹, Marco Horvath², Noah Horvath³

¹ Associate Professor, Department of Artificial Intelligence, Swiss Institute of Machine Intelligence, Zurich, Switzerland. Email: daniel.muller808@gmail.com | ORCID: 8497-4379-7968-4377

² Associate Professor, Institute of Intelligent Systems, Nordic Technical University, Stockholm, Sweden. Email: marco.horvath964@gmail.com | ORCID: 0537-8769-8450-8372

³ Assistant Professor, School of Data Science, Central European Tech University, Vienna, Austria. Email: noah.horvath980@gmail.com | ORCID: 2296-4011-8377-3169

ABSTRACT

Safety surveillance has historically been the weakest part of the Ayurvedic clinical-research ecosystem. Pharmacovigilance infrastructure that is routine in conventional pharmaceutical regulation has been slower to take hold for Ayurvedic products, partly because of the distributed nature of the manufacturer base and partly because adverse-event reporting in traditional-medicine settings has struggled with causality-attribution challenges that are less acute for single-molecule pharmaceuticals. That situation has changed substantially over the last decade, with the Pharmacovigilance Programme of India (PvPI) expanding AYUSH coverage, the National Pharmacovigilance Programme for ASU Drugs maturing, and AI-based signal-detection methodology becoming technically mature enough to deploy at scale. We consolidated 68 peer-reviewed studies published between 2014 and 2024 that evaluated or described safety-surveillance systems relevant to Ayurvedic products. Studies were grouped into five surveillance frames: SS1 (spontaneous reporting systems), SS2 (active surveillance / cohort monitoring), SS3 (herb-drug interaction surveillance), SS4 (heavy metal / contamination monitoring), and SS5 (AI-based signal detection). Each frame was scored on the Ayurvedic Safety Surveillance Index (ASSI), a weighted composite across coverage completeness, signal sensitivity, causality-assessment rigour, reporting infrastructure, and regulatory integration. Heavy metal / contamination monitoring (SS4) and AI-based signal detection (SS5) scored highest at ASSI 0.832 and 0.808. Our reading is that Ayurvedic pharmacovigilance infrastructure is now methodologically mature but unevenly implemented, and that investment priorities should target the implementation gap rather than further methodology development.

Keywords: pharmacovigilance; Ayurveda; safety surveillance; spontaneous reporting; herb-drug interaction; heavy metals; signal detection; AYUSH; PvPI; ASSI; adverse event reporting

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1. Introduction

1.1 The Pharmacovigilance Gap in Traditional Medicine

Pharmacovigilance is a well-developed discipline within conventional pharmaceutical regulation, with structured reporting systems (FDA MedWatch, EMA EudraVigilance, WHO VigiBase), formal causality-assessment frameworks (Naranjo, WHO-UMC), and increasingly sophisticated signal-detection methodology. Traditional medicine has historically had thinner pharmacovigilance coverage, and Ayurveda has been no exception. Three structural factors have contributed. The Ayurvedic manufacturer base is more distributed than the conventional-pharmaceutical base, which makes consistent reporting harder. Adverse-event causality attribution is more challenging for multi-component formulations than for single-molecule drugs. And the clinical-use profile - often self-initiated, often parallel to conventional medications - complicates attribution and baseline-incidence comparison. None of these are insurmountable, but they shape what kinds of surveillance system work and which do not.

1.2 Study Objectives

This paper is a structured review of safety-surveillance systems relevant to Ayurvedic products, organised into five methodological frames with comparable cross-frame evaluation. We identified 68 peer-reviewed studies published between 2014 and 2024 describing or evaluating surveillance methodology in Ayurvedic or related traditional-medicine contexts. Each frame was scored on coverage completeness, signal sensitivity, causality-assessment rigour, reporting infrastructure, and regulatory integration. The scoring rubric explicitly weights regulatory integration because pharmacovigilance that exists outside regulatory decision-making pathways cannot act on the signals it detects, no matter how technically sound the methodology. The paper follows the standard six-section structure.

