

Bridging Two Paradigms: A Reverse-Pharmacology Framework for CTRI/ICMR-Compliant Ayurvedic Clinical Trial Design

Shirin Dastagir Kazi^{*1}, Manaswi Rajurkar², Chirag Warty³,

¹Associate Research Scientist, Ved Sanjeevani Private Limited, Nagpur, Maharashtra, India

²Resident Medical Officer, Ved Sanjeevani Private Limited, Nagpur, India

³Director Research and Development, Ved Sanjeevani Private Limited, Nagpur, India

*Corresponding Author: C: +91 787 511 6345; E: shirin.kazi@vedsanjeevani.com

Abstract

Objective: To propose a framework that maps the three stages of reverse pharmacology (RP) onto the ethical and regulatory requirements for Ayurvedic clinical trials in India [1-6].

Methods: We conducted a narrative synthesis of published literature on RP and of the principal Indian instruments: the Clinical Trials Registry – India (CTRI), the ICMR National Ethical Guidelines (2017), the New Drugs and Clinical Trials Rules, 2019 (NDCT 2019), and Good Clinical Practice guidelines for Ayurveda, Siddha and Unani drugs [1-3,7]. CTRI data were not independently retrieved or analysed; all registry figures were taken from previously published analyses of CTRI records [8,9].

Results: A published analysis reported that Ayurveda accounted for 56.6% (2,054/3,632) of AYUSH trials registered with CTRI between 2009 and 2020 [8]. A separate published audit of 140 CTRI-registered Ayurveda protocols for COVID-19 (2020–2021) found that 90 were described as randomised and 29 as blinded, and that sample-size calculations were rarely reported [9]. Drawing on this evidence, we propose a five-checkpoint framework that links

each RP stage (documentation, exploratory studies, and pilot and confirmatory clinical research) to a specific ethical or regulatory deliverable, and we illustrate it with an anonymised, in-progress institutional pilot-protocol series.

Conclusion: RP stages can be mapped onto CTRI, ICMR and NDCT 2019 requirements. The proposed framework has not been empirically validated; it is offered as a planning template for sponsors and Ethics Committees, and its usefulness should be evaluated prospectively.

Keywords: reverse pharmacology; Ayurveda; Clinical Trials Registry - India; CTRI; ICMR ethical guidelines; Good Clinical Practice; regulatory science; Nabhi-route drug delivery

1. Introduction

This paper (i) reviews the conceptual basis and documented critiques of reverse pharmacology; (ii) summarises the current Indian regulatory landscape for Ayurvedic and phytopharmaceutical drug development; (iii) summarises published, registry-derived evidence on how Ayurvedic trials are actually being registered and conducted; and (iv) proposes an integrated RP-regulatory bridge

framework, illustrated with reference to an in-progress institutional pilot-protocol series for periumbilical (Nabhi-route) herbal oil formulations.

Material and Methods:

We conducted a narrative synthesis of published literature on RP and of the principal Indian instruments: the Clinical Trials Registry – India (CTRI), the ICMR National Ethical Guidelines (2017), the New Drugs and Clinical Trials Rules, 2019 (NDCT 2019), and Good Clinical Practice guidelines for Ayurveda, Siddha and Unani drugs [1-3,7]. CTRI data were not independently retrieved or analysed; all registry figures were taken from previously published analyses of CTRI records [8,9].

Review of Literature:

Conventional drug discovery moves from target identification to preclinical and clinical testing; it costs more than US\$2 billion per new molecular entity, and only about 10–14% of candidates entering Phase I are approved [10-14]. Reverse pharmacology (RP), formalised by Patwardhan and Vaidya, inverts this sequence: it starts from documented clinical experience, which Ayurveda has accumulated over centuries [15,16], and proceeds through documentation, exploratory studies and confirmatory clinical research [4-6,17,18]. Because the starting material has a record of human use, proponents argue that RP can shorten timelines and reduce toxicity risk [4,10,19].

Yet the RP literature has focused on scientific methodology, and calls to “build bridges” between Ayurveda and biomedical science have mainly addressed epistemology and study design [22-24]. How RP’s stages correspond to the checkpoints that an Ayurvedic sponsor in India must clear has received little systematic attention: prospective CTRI registration [7], Ethics Committee review under the ICMR 2017 guidelines [1], and, where applicable, the New Drugs and Clinical Trials Rules, 2019 [2] and the Good Clinical Practice guidelines for Ayurveda, Siddha and Unani (ASU) drugs following Rule 158-B [3,20,21]. The gap has

practical consequences: Ayurveda accounts for most AYUSH trials registered with CTRI [8], yet a published audit of Ayurveda COVID-19 protocols registered in 2020–2021 found incomplete reporting of randomisation, blinding and sample-size calculation [9].

Mapping each RP stage to its regulatory deliverable could help sponsors plan the evidence each checkpoint requires before a trial begins, give Ethics Committees a consistent basis for reviewing Ayurvedic protocols, and support an early decision between the classical ASU and phytopharmaceutical pathways [21]. The intended contribution is not new rules but a single planning sequence linking scientific development with regulatory compliance, which may be most useful to academic institutions and smaller sponsors without dedicated regulatory-affairs teams.

