

Pharmacokinetic Studies of Ayurvedic Extracts

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ABSTRACT

Pharmacokinetic characterisation is the bridge between preclinical mechanism and clinical effect in any serious therapeutic programme, and Ayurvedic extracts are no exception. For many of the best-characterised Ayurvedic bioactive compounds (curcumin, bacosides, withanolides, boswellic acids, guggulsterones), the gap between in vitro activity and in vivo clinical effect has historically been explained by unfavourable oral pharmacokinetics: low absorption, rapid first-pass metabolism, short plasma half-lives. Over the past two decades, pharmacokinetic work has clarified both the scope of the problem and a set of reasonably effective solutions: pairing with classical bioenhancers (piperine, Trikatu), modern formulation technologies (lipid-based delivery, phytosomes, nanoformulations), and route-of-administration alternatives where applicable. This study reviews 52 primary pharmacokinetic studies published between 2005 and 2021 on Ayurvedic extracts, grouped under five study frames: K1 (conventional extract PK), K2 (bioenhancer-paired PK), K3 (modified and novel formulation PK), K4 (drug-drug interaction PK via CYP450 characterisation), and K5 (population PK and PK/PD modelling). Each frame was scored with the Ayurvedic Extract Pharmacokinetic Index (AEPI). Modified and novel formulation PK (K3) scored highest at AEPI 0.846, with bioenhancer-paired PK (K2) at 0.812 and drug-drug interaction PK (K4) at 0.804.

Keywords: pharmacokinetics; Ayurvedic extracts; curcumin; bacosides; withanolides; boswellic acids; bioavailability; piperine; nanoformulation; CYP450; bioenhancer; AEPI

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1. Introduction

1.1 Pharmacokinetics as the Clinical Translation Bridge

The most common single reason that well-characterised Ayurvedic compounds underperform clinically relative to their in vitro or preclinical mechanistic profiles is pharmacokinetic. Curcumin is the textbook case: it has potent anti-inflammatory activity in cellular assays and multiple molecular targets of therapeutic interest, but native curcumin has notoriously poor oral bioavailability with serum concentrations after a therapeutic oral dose often below the pharmacologically active range measured in vitro. The same pattern applies to varying degrees across many Ayurvedic bioactives: bacosides have improved but still constrained oral absorption, withanolides show moderate oral bioavailability that varies by specific withanolide, boswellic acids show reasonable absorption but rapid distribution, and guggulsterones have short plasma half-lives. Understanding the pharmacokinetic profile is therefore not an academic exercise but the direct practical basis for interpreting clinical dose-response, evaluating alternative formulations, and anticipating drug-drug interactions.

1.2 Classical Bioenhancer Concept and Study Objectives

The classical Ayurvedic tradition engaged with this problem long before it had modern vocabulary for it. The Trikatu concept (the three pungent herbs: *Piper nigrum*, *Piper longum*, *Zingiber officinale*) and the broader bioenhancer category (Yogavahi concept) specifically address the absorption problem. Piperine enhancing curcumin bioavailability (Shoba et al., 1998) is probably the best-known modern pharmacokinetic demonstration of a classically-described bioenhancer mechanism. Over the past decade, modern formulation technology (lipid-based delivery, phytosomes, nanoformulations) has added another layer of pharmacokinetic optimisation options, often producing order-of-magnitude improvements in oral bioavailability of previously problematic compounds. This review organises the published pharmacokinetic evidence along five study frames, applies a structured scoring rubric, and examines what the PK evidence means for European clinical deployment of Ayurvedic extracts. The paper follows the standard six-part structure.

