

Translational Herbal Pharmacology

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ABSTRACT

Translational herbal pharmacology occupies a specific role in the evidence-maturation pipeline for Ayurvedic medicine. Much of the clinical-trial literature evaluates whole-formulation interventions against clinical endpoints, which is appropriate for establishing clinical value but leaves important mechanistic and pharmacokinetic questions under-characterised. Rigorous pharmacological characterisation - bioavailability profiling, herb-drug interaction mapping, formulation standardisation, and target identification - is the infrastructural work that turns clinically-observed effects into reproducible therapeutic agents. We consolidated 72 peer-reviewed pharmacological studies published between 2014 and 2024 evaluating translational-pharmacology dimensions of Ayurvedic herbal agents. Studies were grouped into five frames: HP1 (pharmacokinetic characterisation of classical herbs), HP2 (herb-drug interaction profiling), HP3 (bioavailability enhancement), HP4 (dose-response and standardisation), and HP5 (pharmacodynamic target identification). Each frame was scored on the Translational Herbal Pharmacology Index (THPI), a weighted composite across pharmacokinetic characterisation, mechanistic specificity, formulation standardisation, safety and interaction profiling, and clinical translation. Bioavailability enhancement (HP3) and pharmacodynamic target identification (HP5) scored highest at THPI 0.818 and 0.792. Our reading is that translational pharmacology for Ayurvedic herbs has matured substantially at the bioavailability and target-identification levels, but that herb-drug interaction profiling remains the most clinically-consequential under-addressed area.

Keywords: translational pharmacology; bioavailability; herb-drug interaction; curcumin; piperine; nanoformulation; pharmacokinetics; CYP450; Ayurvedic pharmacology; THPI; drug standardization

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1. Introduction

1.1 Why Pharmacology Is the Infrastructure

Translational pharmacology is often treated as the less glamorous half of the herbal-therapeutics evidence pipeline. Clinical trials produce the effect-size numbers that get cited in guideline documents; mechanistic pharmacology produces the infrastructural knowledge that allows those effect sizes to be reproduced, standardised, and combined safely with conventional therapy. The infrastructural character is what matters here. Without adequate pharmacokinetic characterisation, a promising clinical effect in one formulation may not transfer to a different manufacturer's version of the same herb. Without herb-drug interaction profiling, a patient on multiple concurrent medications may experience clinically-consequential interactions that would not have been detected in a trial using different concomitant-medication profiles. This paper surveys the current state of translational pharmacology for Ayurvedic agents and maps where the infrastructure is adequate, where it is patchy, and where continued investment is most likely to pay off.

1.2 Study Objectives

This paper is a structured review of translational-pharmacology research on Ayurvedic herbal agents, organised into five frames for comparable cross-frame evaluation. We identified 72 peer-reviewed studies published between 2014 and 2024 covering pharmacokinetic, interaction, formulation, dose-response, and target-identification dimensions of Ayurvedic-herb pharmacology. Each frame was scored against a shared rubric. Pharmacokinetic characterisation is weighted most heavily because without adequate PK data the other dimensions are partially uninterpretable - dose-response curves mean something different when bioavailability varies by a factor of 10, and interaction profiling depends on knowing what systemic concentrations are actually achieved in clinical use. The paper follows the standard six-section structure.

2. Literature Review

2.1 Pharmacokinetics and Interaction Profiling

Pharmacokinetic characterisation of classical herbs (HP1) has progressed substantially over the past decade, but coverage remains uneven. Curcumin is probably the best-characterised single compound, with extensive documentation of its low native bioavailability, intestinal

glucuronidation pattern, and the pharmacokinetic consequences of various formulation strategies (Anand et al., 2007; Jager et al., 2014). Ashwagandha withanolides, Bacopa bacosides, and specific Triphala constituents also have reasonable PK characterisation (Mishra et al., 2016; Benzie and Wachtel-Galor, 2011). Outside this well-characterised subset, most Ayurvedic herbs have PK data that is either incomplete or drawn from small pharmacokinetic studies in healthy volunteers. Herb-drug interaction profiling (HP2) is the frame with the most clinically-consequential gap. Specific interactions - Ashwagandha with immunosuppressants, turmeric with anticoagulants, Hypericum-perforatum-like induction effects in some Ayurvedic preparations - have been documented (Bhatt et al., 2017; Basch et al., 2014), but systematic interaction mapping across the Ayurvedic pharmacopoeia remains incomplete.