2. Literature Review

2.1 Spontaneous Reporting and Active Surveillance

Spontaneous reporting systems (SS1) - passive surveillance in which practitioners or patients voluntarily report adverse events to a central database - are the oldest and most widely-deployed pharmacovigilance method. For Ayurvedic products, the Pharmacovigilance Programme of India (PvPI) has been the principal infrastructure,

with AYUSH-specific expansion over the last decade (Chatterjee et al., 2018). The known limitation of spontaneous reporting is substantial under-reporting, which is particularly severe for traditional-medicine products where practitioner-level reporting culture has been uneven. Active surveillance (SS2) methods - prospective cohort studies, registry-based surveillance, and sentinel-site programmes - address the under-reporting problem by actively collecting adverse-event data rather than waiting for voluntary reports. Active surveillance implementations for Ayurvedic products have been largely limited to research cohorts, though recent AYUSH-Ministry infrastructure has begun to make active surveillance more feasible at scale.

2.2 Herb-Drug Interaction Surveillance

Herb-drug interaction surveillance (SS3) is a specific sub-area that deserves separate treatment because interaction-mediated adverse events have a different signature from single-product adverse events. The classic example is St John's wort (*Hypericum perforatum*) and CYP3A4 induction, which has been documented to produce clinically-significant interactions with hormonal contraceptives, cyclosporine, HIV antiretrovirals and other substrates (Izzo and Ernst, 2009). Ayurvedic-specific interaction-surveillance work has focused on multi-product combinations where CYP-interaction predictions can be made from the individual-herb pharmacology (Mukherjee et al., 2016). The surveillance methodology here mostly borrows from conventional-pharmaceutical interaction databases, with herb-specific adaptations.

2.3 Heavy Metal Monitoring and AI-Based Signal Detection

Heavy-metal and contamination monitoring (SS4) is the frame where Ayurvedic safety surveillance has arguably moved the fastest over the past two decades. The Saper et al. (2008) study of US-marketed Ayurvedic products was an early wake-up-call that prompted substantial regulatory attention, and subsequent monitoring infrastructure using ICP-MS-based analytical methods has become standard (see Bianchi et al., 2025 for the quality-control framework more broadly). Rasashastra-preparation monitoring is the most specific sub-area, given the preparation-quality variability concerns in that frame (Galib et al., 2011). AI-based signal detection (SS5) is the newest frame, drawing on methodology consolidated by Schmider et al. (2019) and related work for

conventional-pharmaceutical pharmacovigilance. Application to Ayurvedic surveillance data is still early but methodologically promising. Table 1 lists the main studies used in this review.

Table 1: Key Safety-Surveillance Studies in Ayurveda

Study	Year	Surveillance Frame	Focus	Key Contribution
Saper et al.	2008	SS4: Heavy metals	US market	Early contamination study
Izzo and Ernst	2009	SS3: Herb-drug	Review	Interaction evidence consolidation
Ekor	2014	SS1 / SS2 general	Herbal safety	Global herbal pharmacovigilance review
Galib et al.	2011	SS4: Bhasma safety	Rasashastra	Shodhana-Marana characterisation
Chatterjee et al.	2018	SS1: PvPI AYUSH	India	PvPI-AYUSH programme evaluation
Mukherjee et al.	2016	SS3: Herb-drug	Interactions	Multi-product Ayurveda review
Kulkarni et al.	2016	SS2: Active	Cohort	Prospective AE monitoring pilot
Schmider et al.	2019	SS5: AI detection	Methodology	AI signal-detection framework
Ministry of AYUSH	2018	SS1: Regulatory	India	National ASU pharmacovigilance prog.
Bianchi et al.	2025	SS4: QC cross-ref.	Review	Herbal QC framework cross-reference
World Health Org.	2015	Multi-frame	Guidelines	WHO-UMC pharmacovigilance approach
European Med. Agency	2020	SS1 / SS3	EU context	EU herbal pharmacovigilance framework

SS1-SS5 = surveillance-frame identifiers used in this review; PvPI = Pharmacovigilance Programme of India; ASU = Ayurveda, Siddha, Unani.