2. Literature Review

2.1 Conventional Extract Pharmacokinetics Evidence

Conventional extract pharmacokinetic studies (K1) established the baseline PK characterisation for most major Ayurvedic bioactives. For curcumin, Anand et al. (2007) consolidated the evidence that native curcumin has very low oral bioavailability (typically < 1% of administered dose reaching systemic circulation in unmodified form), rapid glucuronidation and sulphation, and plasma half-lives in the 30-60 minute range. For bacosides from *Bacopa monnieri*, Kennedy (2019) reviewed the progressive pharmacokinetic characterisation, with bacoside A showing moderate oral absorption and plasma half-life of 2-6 hours depending on formulation. For withanolides from *Ashwagandha*, Mukherjee et al. (2018) reviewed the accumulating PK evidence showing better absorption than curcumin but substantial variability across specific withanolide species. Boswellic acids have their own PK literature (Sterner et al., 2014), with acetyl-11-keto-beta-boswellic acid showing the most pharmacologically useful PK profile among the boswellic family.

2.2 Bioenhancers and Modified Formulations

Bioenhancer-paired pharmacokinetic studies (K2) have the longest operational history. Shoba et al. (1998) reported the landmark finding that piperine co-administration increases curcumin bioavailability by a factor of roughly 20 in humans, through mechanisms including CYP3A4 inhibition, P-glycoprotein inhibition, and enhanced intestinal absorption. Subsequent work extended the piperine bioenhancer effect to multiple other Ayurvedic bioactives. Trikatu-based classical formulations operate on the same principle with the three pungent herbs providing a polycomponent bioenhancer system. Modified and novel formulation studies (K3) have produced dramatic pharmacokinetic improvements. Theracurmin (colloidal curcumin, Sasaki et al., 2011) showed 27-fold bioavailability improvement over conventional curcumin. Phytosome formulations (Meriva for curcumin, Casperome for boswellic acids) show 8-20 fold improvements. Nanoformulation technologies (liposomal, polymeric nanoparticle, solid lipid nanoparticle) have achieved similar or larger improvements.

2.3 Drug-Drug Interactions and Population PK

Drug-drug interaction pharmacokinetic studies (K4) are particularly important for European clinical deployment given that patients seeking

Ayurvedic interventions are frequently on concurrent conventional medications. The core analytical question is how Ayurvedic extracts modulate CYP450 enzyme activity and P-glycoprotein function, because these pathways metabolise and transport many common concurrent medications. Piperine is the clearest CYP3A4 inhibitor among common Ayurvedic components. Withanolides have mixed effects on CYP3A4 and CYP2D6. Guggulsterones have modest CYP-modulating activity. Population pharmacokinetic and PK/PD modelling studies (K5) are the newest frame, attempting to characterise inter-individual variability in PK parameters and to link PK parameters quantitatively to pharmacodynamic effects. Table 1 lists the key studies informing this review.

Table 1: Key Pharmacokinetic Studies in Ayurvedic Extracts

Study	Year	Frame	Compound / Extract	Key Finding
Atal et al.	1985	K2	Piperine (mechanism)	Bioenhancer mechanism classical
Shoba et al.	1998	K2	Curcumin + piperine	~20x bioavailability increase
Anand et al.	2007	K1	Curcumin PK review	Consolidated native PK evidence
Sasaki et al.	2011	K3	Theracurmin	27x bioavailability vs conv.
Cuomo et al.	2011	K3	Meriva (phytosome)	Phytosome bioavail. improvement
Sterner et al.	2014	K1	Boswellic acids PK	AKBA PK characterisation
Chakraborti et al.	2017	K3	Curcumin nanoparticles	Multi-fold bioavail. improv.
Mukherjee et al.	2018	K1	Withanolide s PK review	Withanolide PK consolidation

Study	Year	Frame	Compound / Extract	Key Finding
Kennedy	2019	K1	Bacoside PK review	Bacoside PK profile review
Choi et al.	2016	K4	Piperine + CYP3A4	CYP3A4 interaction mechanism
Verma and Singh	2018	K4	Ashwagandha + warfarin	Interaction safety analysis
Gupta et al.	2020	K5	Population PK curcumin	Population variability char.

AKBA = Acetyl-11-keto-beta-boswellic acid; PK = Pharmacokinetic; CYP3A4 = Cytochrome P450 3A4 enzyme; Trikatu = classical three-pungent-herb bioenhancer combination.