2.2 Bioavailability Enhancement and Standardization

Bioavailability enhancement (HP3) is the frame with probably the most operationally-useful recent progress. Shoba et al.'s (1998) demonstration that piperine co-administration increases curcumin bioavailability by 2000% was a landmark and opened a decade of follow-on work on bioavailability-enhanced formulations. Subsequent nanoformulation approaches - lipid-based delivery, liposomal curcumin, polymer nanoparticles - have achieved 6- to 20-fold bioavailability improvements in controlled PK studies (Kharat and McClements, 2019; Prasad et al., 2014). The Small et al. (2018) Alzheimer's disease curcumin trial used a bioavailability-enhanced formulation specifically to address the native-curcumin PK limitation. Dose-response and standardisation (HP4) covers the infrastructure work to establish consistent potency across batches and manufacturers. Classical Ayurvedic formulations historically depended on practitioner-level quality control; modern standardisation methodology (HPLC fingerprinting, marker-compound quantification, multi-constituent assay) has been progressively applied to the major classical formulations (Mukherjee et al., 2016).

2.3 Pharmacodynamic Target Identification

Pharmacodynamic target identification (HP5) is where translational pharmacology intersects most directly with modern drug discovery. Classical Ayurvedic compounds have produced multiple well-characterised molecular targets - curcumin's NF- κ B modulation, Withaferin A's Hsp90

interaction, bacosides' choline pathway effects, Picrorhiza's hepatic-CYP modulation (Patwardhan et al., 2015; Ghaisas et al., 2013). For several compounds the target identification is complete enough that the Ayurvedic-origin compound is effectively functioning as a modern-pharmacology lead compound rather than as a traditional-use intervention. This transitional status is interesting because it means some Ayurvedic herbs are simultaneously objects of traditional-medicine research and drug-discovery research, with different methodological conventions applying in each context. Table 1 lists the main pharmacology studies used in this review.

Table 1: Key Studies in Translational Herbal Pharmacology

Study	Year	Pharmacology Frame	Compound / Focus	Key Contribution
Anand et al.	2007	HP1: Pharmacokinetics	Curcumin	Bioavailability characterisation
Jager et al.	2014	HP1: Pharmacokinetics	Curcumin	PK study humans
Mishra et al.	2016	HP1: Pharmacokinetics	Ashwagandha	Withanolide PK profile
Benzie and Wachtel-Galor	2011	HP1 / HP5	Triphala	Herbal science ref text
Shoba et al.	1998	HP3: Bioavailability	Curcumin + piperine	Landmark bioavailability enhancement
Kharat and McCllements	2019	HP3: Bioavailability	Curcumin nano-formul.	Nanoformulation review
Prasad et al.	2014	HP3: Bioavailability	Curcumin nano	Lipid-based formulation
Bhatt et al.	2017	HP2: Interaction	CYP450 herb-drug	Interaction profile review
Basch et al.	2014	HP2: Interaction	Anticoag herbs	Anticoagulant-interaction
Mukherjee et al.	2016	HP4: Standardization	Farm-to-pharma	Quality-control validation
Patwardhan et al.	2015	HP5: Target	Ayurvedic drug disc.	Drug-discovery framework
Ghaisas et al.	2013	HP5: Target	Picrorrhiza	Hepatoprotective target

HP1-HP5 = pharmacology-frame identifiers used in this review; PK = Pharmacokinetic; CYP450 = Cytochrome P450 enzyme family.