2. Reverse Pharmacology: Conceptual Framework

Reverse pharmacology reduces three classical bottlenecks of drug discovery - time, cost, and toxicity - by beginning with a lead whose safety profile is already partly established through generations of documented use [4,6,18]. The approach has been described as “bedside to bench to bedside”, in explicit contrast to the forward “bench to bedside” model [17,19], and has been positioned by its proponents as one of the principal contributions Ayurveda can make to global drug discovery [10,25,26].

The process is conventionally described in three overlapping stages [4,19]:

Stage 1 - Documentation: systematic compilation of classical textual references, institutional case records, and ethnopharmacological survey data describing how a formulation has historically been used, in what dose, by what route, and for what indication [5,27,28].

Stage 2 - Exploratory studies: basic and mechanistic research - in vitro assays, animal pharmacology, standardisation and quality-control studies - conducted to translate the documented clinical experience into a testable pharmacological hypothesis [6,11,29].

Stage 3 - Clinical research: safety and efficacy are evaluated in a structured pilot-to-confirmatory clinical trial sequence, with pharmaceutical development and pharmacodynamic study permitted to proceed in parallel with controlled clinical studies rather than strictly beforehand [4,18].

Because the safety of the traditionally used material is already partially established, the RP model allows pharmaceutical development, safety validation and pharmacodynamic study

to run in parallel with controlled clinical studies, rather than in the strict serial sequence required for a wholly novel chemical entity [4,6] (Figure 1). This "safety prior" is not unconditional: pharmacovigilance data on Ayurvedic products document adverse events, drug-herb interactions and heavy-metal contamination of marketed preparations [30-32], so Stage 2 standardisation and safety pharmacology remain obligatory rather than optional.

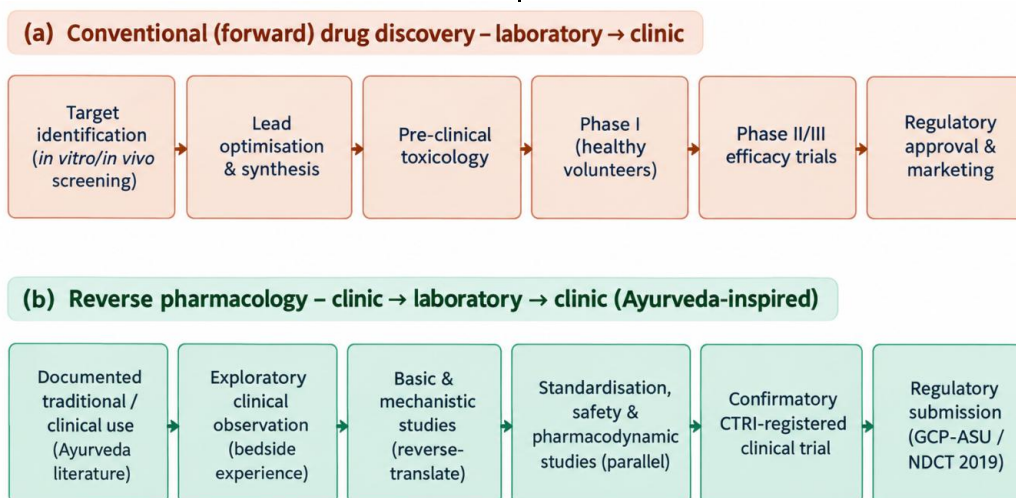


Figure 1. Conventional versus reverse-pharmacology drug-development pathways. (a) Forward discovery proceeds from laboratory target identification to clinical testing. (b) Reverse pharmacology proceeds from documented clinical use to mechanistic study and back to a confirmatory clinical trial; panel (b) is a conceptual redrawing of the sequence described by Patwardhan and Vaidya (reference 4) and is an original schematic, not a reproduction of any published figure. PD, pharmacodynamic.

The approach is not without its critics. Lele has argued that RP, on its own, risks remaining an observational exercise unless it is coupled to genuine mechanism-based screening - receptor-binding assays, target validation, and molecular pharmacology - rather than treating traditional use as self-validating [29]. Related critiques note that the polyherbal, multi-target character of most classical formulations complicates both

mechanistic attribution and marker-based standardisation [27,33]. This critique is directly relevant to the regulatory bridge proposed in Section 9: a documentation stage that is not followed by rigorous exploratory pharmacology will not satisfy the scientific-justification requirements of an Institutional Ethics Committee or CDSCO reviewer, regardless of how well the traditional-use record is compiled [1,2].

RP is not unique to India. A comparable reverse-pharmacology approach guided the development of an artemisinin-based antimalarial phytomedicine in Mali over roughly six years of combined ethnobotanical, mechanistic and clinical work, demonstrating that the model can meet international efficacy and safety expectations when rigorously executed [34]. The World Health Organization's traditional-medicine strategy similarly calls for research approaches that respect the accumulated clinical experience of

traditional systems while applying contemporary standards of evidence [35].

3. The Regulatory Landscape for Ayurvedic Drug Development in India

Ayurvedic and other ASU formulations occupy an intermediate regulatory position: they are neither wholly exempt from clinical evidentiary requirements nor subject to the identical

pathway used for new chemical entities [3,20,36]. Table 1 summarises the principal regulatory and ethical milestones relevant to designing a CTRI-registrable Ayurvedic trial in India [1,2,7,20,37].

Table 1. Key regulatory and ethical milestones for Ayurvedic/ASU clinical research in India.