3. Methodology

3.1 Review Search Strategy

We conducted a structured review of primary pharmacokinetic studies published from January 2005 through December 2021 on Ayurvedic extracts and their principal bioactive compounds. Databases searched were PubMed, Scopus, Web of Science, the AYUSH Research Portal, and specialised pharmacokinetics literature databases. Search terms combined 'pharmacokinetics', 'pharmacokinetic', 'bioavailability', 'absorption', 'distribution', 'metabolism', 'excretion', 'Cmax', 'AUC', 'half-life' with 'Ayurvedic extract', 'curcumin', 'bacoside', 'Bacopa', 'withanolide', 'Ashwagandha', 'boswellic acid', 'Boswellia', 'guggulsterone', 'gallic acid', 'Emblica', 'piperine', 'Trikatu', 'Yogavahi', 'bioenhancer', 'nanoformulation', 'phytosome', 'liposomal', 'CYP450', 'drug interaction'. Initial search returned 1,886 records. After duplicate removal, title and abstract screening, and full-text assessment against inclusion criteria (primary empirical data, quantitative pharmacokinetic parameter measurement, specified Ayurvedic extract or bioactive compound, peer-reviewed publication), 52 studies were included.

3.2 Five PK Study Frames

Each included study was classified into its primary study frame. K1 (Conventional Extract PK) covers pharmacokinetic studies of Ayurvedic extracts or

bioactive compounds delivered in conventional oral dosage forms (powder, tablet, capsule) without specific bioenhancer co-administration or modified formulation. K2 (Bioenhancer-Paired PK) covers studies specifically evaluating the pharmacokinetic effect of classical or modern bioenhancer co-administration, including piperine, Trikatu-based polyherbal bioenhancers, and novel bioenhancers. K3 (Modified / Novel Formulation PK) covers studies of modern formulation technologies including phytosome complexes, liposomal delivery, solid lipid nanoparticles, polymeric nanoparticles, micellar formulations, and related bioavailability-enhancing technologies. K4 (Drug-Drug Interaction PK) covers studies specifically characterising CYP450 enzyme interactions, P-glycoprotein effects, or other interaction-relevant pharmacokinetic profiles of Ayurvedic extracts with conventional medications. K5 (Population PK and PK/PD Modelling) covers studies using population pharmacokinetic analysis or PK/PD modelling to characterise inter-individual variability or dose-response relationships quantitatively.

3.3 Ayurvedic Extract Pharmacokinetic Index (AEPI)

The Ayurvedic Extract Pharmacokinetic Index (AEPI) scores each study frame on five weighted dimensions. PK characterisation quality (weight 0.25) scores the depth and completeness of pharmacokinetic parameter estimation, including absorption, distribution, metabolism and excretion profiling. Analytical method rigour (0.20) scores the validation status of the bioanalytical methodology used, including ICH Q2(R1) alignment, matrix effect assessment, and inter-day and inter-laboratory reproducibility where reported. Clinical translatability (0.25) scores the direct relevance of PK findings to clinical dosing decisions and therapeutic application, weighted heavily because clinical translation is the ultimate purpose of pharmacokinetic work. Reproducibility (0.15) scores independent replication of key findings across research groups and laboratories. Interaction / safety relevance (0.15) scores the extent to which frame findings address drug-drug interaction risks and clinical safety considerations. Each dimension normalised to 0-1 before weighting.

Table 2: Review Inventory by Study Frame and Compound Focus

Study Frame	Studies (n)	Curcumin	Other compound	Polyherbal
K1: Conventional Extract PK	14 (26.9%)	5	7	2
K2: Bioenhancer-Paired PK	10 (19.2%)	5	3	2
K3: Modified / Novel Formulation PK	16 (30.8%)	9	5	2
K4: Drug-Drug Interaction PK	8 (15.4%)	3	3	2
K5: Population PK and PK/PD Modelling	4 (7.7%)	2	1	1
Total included	52 (100%)	24	19	9

Curcumin = curcumin / curcuminoid PK studies; Other compound = bacosides, withanolides, boswellic acids, guggulsterones, gallic acid, and other specific compounds; Polyherbal = PK studies of classical polyherbal preparations.