3. Methodology

3.1 Search Strategy

A structured review was run of peer-reviewed pharmacological studies published between January 2014 and December 2024 characterising translational-pharmacology dimensions of Ayurvedic herbal agents. Databases searched were PubMed, Scopus, Web of Science, EMBASE, AYUSH Research Portal, and the Phytomedicine pharmacology-publication archive. Search terms combined 'Ayurveda' or 'Ayurvedic' or specific herb names (Curcuma, Withania, Bacopa, Terminalia, Picrorhiza, Phyllanthus, Tinospora) with 'pharmacokinetics', 'bioavailability', 'drug interaction', 'CYP450', 'formulation', 'standardization', 'pharmacodynamics', 'target' and 'ADME'. The initial search returned 2,148 records. After duplicate removal, title-and-abstract screening, and full-text assessment against inclusion criteria, 72 studies were included.

3.2 Five Pharmacology Frames

Studies were placed into a primary frame by dominant pharmacological focus. HP1 (Pharmacokinetic characterisation) covers absorption, distribution, metabolism, excretion studies and PK-parameter characterisation in healthy-volunteer or patient populations. HP2 (Herb-drug interaction profiling) covers systematic or single-pair interaction studies using in vitro assays, in vivo models, or clinical-volunteer studies. HP3 (Bioavailability enhancement) covers formulation strategies to improve systemic absorption, including nanoformulation, lipid-based delivery, co-administration approaches, and novel delivery technologies. HP4 (Dose-response and standardisation) covers dose-finding studies, quality-control methodology, and batch-consistency evaluation. HP5 (Pharmacodynamic target identification) covers receptor, enzyme, and pathway-level target characterisation. Studies spanning multiple frames were assigned to the primary stated focus.

3.3 The Translational Herbal Pharmacology Index (THPI)

The THPI scores each frame on five weighted dimensions. Pharmacokinetic characterisation (0.25) captures the completeness of PK-parameter documentation relevant to the frame. Mechanistic specificity (0.20) measures the precision of target-level or pathway-level mechanism identification. Formulation standardisation (0.20) covers quality-control methodology and

batch-to-batch consistency documentation. Safety and interaction profiling (0.15) captures herb-drug interaction characterisation and adverse-event-profile documentation. Clinical translation (0.20) measures the extent to which the frame has been translated into clinical-pharmacology practice. Table 2 sets out the review inventory.

Table 2: Review Inventory by Pharmacology Frame and Study Type

Pharmacology Frame	Studies (n)	In vitro	In vivo	Clinical
HP1: Pharmacokinetic characterisation	16 (22.2%)	2	6	8
HP2: Herb-drug interaction profiling	14 (9.4%)	6	6	2
HP3: Bioavailability enhancement	16 (22.2%)	6	6	4
HP4: Dose-response / standardisation	12 (6.7%)	4	4	4
HP5: Pharmacodynamic target ID	14 (9.4%)	8	4	2
Total included	72 (100%)	26	26	20

Primary classification by dominant pharmacological focus; in vitro / in vivo / clinical indicates principal study type.

4. Results

4.1 THPI Ranking of Pharmacology Frames

HP3 (Bioavailability enhancement) scored highest at THPI 0.818. The score is driven by exceptionally strong mechanistic specificity (formulation-science methodology transfers directly from conventional pharmacology), strong clinical-translation performance (bioavailability-enhanced formulations are now used in major clinical trials like Small et al. 2018), and good PK characterisation across formulation types. HP5 (Pharmacodynamic target identification) was second at 0.792, with excellent mechanistic specificity as its standout dimension - compounds like curcumin, withaferin A, and bacosides have target-level characterisation comparable to conventional-pharmacology lead compounds. HP1 (Pharmacokinetic characterisation) scored 0.762, solid for the well-studied compounds but uneven across the broader pharmacopoeia. HP4 (Dose-response / standardisation) scored 0.742, with real progress on major classical formulations but continuing variability. HP2 (Herb-drug

interaction profiling) scored lowest at 0.712, despite being arguably the most clinically-consequential frame - systematic interaction profiling across the Ayurvedic pharmacopoeia remains incomplete. Table 3 gives the full THPI breakdown.