Year	Instrument / milestone	Regulatory significance
2007	Clinical Trials Registry - India (CTRI) launched by ICMR-NIMS	Establishes voluntary, later mandatory, prospective public registration of all interventional trials, including AYUSH.
2009	CTRI registration made mandatory by CDSCO / DCGI	All new clinical trials in India, including Ayurveda, Siddha, Unani and Homoeopathy (ASU-H) trials, require prospective CTRI registration before enrolment of the first participant.
2010	Rule 158-B, Drugs and Cosmetics Rules (AYUSH)	Introduces a requirement for proof of effectiveness for licensing of patent/proprietary ASU medicines, followed by GCP guidelines for ASU clinical trials (2013).
2015	CDSCO Gazette Notification on phytopharmaceuticals (G.S.R. 918(E))	Creates a distinct 'phytopharmaceutical drug' category under Schedule Y, Appendix I-B, with defined quality, safety and efficacy data requirements.
2017	ICMR National Ethical Guidelines for Biomedical and Health Research (3rd revision)	Sets Ethics Committee review, informed-consent, data-integrity and confidentiality standards applicable to all human-participant research, including Ayurveda trials.
2019	New Drugs and Clinical Trials Rules (NDCT 2019), G.S.R. 227(E)	Replaces Part XA and Schedule Y for new/investigational drugs; introduces time-bound (90-working-day) review, revised Ethics Committee registration, and compensation provisions.

ASU, Ayurveda, Siddha and Unani; CDSCO, Central Drugs Standard Control Organisation; DCGI, Drugs Controller General of India; ICMR-NIMS, ICMR National Institute of Medical Statistics.

A distinct but overlapping pathway applies to standardised, multi-compound herbal extracts that seek approval as 'phytopharmaceutical drugs' under CDSCO rather than as classical ASU medicines - a route requiring a minimum of four qualitatively and quantitatively characterised bioactive markers and full new-drug-style safety and confirmatory efficacy data

[21,37]. The CTRI itself, launched in 2007 and made mandatory for all interventional trials from June 2009, provides the public, prospective registration layer that applies equally to both pathways [7]; registry data have subsequently been shown to report trial methods more completely than the corresponding Indian journal publications [38]. For an Ayurvedic sponsor, the practical implication is that a single formulation's regulatory strategy must be decided early: it may proceed as a classical ASU product under AYUSH/GCP-ASU guidance [3,20], or, if

standardisation and marker-compound characterisation permit, as a phytopharmaceutical under CDSCO [21,37]. Reverse pharmacology's Stage 1-2 documentation and exploratory work is what generates the evidence needed to make this classification decision defensibly [4,11].

4. Mapping the Three RP Stages to CTRI/ICMR/NDCT Requirements

Table 2 makes explicit the mapping implied but rarely operationalised in the RP literature [4,18,19]: each scientific stage of reverse pharmacology has a corresponding regulatory or ethical deliverable that an Indian Ayurvedic

sponsor must produce [1-3]. The deliverables at Stage 3 are aligned with international protocol and reporting standards - SPIRIT 2013 for protocol content [39] and CONSORT 2010, together with its herbal-intervention extension, for trial reporting [40-42]. This mapping is the authors' own methodological synthesis, developed for institutional protocol-design use, and is offered as a proposed framework rather than an empirically validated outcome.

Table 2. Proposed mapping of reverse-pharmacology stages to CTRI/ICMR/NDCT 2019 regulatory deliverables.

RP stage	Scientific activity	Corresponding regulatory / ethical requirement	Key deliverable
1. Documentation	Classical-text review, institutional case records, prior-use survey	Justification of rationale in Ethics Committee application (ICMR 2017, informed scientific rationale)	Literature / traditional-use dossier
2. Exploratory studies	In vitro / in vivo screening, standardisation, safety pharmacology, permeation studies	Non-clinical data package supporting CT-04 application; GCP-ASU pre-clinical documentation	Standardisation and safety report; chemistry, manufacturing and controls (CMC) data
3a. Pilot clinical study	Small-sample feasibility trial; CRF / ICF development	Prospective CTRI registration before first enrolment; EC approval valid throughout trial duration	CTRI registration number; approved ICF / CRF
3b. Confirmatory RCT	Double-blind / double-dummy, placebo- or active-controlled trial with pre-defined endpoints	Full NDCT 2019 / GCP-ASU compliance; data-safety monitoring; adverse-event reporting	Locked database; CONSORT-compliant manuscript
Post-trial	Data analysis, manuscript preparation, journal submission	Public disclosure of results (WHO / ICMR joint statement); CTRI results reporting	Peer-reviewed publication; updated CTRI record

CRF, case record form; CT-04, application form for permission to conduct a clinical trial under NDCT 2019; EC, Ethics Committee; ICF, informed consent form; RCT, randomised controlled trial; RP, reverse pharmacology.

5. Institutional Illustration: Periumbilical (Nabhi-Route) Oil Formulations

To illustrate how the framework in Table 2 can be operationalised, we describe - in general,

non-proprietary terms - its application to an in-progress pilot-protocol series for periumbilical ("Nabhi-route") herbal oil formulations developed under a reverse-pharmacology model.

Stage 1 documentation draws on the traditional and institutional use record of navel-route oil application described in Ayurvedic dietetics and external-therapy (Bahya Chikitsa) literature

[15,27]. Stage 2 exploratory work is directed at mechanistic validation of the underlying Pechoti absorption hypothesis - the proposition that the periumbilical skin permits systemic or loco-regional drug absorption - using permeation modelling with Franz diffusion cell methodology [43,44] alongside standard in vitro cytotoxicity and neuropharmacological screening panels appropriate to the intended indication [11,29]. Standardisation of the oil base and marker constituents follows the quality requirements of the GCP-ASU guidelines [3], with heavy-metal and microbial testing included in view of documented contamination risks in marketed Ayurvedic products [30,31].