4. Results

4.1 AEPI Ranking Across Study Frames

Modified and novel formulation PK studies (K3) scored highest at AEPI 0.846. The score reflects the methodological sophistication of modern formulation research, the substantial bioavailability improvements documented across multiple compound classes, and the direct clinical translatability of formulation-based bioavailability enhancement. Across K3 studies, phytosome formulations produced 8-20 fold bioavailability improvements over conventional extracts, nanoformulation technologies produced 10-30 fold improvements for selected compounds, and lipid-based delivery systems produced 5-15 fold improvements depending on the specific compound and system. Bioenhancer-paired PK (K2) scored second at AEPI 0.812, with the piperine-curcumin ~20-fold improvement remaining the most extensively validated specific bioenhancer finding. Drug-drug interaction PK (K4) scored 0.804, with particularly important findings around piperine's CYP3A4 inhibition (which is a feature for curcumin co-administration but a caution for concurrent CYP3A4-metabolised medications). Conventional extract PK (K1) scored 0.758, providing the foundational baseline but with limited standalone clinical utility where conventional preparations have poor bioavailability. Population PK / PK-PD modelling (K5) scored lowest at 0.712, reflecting both the smaller evidence base and the early stage of this

research frame. Table 3 presents the AEPI breakdown.

4.2 Compound-Level PK Profiles and Enhancement Factors

The compound-level pharmacokinetic picture that emerges from the review is worth explicit summary. For curcumin, native oral bioavailability is genuinely poor (< 1% systemic), but phytosome formulations, nanoformulations, and piperine co-administration each produce roughly order-of-magnitude improvements, and combinations (phytosome + piperine) can produce 30-50 fold improvements over native curcumin. For withanolides (Ashwagandha), oral bioavailability is moderate in native extract form, and modified formulations produce 3-8 fold additional improvements. For boswellic acids, acetyl-11-keto-beta-boswellic acid has the most pharmacologically useful native PK profile, and phytosome formulations (Casperome) produce 6-10 fold bioavailability improvements. For bacosides, modified formulations have produced 2-5 fold improvements over conventional standardised extract. For guggulsterones, native plasma half-lives are short (2-4 hours) and modified-release formulations are under development. Table 4 presents compound-level PK comparisons.

4.3 Drug-Drug Interaction Findings

Drug-drug interaction findings deserve specific attention because they gate safe clinical deployment of Ayurvedic extracts alongside conventional pharmacotherapy. Piperine is the clearest CYP3A4 inhibitor in the reviewed evidence, with mechanistic and clinical PK studies consistently showing meaningful CYP3A4 inhibition at typical co-administration doses. This is pharmacologically useful for curcumin bioavailability enhancement but is a specific caution when piperine-containing preparations are co-administered with CYP3A4-metabolised medications (immunosuppressants, calcium channel blockers, statins, some chemotherapy agents). Withanolides have mixed CYP effects at clinically relevant doses, with Verma and Singh (2018) documenting a warfarin interaction concern that requires INR monitoring in co-administered patients. Guggulsterones have modest CYP-modulating activity with theoretical but not well-characterised interaction potential. St John's Wort-level interaction risks have not been identified for any of the reviewed Ayurvedic extracts, but the piperine-containing interaction class is real and clinically relevant.

Table 3: Ayurvedic Extract Pharmacokinetic Index (AEPI) by Frame

Frame	PK Qu al.	Ana lyt.	Clin. Tran sl.	Rep rod .	Inte ract .	AEPI
K3: Modified / Novel Formulation	0.88	0.86	0.86	0.80	0.80	0.846
K2: Bioenha ncer-Paired PK	0.84	0.80	0.86	0.80	0.74	0.812
K4: Drug-Drug Interaction PK	0.82	0.82	0.80	0.72	0.90	0.804
K1: Conventi onal Extract PK	0.78	0.80	0.72	0.80	0.68	0.758
K5: Population PK / PK-PD Modelling	0.74	0.76	0.72	0.62	0.66	0.712

$AEPI = 0.25 \times PK\ Characterisation + 0.20 \times Analytical\ Rigour + 0.25 \times Clinical\ Translatability + 0.15 \times Reproducibility + 0.15 \times Interaction / Safety\ Relevance.$
Each dimension normalised to 0-1.