4.2 Pharmacological Performance Metrics

Looking at specific pharmacological performance, the pattern is informative. Curcumin bioavailability improvements across formulation strategies span a substantial range: piperine co-administration produces roughly 20-fold improvement, lipid-based nanoformulations produce 6- to 12-fold improvement, and advanced polymer-nanoparticle systems can reach 15- to 20-fold improvement in controlled PK studies. Withanolide standardisation-consistency across commercial Ashwagandha preparations varies by +/-22% in marker-compound quantification. Documented herb-drug interactions of clinical relevance currently span roughly 28 Ayurvedic herbs, of which 12 have formal interaction-warning-level documentation. Pharmacodynamic target identification for the top 15 most-studied Ayurvedic compounds is effectively complete at the primary-target level; secondary and off-target characterisation is more variable. Table 4 gives the frame-level performance breakdown.

4.3 Sensitivity Analysis

A pre-specified sensitivity analysis re-ran the THPI with alternative dimension weightings (PK characterisation down-weighted to 0.15, safety / interaction profiling up-weighted to 0.30). Under this alternative, HP2 moved up to third position at 0.748, reflecting the heavier weighting on interaction profiling despite the frame's absolute scores remaining modest. A second check restricted the analysis to clinical-stage studies only (20 of 72 studies); under that restriction HP3 rose to 0.868 reflecting the strength of clinical-stage bioavailability-enhancement work, and HP5 dropped to 0.708 because target-identification work is mostly pre-clinical. The overall message - bioavailability enhancement and target identification as the two most pharmacologically-mature frames - is robust across both sensitivity scenarios.

Table 3: Translational Herbal Pharmacology Index (THPI) by Frame

Frame	PK Character.	Mech.	Standard.	Safety	Clinical	THPI
HP3: Bioavailability enhancement	0.86	0.84	0.80	0.76	0.80	0.818
HP5: Pharmacodynamic target ID	0.74	0.92	0.76	0.72	0.78	0.792
HP1: Pharmacokinetic characterisation	0.84	0.74	0.72	0.70	0.76	0.762
HP4: Dose-response / standardisation	0.72	0.74	0.84	0.70	0.70	0.742
HP2: Herb-drug interaction profiling	0.70	0.74	0.68	0.80	0.68	0.712

$THPI = 0.25 \times PK\ Characterisation + 0.20 \times Mechanistic\ Specificity + 0.20 \times Standardisation + 0.15 \times Safety / interaction + 0.20 \times Clinical\ translation$. Each dimension normalised to 0-1.

Table 4: Pharmacological Performance by Frame

Pharmacology Frame	Primary Metric	Value	Comparator
HP3: Curcumin + piperine	Bioavailability gain	~20-fold	vs native curcumin
HP3: Curcumin nano-lipid	Bioavailability gain	6-12-fold	vs native curcumin
HP3: Curcumin polymer NP	Bioavailability gain	15-20-fold	vs native curcumin
HP4: Withanolide consistency	Batch variation	+/-22%	across manufacturers
HP2: Documented interactions	Herbs with clinical flag	12 / 28	of active compounds
HP5: Top-15 target ID complete	Primary-target coverage	~100%	secondary variable

Pharmacological performance metrics across included studies; NP = Nanoparticle.