Stage 3 clinical research follows a pilot-to-confirmatory sequence: small, CTRI-registrable pilot protocols precede larger double-blind, double-dummy, placebo- or comparator-controlled trials, with pre-specified biomarker and patient-reported outcome endpoints appropriate to each indication (e.g., digestive, sleep/stress-relief, or joint-health applications) [39,40,42]. Every protocol in the series is prospectively registered with CTRI and reviewed by an Institutional Ethics Committee constituted under the ICMR 2017 guidelines and registered under NDCT 2019 [1,2,7].

This example is presented purely as a methodological illustration of how the RP-regulatory bridge in Table 2 can structure protocol development. It is not a report of

completed trial results, and no efficacy or safety conclusions are drawn or implied for any specific formulation; the underlying trials are, at the time of writing, in pilot or protocol-development stages and have not yet generated confirmatory clinical data.

6. Current Evidence Base: CTRI-Registered AYUSH Trials

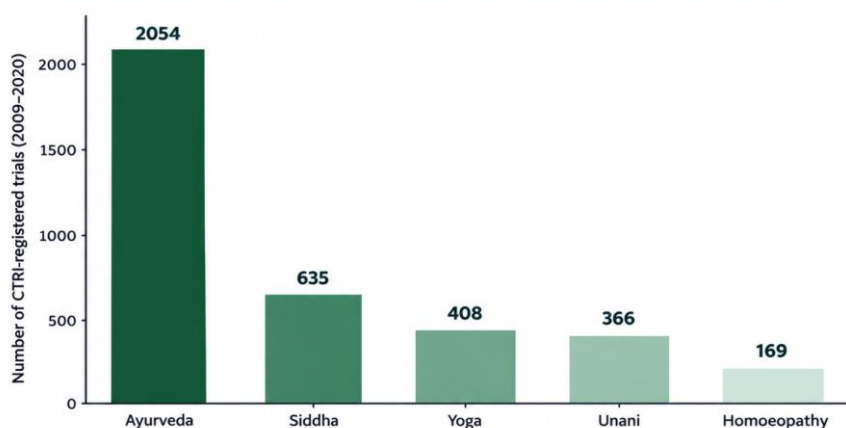
A retrospective cross-sectional analysis of the CTRI database identified 3,632 AYUSH-stream trial registrations between 2009 and 2020, of which Ayurveda accounted for the largest share (Table 3, Figure 2) [8]. Interventional study designs dominated over observational designs across all streams [8]. This registry footprint reflects both the mandatory-registration requirement introduced in 2009 [7] and the expansion of publicly funded AYUSH research infrastructure over the same period [23,36].

Table 3. AYUSH clinical trials registered with CTRI, 2009-2020, by stream.

AYUSH stream	Registered trials (2009-2020)	% of total AYUSH trials
Ayurveda	2,054	56.6
Siddha	635	17.5
Yoga	408	11.2
Unani	366	10.1
Homoeopathy	169	4.7
Total	3,632	100

Data from Shree Devi et al., 2021 (reference 8).

Figure 2. Distribution of AYUSH Clinical Trials Registered with CTRI, 2009-2020 (N = 3632)



Source: data reported in Shree Devi et al., J Ayurveda Integr Med 2021;12(2):346-350.

Figure 2. Distribution of AYUSH clinical trials registered with the Clinical Trials Registry - India (CTRI), 2009-2020 (N = 3,632). Bars show the number of registered trials per stream with the percentage of the total in parentheses. Drawn from data reported by Shree Devi et al., 2021 (reference 8).

The scale of Ayurveda's registry footprint indicates substantial trial volume, but volume alone is not evidence of methodological rigour [24,28]. Section 7 reviews audits that examined the quality of these registrations.

7. Methodological Gaps Identified in CTRI-Registered Ayurvedic Trials

A methodological audit of 140 CTRI-registered Ayurveda interventional protocols for COVID-19 (2020-2021) found that while most trials were described as randomised, fewer than a quarter reported any blinding procedure, and sample-size calculations were rarely documented (Table 4) [9]. These shortfalls correspond to core items of the CONSORT statement and its herbal-medicine extensions, which require explicit description of sequence generation, allocation concealment, blinding and sample-size determination [40-42,45].

Table 4. Methodological gaps identified in audited CTRI-registered Ayurvedic clinical trials.

Audited parameter	Finding	Source
Trial protocols analysed (Ayurveda, COVID-19, 2020-2021)	140 CTRI-registered interventional protocols	Chaudhari et al., 2023
Randomisation reported	90 of 140 trials described as randomised; method of randomisation frequently unspecified	Chaudhari et al., 2023
Blinding reported	Only 29 of 140 trials described as blinded	Chaudhari et al., 2023
Sample-size justification	Hospital-based studies: 30-500 participants; community-based studies: 500-80,000; sample-size calculation rarely reported	Chaudhari et al., 2023
Registration timing / EC documentation	Persistent concerns nationally over inconsistent Ethics Committee constitution and functioning	Pandey et al., 2011

EC, Ethics Committee. These findings echo a longer-standing concern raised in correspondence to the Indian Journal of Medical Research, which noted that fewer than 40 Ethics Committees in India were, at the time, properly constituted and functioning, and recommended strengthening EC oversight as part of the CTRI registration workflow [46]. Comparative analyses have also shown that, although CTRI records report methods more completely than the resulting journal articles, important design elements remain under-reported in both [38].