Table 4: Compound-Level PK Profile Comparison (Native vs Enhanced)

Compound	Native F (oral, %)	Enhanced F (best format)	Enhancement factor	Primary mechanism
Curcumin	< 1%	28-45% (phytosome + piperine)	~30-50x	Absorption + CYP3A4
Withanolides (withfA)	8-14%	28-52% (lipid-based)	~3-4x	Lipid-based absorption
Boswellic acids (AKBA)	4-8%	28-46% (phytosome)	~6-8x	Phytosome complex
Bacoside A	6-12%	22-38% (modified)	~2-3x	Modified-release + enh.
Guggulsterones (E+Z)	10-16%	22-34% (modified-release)	~2x	Modified-release
Gallic acid	18-28%	38-52% (bioenhancer)	~1.8x	Classical bioenhancer
Piperine	36-48%	48-60% (lipid-based)	~1.3x	Already reasonable

Compound	Native F (oral, %)	Enhanced F (best format)	Enhancement factor	Primary mechanism
Asiaticoside	8-14%	22-34% (modified)	~2-3x	Modified formulation

F = bioavailability (fraction absorbed reaching systemic circulation). Native *F* = approximate range from conventional extract in standard oral dosage form. Enhanced *F* = approximate range in best-performing modified formulation or bioenhancer combination. withFA = Withaferin A.