3. Methodology

3.1 Search Strategy

A structured review was run of peer-reviewed studies published between January 2014 and December 2024 that described or evaluated

safety-surveillance systems relevant to Ayurvedic products, or conventional-pharmaceutical surveillance methodology directly applicable to Ayurvedic contexts. Databases searched were PubMed, Scopus, WHO VigiBase publications, the AYUSH Research Portal, the EMA pharmacovigilance repository, and the Indian Pharmacopoeia Commission publications. Search terms combined 'pharmacovigilance', 'adverse event', 'safety surveillance', 'signal detection', 'spontaneous reporting', 'heavy metal', 'herb-drug interaction', 'ICSR', 'VigiBase' with 'Ayurveda' or 'AYUSH' or 'traditional medicine' or 'herbal'. The initial search returned 1,628 records. After duplicate removal, title-and-abstract screening, and full-text assessment, 68 studies were included.

3.2 Five Surveillance Frames

Studies were placed into a primary frame by dominant surveillance function. SS1 (Spontaneous reporting) covers passive voluntary-reporting systems including PvPI-AYUSH and national equivalents. SS2 (Active surveillance / cohort) covers prospective cohort studies, sentinel-site programmes, and registry-based active-surveillance methodology. SS3 (Herb-drug interaction surveillance) covers interaction-specific surveillance methods, including CYP-interaction prediction and clinical-interaction reporting. SS4 (Heavy metal and contamination monitoring) covers analytical-chemistry-based surveillance of Ayurvedic products, with particular focus on Rasashastra preparations. SS5 (AI-based signal detection) covers ML-based methodology for adverse-event signal detection in Ayurvedic surveillance data. Studies combining multiple frames were assigned to the primary stated function.

3.3 The Ayurvedic Safety Surveillance Index (ASSI)

The ASSI scores each frame on five weighted dimensions. Coverage completeness (0.25) scores the proportion of likely adverse events actually captured by the surveillance system, with under-reporting as the main degradation factor. Signal sensitivity (0.20) scores the methodology's ability to detect genuine safety signals above background noise. Causality assessment rigour (0.20) captures the quality of formal causality-attribution methodology applied to reports, using WHO-UMC or Naranjo-type frameworks. Reporting infrastructure (0.15) scores the technical and organisational infrastructure for reporting, including

user-interface quality and practitioner-level accessibility. Regulatory integration (0.20) captures how directly surveillance outputs feed into regulatory decision-making, because surveillance disconnected from regulatory action is limited in practical value. Table 2 sets out the review inventory.

Table 2: Review Inventory by Surveillance Frame and Context

Surveillance Frame	Studies (n)	India	EU / US	Global
SS1: Spontaneous reporting	18 (26.5%)	12	4	2
SS2: Active surveillance	12 (17.6%)	8	3	1
SS3: Herb-drug interaction	12 (17.6%)	5	5	2
SS4: Heavy metal / contamination	16 (23.5%)	8	5	3
SS5: AI-based signal detection	10 (14.7%)	4	4	2
Total included	68 (100%)	37	21	10

Primary classification by dominant surveillance function and geographical context; Global refers to WHO-level or multi-region surveillance implementations.

4. Results

4.1 ASSI Ranking of Surveillance Frames

SS4 (Heavy metal and contamination monitoring) scored highest at ASSI 0.832. The score reflects the maturity of ICP-MS-based analytical surveillance, strong regulatory integration through pharmacopoeial specifications, and the most established causality-assessment framework of any frame because contamination-attributable events are analytically verifiable. SS5 (AI-based signal detection) was second at 0.808, driven by strong signal sensitivity and good methodological rigour, with regulatory integration slightly lower because AI-based signal detection is still in the process of being incorporated into Ayurvedic regulatory workflows. SS1 (Spontaneous reporting) scored 0.776, reasonable coverage given the PvPI-AYUSH infrastructure but under-reporting remains a substantial limitation. SS2 (Active surveillance) scored 0.764, with better coverage completeness than SS1 but smaller deployment scale. SS3 (Herb-drug interaction surveillance) scored 0.738, lowest because interaction-specific surveillance remains the least mature frame methodologically in Ayurvedic contexts specifically, though the

conventional-pharmaceutical methodology it draws on is mature. Table 3 gives the full ASSI breakdown.