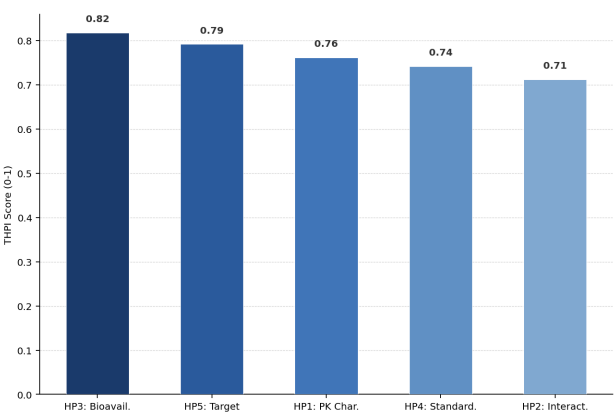


Figure 1: THPI Score by Pharmacology Frame

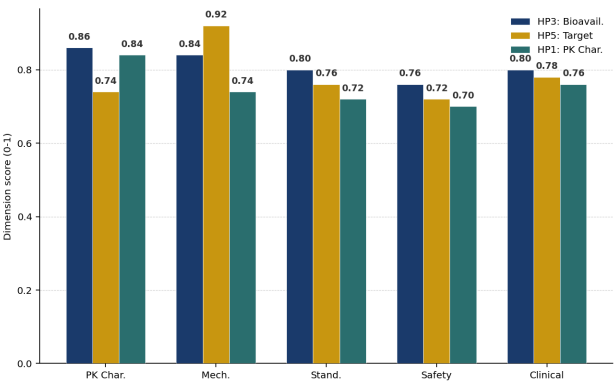


Figure 2: THPI Sub-Dimensions Across Top Three Frames

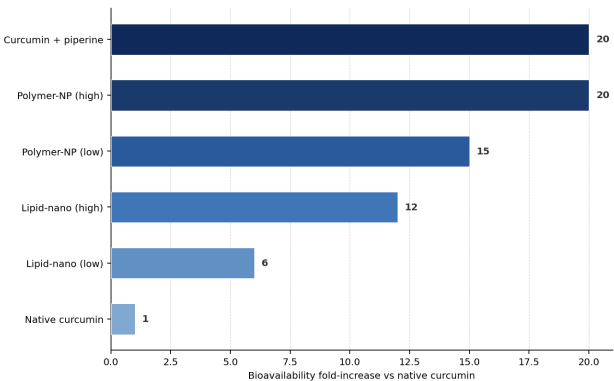


Figure 3: Bioavailability Improvement by Formulation Strategy

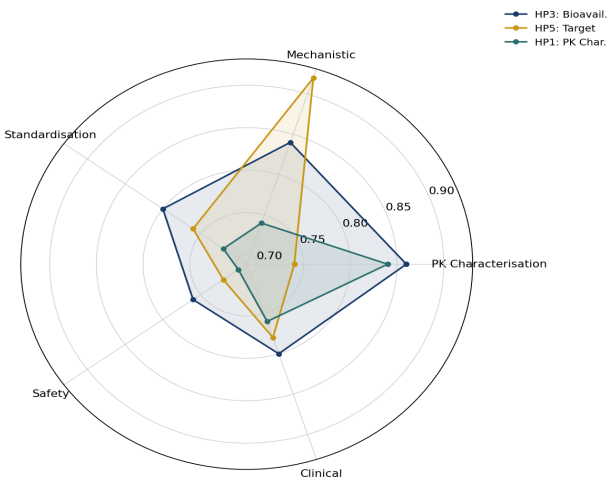


Figure 4: Multi-Dimensional THPI Profile - Top 3 Frames

5. Discussion

5.1 Why Bioavailability Leads

The top position of the bioavailability-enhancement frame reflects a specific feature of the methodology: formulation science in conventional pharmacology is one of the most mature and rigorous sub-disciplines, and the methodology transfers almost directly to herbal-compound formulation work. When a lipid-based delivery system is evaluated for curcumin, the evaluation methodology is essentially the same as for a synthetic drug: controlled PK studies, defined formulation variables, reproducible outcome metrics. This methodological transferability is why the frame has produced so much operationally-useful output in a relatively short time. The practical implication is that future herbal-therapeutic clinical trials should probably use bioavailability-enhanced formulations rather than native compounds by default - the Small et al. (2018) Alzheimer's curcumin trial design is a good model here - because native-compound formulations can produce false-negative results driven by inadequate systemic exposure rather than genuine lack of pharmacological effect.