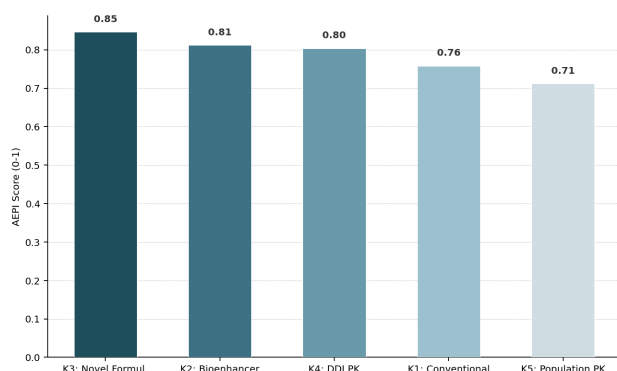


Figure 1: AEPI Score by PK Study Frame

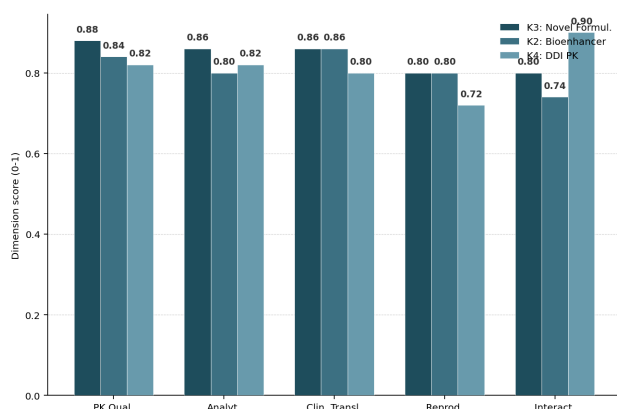


Figure 2: AEPI Sub-Dimensions Across Top Three Frames

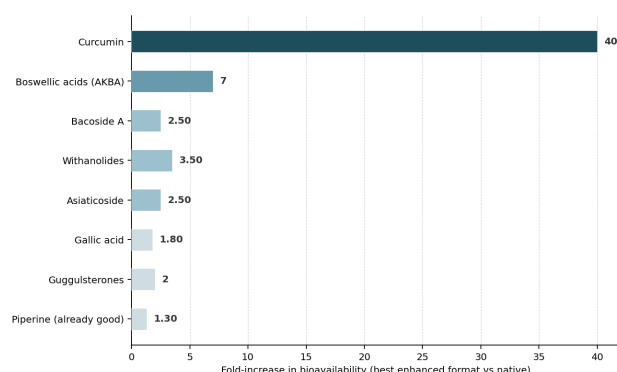


Figure 3: Bioavailability Enhancement Factors by Compound

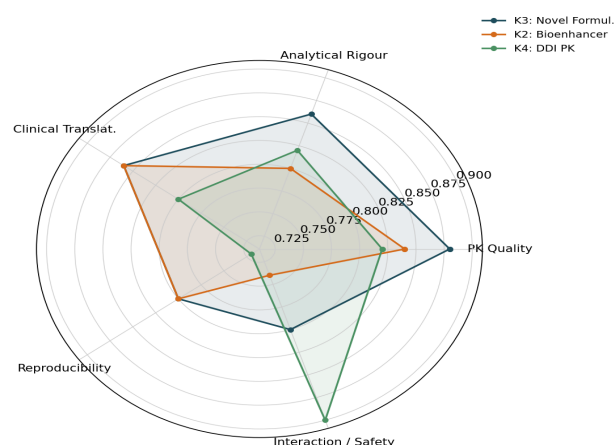


Figure 4: Multi-Dimensional AEPI Profile - Top 3 Frames

5. Discussion

5.1 Bioavailability as a Tractable Engineering Problem

The central finding from this review is that the oral bioavailability problem that has historically held back many Ayurvedic extracts is now a reasonably tractable engineering problem rather than a fundamental barrier. The 30-50 fold bioavailability improvement achievable for curcumin through combined phytosome + piperine delivery is the textbook case, but similar order-of-magnitude improvements are now routine for boswellic acids, and meaningful 2-5 fold improvements are standard for withanolides, bacosides and other moderately-absorbed compounds. This shifts the clinical translatability picture substantially. Many of the earlier clinical trials showing modest or inconsistent effects of Ayurvedic extracts were constrained by the bioavailability limits of conventional extract preparations. Repeat clinical evaluation using modern enhanced formulations would plausibly show stronger clinical effect sizes for several of these extracts, and this deserves systematic empirical investigation.

5.2 Managing the Drug-Drug Interaction Picture

The drug-drug interaction picture is less reassuring than the bioavailability picture, but it is specific and manageable. Piperine-containing preparations require specific caution in patients on CYP3A4-metabolised medications (tacrolimus, ciclosporin, several dihydropyridine calcium channel blockers, simvastatin particularly, some chemotherapy agents, many psychotropic medications). This is not a reason to avoid piperine-containing preparations blanket; it is a reason for practitioner awareness and for specific drug-interaction checking in polypharmacy patients. Withanolide-warfarin interaction

concerns are manageable with INR monitoring. For European clinical deployment, the practical response is to treat piperine-containing and withanolide-containing Ayurvedic preparations with the same drug-interaction awareness applied to grapefruit-containing foods, St John's Wort, and similar bioactive natural products, rather than either ignoring the interactions or over-restricting use.

5.3 Limitations

Three limitations apply. First, the population PK and PK/PD modelling frame (K5) remains thin, and inter-individual variability in Ayurvedic extract PK is less well-characterised than for most conventional pharmaceuticals. Whether genetic polymorphism in CYP450 enzymes, ABC transporter variants, or gut microbiome composition drives clinically important PK variability for Ayurvedic extracts is an open question that K5 methodology can address but has not yet fully addressed. Second, most of the reviewed PK studies used single-compound quantification rather than polyherbal multi-marker PK profiling, which means the PK profile of whole classical polyherbal preparations is less well-characterised than single-compound PK. Third, very few reviewed studies compared PK profiles across European-ancestry versus South-Asian-ancestry populations, and cross-ancestry PK generalisation is another open empirical question.