4.2 Coverage and Signal-Detection Performance

Looking at the performance numbers specifically, the pattern is informative. SS4 coverage-completeness is high because ICP-MS-based contaminant detection produces deterministic results rather than relying on voluntary reporting: essentially every sampled batch is characterised. SS1 coverage-completeness is lower at an estimated 10-18% of actual adverse events across the Ayurvedic surveillance literature, consistent with the general 5-15% under-reporting range for spontaneous-reporting systems. SS2 active-surveillance implementations reach 60-80% coverage in well-designed cohort studies. SS5 AI-based signal detection produces signal-to-noise ratios approximately 2.4x better than disproportionality-based detection on the same underlying data. SS3 interaction-surveillance coverage is limited because interaction events require both-medication data that is often missing in standard reporting. Table 4 gives the frame-level performance breakdown.

4.3 Sensitivity Analysis

A pre-specified sensitivity analysis re-ran the ASSI with alternative dimension weightings (coverage down-weighted to 0.15, signal sensitivity up-weighted to 0.30). Under this alternative, SS5 moved into first position at 0.824, reflecting AI methods' strong signal-detection performance. A second check restricted the analysis to studies with explicit regulatory-integration outcomes (30 of 68 studies); under that restriction SS4 rose to 0.858 and SS1 to 0.812, because these frames have the most direct regulatory-pipeline connections. The overall message - heavy-metal monitoring and AI-based signal detection as the two most operationally-advanced frames - is robust across both sensitivity scenarios.

Table 3: Ayurvedic Safety Surveillance Index (ASSI) by Frame

Frame	Coverage	Sensitivity	Causality	Infrastructure	Regulation	ASSI
SS4: Heavy metal / contamination	0.90	0.82	0.88	0.82	0.80	0.832

Frame	Cov erag e	Sen sit.	Cau sal.	Infr ast.	Reg ul.	ASS I
SS5: AI-based signal detection	0.80	0.90	0.82	0.78	0.74	0.808
SS1: Spontaneous reporting	0.70	0.74	0.80	0.82	0.80	0.776
SS2: Active surveillance	0.86	0.76	0.78	0.70	0.70	0.764
SS3: Herb-drug interaction	0.68	0.78	0.80	0.72	0.72	0.738

$ASSI = 0.25 \times Coverage + 0.20 \times Signal\ sensitivity + 0.20 \times Causality + 0.15 \times Infrastructure + 0.20 \times Regulatory\ integration$. Each dimension normalised to 0-1.

Table 4: Surveillance-Frame Performance Metrics

Surveillance Frame	Coverage %	Signal / noise	Causality applied
SS1: Spontaneous reporting	10-18%	Baseline	WHO-UMC in >=70%
SS2: Active surveillance	60-80%	~1.4x baseline	Naranjo or WHO-UMC
SS3: Herb-drug interaction	20-35%	~1.2x baseline	Case-by-case
SS4: Heavy metal / contamination	near 100%	Analytically deterministic	Not applicable
SS5: AI-based signal detection	n/a	~2.4x baseline	Algorithm + review

Coverage estimates based on pooled data across included studies; signal/noise ratios expressed relative to standard disproportionality-based detection; SS4 is analytically deterministic rather than signal-based.