For a reverse-pharmacology-based development programme, this evidence underscores that Stage 3 confirmatory trials

cannot rely on the credibility conferred by Stage 1 traditional-use documentation alone [24,29]: randomisation, blinding, and pre-specified sample-size calculation must be built into the protocol from the pilot stage [39,40], and reported transparently at CTRI registration [7,38].

8. Ethical and Regulatory Compliance Checklist

Table 5 consolidates the ethical and regulatory domains that a reverse-pharmacology-based Ayurvedic protocol must satisfy, drawn from the ICMR 2017 guidelines [1], NDCT 2019 [2], GCP-ASU and phytopharmaceutical provisions [3,21,37], and the international ethical and GCP

standards on which these instruments draw [47,48].

Table 5. Consolidated ethical and regulatory compliance checklist for Ayurvedic clinical trials in India.

Domain	Requirement	Applicable instrument
Prospective registration	Register with CTRI before enrolment of the first participant	CTRI / ICMR
Ethics Committee review	Independent EC review and approval, valid for the trial's full duration	ICMR 2017; NDCT 2019, Rules 7-8
Informed consent	Voluntary, comprehensible, documented consent; provision for broad consent where applicable	ICMR 2017
Data integrity and confidentiality	Accurate, complete and authentic trial data; protection of participant confidentiality	ICMR 2017; NDCT 2019
Adverse-event and compensation provision	Defined process for injury/death compensation and reporting	NDCT 2019
Non-clinical / standardisation data	Quality, safety and (where applicable) marker-compound characterisation	GCP-ASU guidelines; phytopharmaceutical notification, 2015
Results disclosure	Public disclosure of trial results in line with the WHO / ICMR joint statement	CTRI; ICMR 2017

CTRI, Clinical Trials Registry - India; EC, Ethics Committee; GCP-ASU, Good Clinical Practice guidelines for Ayurveda, Siddha and Unani drugs; NDCT, New Drugs and Clinical Trials Rules.

9. Proposed Integrated Reverse-Pharmacology-Regulatory Bridge Framework

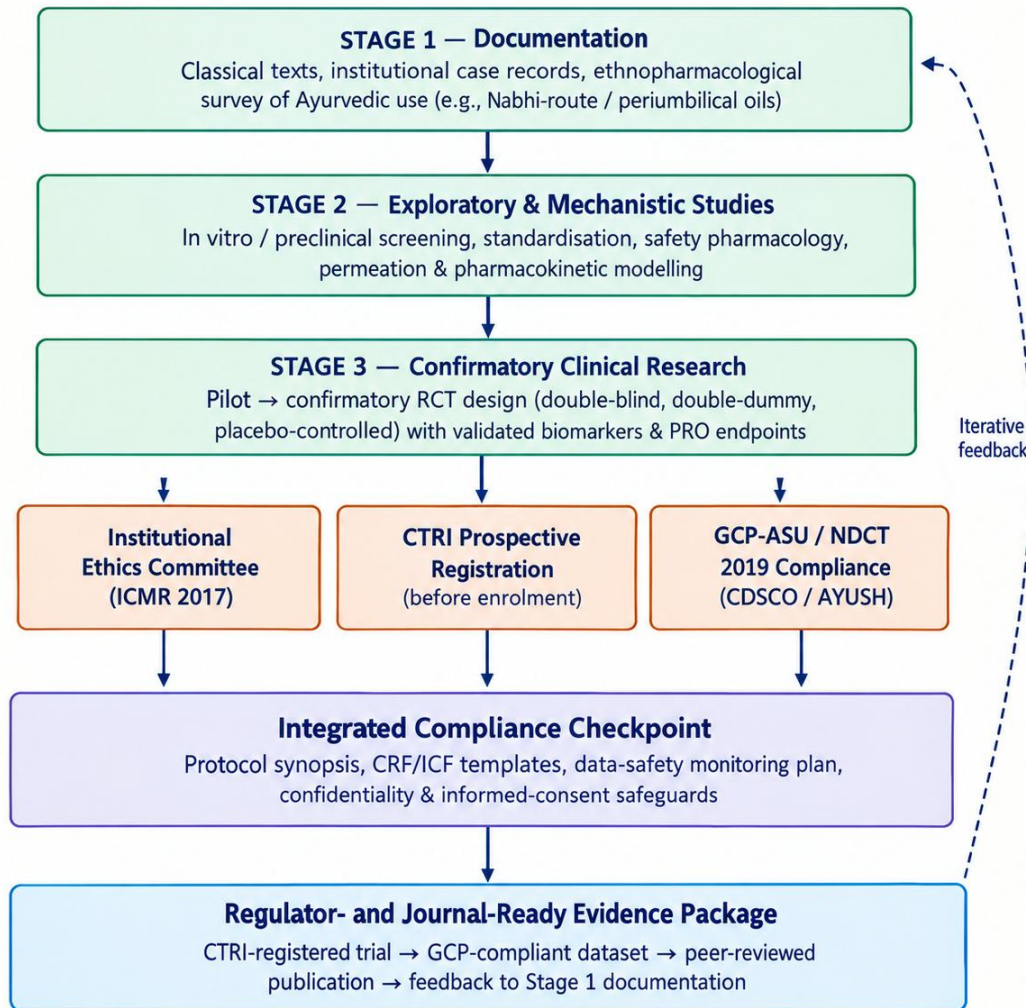
Synthesising Sections 4, 7 and 8, we propose the five-checkpoint framework shown in Figure 3, in which each of the three RP stages [4,19] feeds into a specific regulatory gate (Ethics Committee review [1], CTRI registration [7], GCP-ASU/NDCT compliance [2,3]) before converging on an integrated compliance checkpoint and, ultimately, a regulator- and journal-ready evidence package [40,42].