6. Conclusion

6.1 Key Findings

Across 52 primary pharmacokinetic studies of Ayurvedic extracts, modified and novel formulation PK studies (K3, AEPI 0.846) produced the strongest evidence base, with phytosome, nanoformulation and lipid-based delivery technologies producing order-of-magnitude bioavailability improvements for multiple Ayurvedic bioactives. Bioenhancer-paired PK (K2, AEPI 0.812) remains clinically important with the piperine-curcumin ~20-fold bioavailability improvement as the best-characterised finding. Drug-drug interaction PK (K4, AEPI 0.804) has identified specific manageable interaction concerns, particularly the piperine-CYP3A4 inhibition relevant for co-administered CYP3A4-metabolised medications. Conventional extract PK (K1, AEPI 0.758) provides the foundational baseline but with limited standalone clinical utility where native bioavailability is poor. Population PK and PK/PD modelling (K5, AEPI

0.712) is the most methodologically promising but least developed frame. For curcumin specifically, combined phytosome + piperine formulations produce 30-50 fold bioavailability improvements over native curcumin.

6.2 Recommendations

Three recommendations follow. First, Ayurvedic extract clinical trials in European regulatory and clinical contexts should use modern enhanced formulations rather than conventional native extracts where bioavailability limits conventional-extract effect sizes; repeat clinical evaluation of previously studied compounds in enhanced formulations would plausibly clarify the true clinical potential of several Ayurvedic extracts. Second, drug-drug interaction checking should be integrated into European integrative-medicine practice for Ayurvedic extract deployment, with particular attention to piperine-containing preparations in patients on CYP3A4-metabolised medications. Third, population pharmacokinetic and PK/PD modelling work for major Ayurvedic compounds in European-ancestry cohorts should be a near-term empirical priority, because cross-ancestry PK generalisation remains incompletely characterised and matters for clinical dosing decisions. The AEPI rubric and the full review 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 has financial or consulting relationships with pharmaceutical companies, Ayurvedic extract manufacturers, formulation technology companies, or bioanalytical service providers relevant to this review.

Data Availability Statement

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

Ethical Approval

As this is a structured review of previously published pharmacokinetic studies with no primary human-subjects or animal 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/AEPI2) prior to the start of screening.

Appendix A

AEPI Scoring Rubric and Study Frame Classification

Full scoring rubric for the Ayurvedic Extract Pharmacokinetic Index (AEPI) together with the study frame classification protocol used in this structured review. All five AEPI dimensions are normalised to the 0-1 range before the weighted sum is computed. PK characterisation quality and clinical translatability are jointly the most heavily weighted dimensions (0.25 each) because they represent the core measurables that determine whether PK work supports clinical decision-making.

Part 1 - AEPI Dimension Scoring Anchors

Family Per-dimension scoring definitions

Dimension	Weight	0.00 anchor	0.50 anchor	1.00 anchor
<i>PK characterisation quality</i>	0.25	Cmax only	Cmax + AUC + t _{1/2}	Full ADME profile
<i>Analytical method rigour</i>	0.20	HPLC-UV unvalidated	HPLC-DAD validated	LC-MS/MS ICH validated
<i>Clinical translatability</i>	0.25	Preclinical-only relev.	Partial clinical application	Direct clinical dosing support
<i>Reproducibility</i>	0.15	Single study only	Partial independent replicn.	Multi-group indep. replication
<i>Interaction / safety relevance</i>	0.15	No interaction data	Partial CYP data	Full DDI + safety character.

Part 2 - Study Frame Classification Protocol

Family Frame assignment criteria

Frame	Primary focus	Typical methodology	Key distinguishing feature
<i>K1: Conventional Extract</i>	Native extract PK	Oral dose + plasma PK	Unmodified delivery form
<i>K2: Bioenhancer-Paired</i>	Bioenhancer effect	Paired vs unpaired PK	Bioenhancer comparison focus
<i>K3: Novel Formulation</i>	Formulation technology PK	Formulation vs conventional	Modified-delivery comparison
<i>K4: Drug-Drug Interaction</i>	CYP / transport interaction	Interaction PK design	Interaction-specific measurement
<i>K5: Population PK / PK-PD</i>	Variability or PK-PD model	PopPK or PK/PD analysis	Quantitative variability focus
<i>Assignment rule</i>	Dominant study focus	Per study design	Cross-reference secondary frame