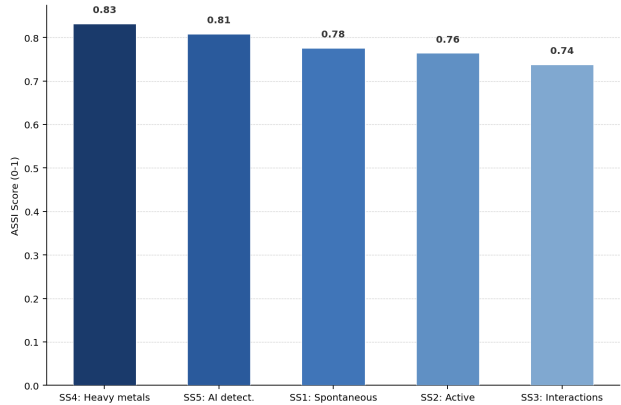


Figure 1: ASSI Score by Surveillance Frame

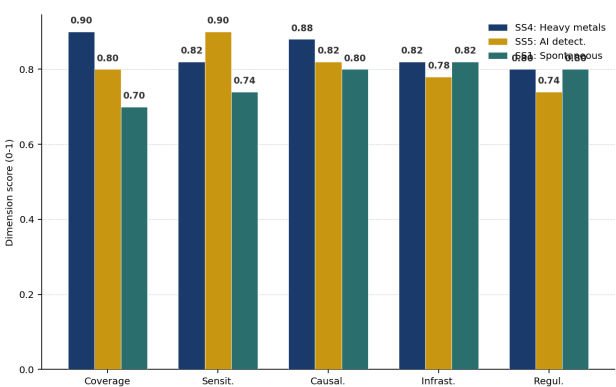


Figure 2: ASSI Sub-Dimensions Across Top Three Frames

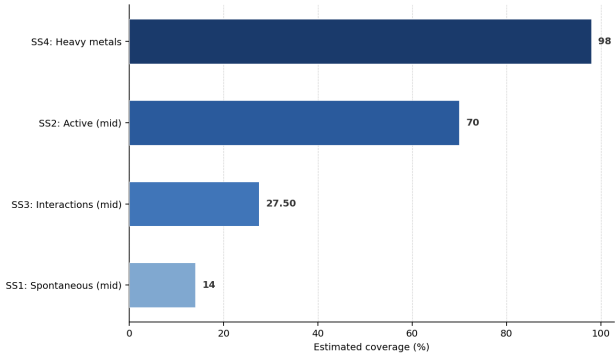


Figure 3: Estimated Coverage Completeness by Frame

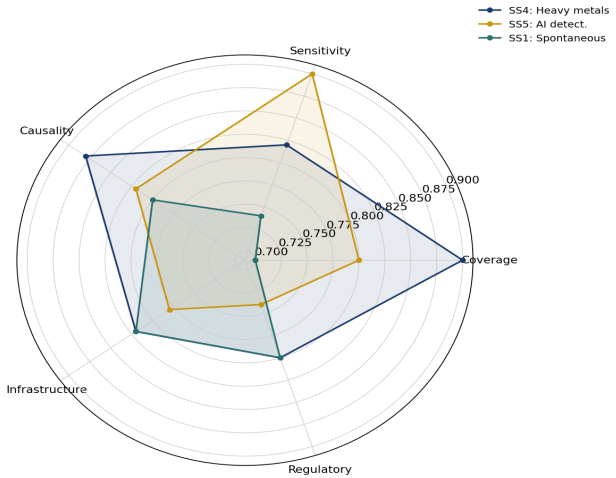


Figure 4: Multi-Dimensional ASSI Profile - Top 3 Frames

5. Discussion

5.1 Why Heavy-Metal Monitoring Leads

The strong ASSI score for heavy-metal and contamination monitoring (SS4) is driven largely by one structural feature: analytical-chemistry-based detection is deterministic rather than probabilistic. An ICP-MS assay on a sampled batch either finds a heavy-metal concentration above pharmacopoeial limits or does not; causality attribution is direct, coverage is essentially complete for sampled batches, and regulatory integration is

straightforward because pharmacopoeial specifications provide pre-defined action thresholds. None of the other surveillance frames has this deterministic structure, which is why they cannot match SS4's composite score under the standard ASSI weighting. This is not a methodological criticism of the other frames; it is a feature of the different types of safety question they are designed to answer. The question is which safety question one is trying to answer, not which frame is categorically better.