Figure 3. Proposed reverse-pharmacology-regulatory bridge framework for aligning Ayurvedic clinical trial design with CTRI/ICMR requirements. Each of the three reverse-pharmacology stages feeds a specific

regulatory gate (Ethics Committee review, CTRI registration, GCP-ASU / NDCT 2019 compliance) before converging on an integrated compliance checkpoint and a regulator- and journal-ready evidence package; the dashed line indicates the iterative feedback of trial results to Stage 1 documentation. Original schematic developed by the authors. CRF, case record form; ICF, informed consent form; PRO, patient-reported outcome; RCT, randomised controlled trial.

The feedback loop from the evidence package back to Stage 1 documentation reflects the iterative nature recommended in the RP literature: findings from a confirmatory trial (including negative or inconclusive results) should update the documented evidence base used to justify subsequent protocols for the same or related formulations, rather than being treated as a terminal output [4,18,24]. Public disclosure of results through the CTRI record and peer-reviewed publication is the mechanism by which this loop is closed [1,7].

Figure 3. Proposed Reverse-Pharmacology-Regulatory Bridge Framework for CTRI/ICMR-Compliant Ayurvedic Clinical Trial Design



10. Limitations and Critiques of the Reverse Pharmacology Approach

Reverse pharmacology is not a substitute for mechanism-based pharmacology; documented traditional use establishes plausibility and a safety prior, not proof of efficacy [24,29]. Lele's critique - that RP must be coupled to genuine target- and mechanism-based screening - remains the central methodological caution for any programme relying on this model [29]. The safety prior itself is bounded by well-documented quality and pharmacovigilance concerns for marketed Ayurvedic products [30-32].

Registry-level evidence also indicates that Ayurveda's high trial volume on CTRI has not been matched by uniformly rigorous reporting

of randomisation, blinding, or sample-size justification [9,38], which limits the strength of conclusions that can currently be drawn from the aggregate Ayurvedic trial literature [24,28]. Finally, RP-derived formulations that involve multi-compound herbal extracts face a further classification decision - whether to proceed as classical ASU products or to pursue the more data-intensive phytopharmaceutical pathway [21,37] - and this decision has downstream implications for the scale of confirmatory clinical evidence required [2,33]. The framework proposed here is a synthesis rather than an empirically tested instrument; its utility should be evaluated prospectively, for example by comparing CTRI-record completeness and

Ethics Committee query rates for protocols developed with and without it.

11. Conclusion

Reverse pharmacology offers a scientifically coherent and historically grounded pathway for developing Ayurvedic formulations [4,18,26], and its three-stage structure maps naturally, if not automatically, onto the ethical and regulatory checkpoints required under Indian law - prospective CTRI registration [7], ICMR 2017 ethical review [1], and, where relevant, NDCT 2019 or GCP-ASU compliance [2,3].

The framework proposed here is intended as a practical planning tool for research teams and Ethics Committees: it does not replace mechanism-based pharmacological validation [29], nor does it substitute for methodologically rigorous randomisation, blinding, and sample-size planning at the confirmatory-trial stage [39,40]. Used alongside these safeguards, an explicit RP-regulatory bridge can help Ayurvedic drug development produce evidence that is simultaneously culturally continuous, scientifically defensible, and regulator- and journal-ready [22,24,35].

Declarations

Funding: No external funding was received for this work.

Conflict of interest: The author is employed by Ved Sanjeevani Private Limited, which develops the periumbilical oil formulations referred to in Section 5. No efficacy or safety claims are made for any product in this article.

Ethical approval: Not applicable; this article is a narrative synthesis of published literature and public registry data and involved no human participants.

Data availability: All data analysed are available in the cited publications and the public CTRI database (www.ctri.nic.in).

References

1. Indian Council of Medical Research. National Ethical Guidelines for Biomedical and Health Research Involving Human Participants. New Delhi: ICMR; 2017.