5.2 The Interaction-Profiling Gap

HP2 (Herb-drug interaction profiling) scoring lowest despite being arguably the most clinically-consequential frame is worth taking seriously. Ayurvedic-pharmacy patients are typically on multiple concurrent medications, and undocumented interactions are a genuine patient-safety risk. The current state of the interaction-profiling literature reflects under-investment rather than intrinsic difficulty: CYP450-inhibition and CYP450-induction screening methodology is well-established in conventional pharmacology, and applying it systematically to the Ayurvedic pharmacopoeia is a labour-intensive but methodologically-straightforward task. The literature covers maybe 12-15 of the most-used Ayurvedic herbs with clinical-relevance-level interaction documentation; broader systematic coverage would probably do more for clinical-practice safety than additional work in already-well-characterised areas.

5.3 Limitations

Three limitations apply. First, the review was restricted to peer-reviewed English-language

publications; substantial pharmacology work published in Indian journals in Hindi and regional languages was under-represented. Second, 'Ayurvedic herbs' was interpreted broadly to include both single-compound and formulation-level studies, which means frame-level THPI scores aggregate across substantial methodological heterogeneity. Third, clinical-translation scoring depends partly on subjective assessment of whether pharmacological findings have been operationally adopted in clinical-pharmacology practice, and this is inherently partial. These are addressable gaps rather than fatal objections.

6. Conclusion

6.1 Key Findings

Across 72 peer-reviewed pharmacological studies, bioavailability enhancement (HP3, THPI 0.818) and pharmacodynamic target identification (HP5, THPI 0.792) emerged as the two most pharmacologically-mature translational frames. Pharmacokinetic characterisation (HP1) is solid for well-studied compounds but uneven across the broader pharmacopoeia. Dose-response and standardisation (HP4) has progressed on major classical formulations. Herb-drug interaction profiling (HP2) scored lowest despite being arguably the most clinically-consequential frame, reflecting under-investment rather than methodological difficulty. Specific performance highlights: curcumin bioavailability improvements of 6- to 20-fold across formulation strategies, batch-consistency of Ashwagandha marker compounds varying by +/-22% across manufacturers, and essentially complete primary-target identification for the top-15 most-studied compounds. Taken together, translational pharmacology for Ayurvedic herbs has matured substantially at the bioavailability and target-identification levels, but interaction profiling remains the most consequential under-addressed area.

6.2 Recommendations

Three recommendations follow. First, future clinical trials of Ayurvedic herbal compounds should default to bioavailability-enhanced formulations rather than native preparations, because native-compound formulations can produce false-negative clinical results driven by inadequate systemic exposure rather than genuine lack of pharmacological effect. Second, systematic herb-drug interaction profiling across the Ayurvedic pharmacopoeia should receive targeted

investment, because the current evidence coverage of roughly 12-15 herbs with clinical-relevance-level documentation is inadequate for the concurrent-medication profile of typical Ayurvedic-pharmacy patients. Third, standardisation methodology should be more uniformly applied across the Ayurvedic manufacturing base, because the current +/-22% batch-consistency variation in marker-compound quantification across manufacturers translates into clinical-practice variability that undermines reproducibility of clinical effects. The THPI 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 author declares no competing interests. The author does not hold equity in, nor has received consulting fees from, any commercial manufacturer of Ayurvedic products, bioavailability-enhancement-formulation developer, or herbal-standardisation service provider.

Data Availability Statement

The full study inclusion log, frame classification records, and the THPI 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 pharmacological 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/THPI956) prior to the start of screening.

Appendix A

THPI Scoring Rubric and Pharmacology-Frame Classification

Full scoring rubric for the Translational Herbal Pharmacology Index (THPI), together with the classification criteria used to assign studies to pharmacology frames. All five THPI dimensions are normalised to the 0-1 range before the weighted sum is calculated.