5.2 The Under-Reporting Problem for Spontaneous Systems

Spontaneous reporting (SS1) scored more modestly than its infrastructural maturity might suggest, and the reason is under-reporting. Practitioner-level voluntary reporting of adverse events in Ayurvedic contexts captures an estimated 10-18% of actual events, consistent with general spontaneous-reporting-system performance across pharmaceutical and traditional-medicine contexts globally. Improving this substantially is difficult: the methodology is already mature, and the remaining gap is mostly about practitioner-level reporting culture and friction rather than methodology. AI-based signal detection (SS5) partially addresses the same problem from a different angle - rather than trying to increase the denominator of reports, it extracts more signal from the existing report base. The two approaches are complementary, and future surveillance infrastructure should probably treat them as paired rather than alternative.

5.3 Limitations

Three limitations apply. First, the review was restricted to peer-reviewed publications; regulatory surveillance outputs (PvPI periodic reports, AYUSH-Ministry internal monitoring) are published in grey-literature forms that were not systematically captured. Second, coverage-completeness estimates for SS1 are pooled across studies with substantial methodological variation, and should be read as approximate rather than precise. Third, the ASSI weighting places substantial weight on regulatory integration, which reflects a deliberate focus on operationally-useful surveillance rather than surveillance as a pure research activity. These are addressable gaps rather than fatal objections.

6. Conclusion

6.1 Key Findings

Across 68 peer-reviewed studies, heavy-metal and contamination monitoring (SS4, ASSI 0.832) and AI-based signal detection (SS5, ASSI 0.808) emerged as the two most operationally-advanced surveillance frames. Spontaneous reporting (SS1) has reasonable regulatory integration but substantial under-reporting limitations. Active surveillance (SS2) has better coverage but smaller deployment scale. Herb-drug interaction surveillance (SS3) is the least mature frame in Ayurvedic contexts, though the underlying conventional-pharmaceutical methodology it inherits is well-developed. Coverage estimates for spontaneous reporting remain in the expected 10-18% range; active-surveillance implementations reach 60-80% coverage; heavy-metal monitoring is essentially analytically deterministic. Taken together, Ayurvedic pharmacovigilance infrastructure is now methodologically mature but unevenly implemented.

6.2 Recommendations

Three recommendations follow. First, investment in Ayurvedic pharmacovigilance should prioritise the implementation gap rather than further methodology development, because the principal methodology across frames is now mature. Specifically, practitioner-level reporting-culture interventions - training, reporting-interface simplification, feedback loops from reports to practice - are probably the highest-leverage investment for SS1 improvement. Second, AI-based signal detection (SS5) should be formally integrated into PvPI-AYUSH workflow rather than remaining a research-methodology activity, because the signal-detection performance gap (2.4x over baseline) is large enough to matter operationally. Third, herb-drug interaction surveillance (SS3) should receive targeted infrastructural investment, because the frame is the least mature in Ayurvedic contexts and interaction-mediated adverse events are a well-documented real clinical risk. The ASSI rubric and the full study inventory are available from the corresponding author.

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Declarations

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Conflict of Interest

The authors declare no competing interests. None of the authors holds equity in, or has received consulting fees from, any commercial pharmacovigilance-services provider or Ayurvedic product manufacturer.

Data Availability Statement

The full study inclusion log, frame classification records, and the ASSI scoring spreadsheet are available as supplementary material from the corresponding author on reasonable request. Individual study-level data remain subject to the original publishers' data-sharing policies.

Ethical Approval

As this is a structured review of previously published pharmacovigilance-methodology studies with no primary human-subjects data collection, formal ethical approval was not required. The review protocol was registered on the Open Science Framework (OSF registration DOI 10.17605/OSF.IO/ASSI23) prior to the start of screening.

Appendix A

ASSI Scoring Rubric and Surveillance-Frame Classification

Full scoring rubric for the Ayurvedic Safety Surveillance Index (ASSI), together with the classification criteria used to assign studies to surveillance frames. All five ASSI dimensions are normalised to the 0-1 range before the weighted sum is calculated.