2. Government of India, Ministry of Health and Family Welfare. New Drugs and Clinical Trials Rules, 2019 (G.S.R. 227(E), dated 19 March 2019). New Delhi: Central Drugs Standard Control Organisation; 2019.
3. Department of AYUSH, Ministry of Health and Family Welfare, Government of India. Good Clinical Practice Guidelines for Clinical Trials in Ayurveda, Siddha and Unani Medicine. New Delhi; 2013.
4. Patwardhan B, Vaidya ADB. Natural products drug discovery: accelerating the clinical candidate development using reverse pharmacology approaches. *Indian J Exp Biol*. 2010;48(3):220-227.
5. Patwardhan B, Vaidya ADB, Chorghade M. Ayurveda and natural products drug discovery. *Curr Sci*. 2004;86(6):789-799.
6. Patwardhan B, Vaidya ADB, Chorghade M, Joshi PS. Reverse pharmacology and systems approaches for drug discovery and development. *Curr Bioact Compd*. 2008;4(4):201-212. doi:10.2174/157340708786847870
7. Pandey A, Aggarwal AR, Seth SD, Maulik M, Bano R, Juneja A. Clinical Trials Registry - India: redefining the conduct of clinical trials. *Indian J Cancer*. 2008;45(3):79-82. doi:10.4103/0019-509X.44060
8. Shree Devi MS, Sathiyarajeswaran P, Kanakavalli K, Vinod NP, Baskar V. Analysis of AYUSH studies registered in Clinical Trials Registry of India from 2009 to 2020. *J Ayurveda Integr Med*. 2021;12(2):346-350. doi:10.1016/j.jaim.2021.02.010
9. Chaudhari SS, et al. A methodological analysis of CTRI registered clinical trials on Ayurveda interventions for COVID-19 management. *J Ayurveda Integr Med*. 2023;14(1):100631. doi:10.1016/j.jaim.2022.100631
10. Patwardhan B, Mashelkar RA. Traditional medicine-inspired approaches to drug discovery: can Ayurveda show the way forward? *Drug Discov Today*. 2009;14(15-16):804-811. doi:10.1016/j.drudis.2009.05.009
11. Katiyar C, Gupta A, Kanjilal S, Katiyar S. Drug discovery from plant sources: an integrated approach. *Ayu*. 2012;33(1):10-19. doi:10.4103/0974-8520.100295
12. DiMasi JA, Grabowski HG, Hansen RW. Innovation in the pharmaceutical industry: new estimates of R&D costs. *J Health Econ*.

- 2016;47:20-33.
doi:10.1016/j.jhealeco.2016.01.012
13. Hay M, Thomas DW, Craighead JL, Economides C, Rosenthal J. Clinical development success rates for investigational drugs. *Nat Biotechnol.* 2014;32(1):40-51. doi:10.1038/nbt.2786
 14. Wong CH, Siah KW, Lo AW. Estimation of clinical trial success rates and related parameters. *Biostatistics.* 2019;20(2):273-286. doi:10.1093/biostatistics/kxx069
 15. Jaiswal YS, Williams LL. A glimpse of Ayurveda - the forgotten history and principles of Indian traditional medicine. *J Tradit Complement Med.* 2017;7(1):50-53. doi:10.1016/j.jtcme.2016.02.002
 16. Patwardhan B, Warude D, Pushpangadan P, Bhatt N. Ayurveda and traditional Chinese medicine: a comparative overview. *Evid Based Complement Alternat Med.* 2005;2(4):465-473. doi:10.1093/ecam/neh140
 17. Vaidya ADB. Reverse pharmacological correlates of Ayurvedic drug actions. *Indian J Pharmacol.* 2006;38(5):311-315. doi:10.4103/0253-7613.27697
 18. Vaidya ADB. Reverse pharmacology - a paradigm shift for drug discovery and development. *Curr Res Drug Discov.* 2014;1(2):39-44. doi:10.3844/crddsp.2014.39.44
 19. Raut AA, Chorghade MS, Vaidya ADB. Reverse pharmacology. In: Patwardhan B, Chaguturu R, editors. *Innovative Approaches in Drug Discovery.* Cambridge, MA: Academic Press; 2017. p. 89-126. doi:10.1016/B978-0-12-801814-9.00004-0
 20. Government of India, Ministry of Health and Family Welfare. *Drugs and Cosmetics Rules, 1945: Rule 158-B (requirements for licensing of Ayurvedic, Siddha and Unani patent or proprietary medicines), inserted by the Drugs and Cosmetics (Amendment) Rules, 2010.* New Delhi; 2010.
 21. Bhatt A. Phytopharmaceuticals: a new drug class regulated in India. *Perspect Clin Res.* 2016;7(2):59-61. doi:10.4103/2229-3485.179435
 22. Rastogi S. Building bridges between Ayurveda and modern science. *Int J Ayurveda Res.* 2010;1(1):41-46. doi:10.4103/0974-7788.59943
 23. Sen S, Chakraborty R. Revival, modernization and integration of Indian traditional herbal medicine in clinical practice: importance, challenges and future. *J Tradit Complement Med.* 2017;7(2):234-244. doi:10.1016/j.jtcme.2016.05.006
 24. Patwardhan B. The quest for evidence-based Ayurveda: lessons learned. *Curr Sci.* 2012;102(10):1406-1417.
 25. Padma TV. Ayurveda. *Nature.* 2005;436(7050):486. doi:10.1038/436486a
 26. Patwardhan B. Where lies the future of Ayurveda-inspired drug discovery? *Expert Opin Drug Discov.* 2023;18(9):947-949. doi:10.1080/17460441.2023.2232811
 27. Mukherjee PK, Harwansh RK, Bahadur S, Banerjee S, Kar A, Chanda J, et al. Development of Ayurveda - tradition to trend. *J Ethnopharmacol.* 2017;197:10-24. doi:10.1016/j.jep.2016.09.024
 28. Narahari SR, Aggithaya MG, Suraj KR. A protocol for systematic reviews of Ayurveda treatments. *Int J Ayurveda Res.* 2010;1(4):254-267. doi:10.4103/0974-7788.76791
 29. Lele RD. Beyond reverse pharmacology: mechanism-based screening of Ayurvedic drugs. *J Ayurveda Integr Med.* 2010;1(4):257-265. doi:10.4103/0975-9476.74435
 30. Gogtay NJ, Bhatt HA, Dalvi SS, Kshirsagar NA. The use and safety of non-allopathic Indian medicines. *Drug Saf.* 2002;25(14):1005-1019. doi:10.2165/00002018-200225140-00003
 31. Saper RB, Phillips RS, Sehgal A, Khouri N, Davis RB, Paquin J, et al. Lead, mercury, and arsenic in US- and Indian-manufactured Ayurvedic medicines sold via the Internet. *JAMA.* 2008;300(8):915-923. doi:10.1001/jama.300.8.915
 32. Thatte U, Bhalerao S. Pharmacovigilance of ayurvedic medicines in India. *Indian J Pharmacol.* 2008;40(Suppl 1):S10-S12.
 33. Parasuraman S, Thing GS, Dhanaraj SA. Polyherbal formulation: concept of Ayurveda. *Pharmacogn Rev.* 2014;8(16):73-80. doi:10.4103/0973-7847.134229
 34. Willcox ML, Graz B, Falquet J, Diakite C, Giani S, Diallo D. A "reverse pharmacology" approach for developing an anti-malarial phytomedicine. *Malar J.* 2011;10(Suppl 1):S8. doi:10.1186/1475-2875-10-S1-S8
 35. World Health Organization. *WHO Traditional Medicine Strategy 2014-2023.* Geneva: WHO; 2013.
 36. Chandra S. Status of Indian medicine and folk healing: with a focus on integration of AYUSH medical systems in healthcare delivery. *Ayu.*

- 2012;33(4):461-465. doi:10.4103/0974-8520.110504
37. Government of India, Ministry of Health and Family Welfare. Gazette Notification G.S.R. 918(E): Drugs and Cosmetics (Eighth Amendment) Rules, 2015 - phytopharmaceutical drugs (Schedule Y, Appendix I-B). New Delhi; 30 November 2015.
 38. Tharyan P, George AT, Kirubakaran R, Barnabas JP. Reporting of methods was better in the Clinical Trials Registry-India than in Indian journal publications. *J Clin Epidemiol*. 2013;66(1):10-22. doi:10.1016/j.jclinepi.2011.11.011
 39. Chan AW, Tetzlaff JM, Altman DG, Laupacis A, Gotzsche PC, Krleza-Jeric K, et al. SPIRIT 2013 statement: defining standard protocol items for clinical trials. *Ann Intern Med*. 2013;158(3):200-207. doi:10.7326/0003-4819-158-3-201302050-00583
 40. Schulz KF, Altman DG, Moher D; CONSORT Group. CONSORT 2010 statement: updated guidelines for reporting parallel group randomised trials. *BMJ*. 2010;340:c332. doi:10.1136/bmj.c332
 41. Moher D, Hopewell S, Schulz KF, Montori V, Gotzsche PC, Devereaux PJ, et al. CONSORT 2010 explanation and elaboration: updated guidelines for reporting parallel group randomised trials. *BMJ*. 2010;340:c869. doi:10.1136/bmj.c869
 42. Gagnier JJ, Boon H, Rochon P, Moher D, Barnes J, Bombardier C; CONSORT Group. Reporting randomized, controlled trials of herbal interventions: an elaborated CONSORT statement. *Ann Intern Med*. 2006;144(5):364-367. doi:10.7326/0003-4819-144-5-200603070-00013
 43. Franz TJ. Percutaneous absorption on the relevance of in vitro data. *J Invest Dermatol*. 1975;64(3):190-195. doi:10.1111/1523-1747.ep12533356
 44. Ng SF, Rouse JJ, Sanderson FD, Meidan V, Eccleston GM. Validation of a static Franz diffusion cell system for in vitro permeation studies. *AAPS PharmSciTech*. 2010;11(3):1432-1441. doi:10.1208/s12249-010-9522-9
 45. Cheng CW, Wu TX, Shang HC, Li YP, Altman DG, Moher D, et al. CONSORT Extension for Chinese Herbal Medicine Formulas 2017: recommendations, explanation, and elaboration. *Ann Intern Med*. 2017;167(2):112-121. doi:10.7326/M16-2977
 46. Pandey A, Aggarwal A, Seth SD, Maulik M, Juneja A. Strengthening ethics in clinical research. *Indian J Med Res*. 2011;133(3):339-340.
 47. World Medical Association. World Medical Association Declaration of Helsinki: ethical principles for medical research involving human subjects. *JAMA*. 2013;310(20):2191-2194. doi:10.1001/jama.2013.281053
 48. International Council for Harmonisation. Integrated Addendum to ICH E6(R1): Guideline for Good Clinical Practice E6(R2). Geneva: ICH; 2016.

Conflict of Interest: *Non*

Source of funding: *Nil*

Cite this Article:

Shirin Dastagir Kazi, Manaswi Rajurkar, Chirag Warty. "Bridging Two Paradigms: A Reverse-Pharmacology Framework for CTRI/ICMR-Compliant Ayurvedic Clinical Trial Design".(2026), Ayurline: International Journal of Research In Indian Medicine:10(6),

Article Url: <https://www.ayurline.in/index.php/ayurline/article/view/1120>

Crossref DOI: <https://doi.org/10.52482/ayurline.v10i6.1120>