Observability and pharmacological calibration in psychoactive ethnobotany: Admixture selection and the discovery of Ayahuasca

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Research

Abstract

Background: Traditional pharmacopoeias, including psychoactive plant traditions, contain pharmacologically active compounds at rates far above chance. The Amazonian ayahuasca complex — a brew requiring co-administration of an *N,N*-dimethyltryptamine (DMT) source with a monoamine-oxidase inhibitor (MAO-I) — is the paradigm case: indigenous practitioners arrived at a highly specific pharmacological pairing navigating a flora of 14003 species. We apply the observability gradient framework to evaluate when traditional pharmacological knowledge tracks empirical reality.

Methods: Three tests: (i) cross-cultural comparison of ceremony versus pharmacokinetic effect duration across eleven independent traditions spanning five continents and seven pharmacological classes; (ii) a 118-plant Amazonian admixture catalogue cross-classified by purpose observability and pharmacological validity (70 years of documentation); (iii) an agent-based simulation of guided iterative search for the DMT + MAO-I combination.

Results: Ceremony duration tracks pharmacokinetic duration log-log (Pearson $r = 0.977$, $p = 2.5 \times 10^{-7}$, $n = 11$; slope 1.010). Active admixture plants cluster at the extremes of the purpose-observability distribution while candidate plants concentrate in the middle ($\chi^2(2) = 20.2$, $p = 4.2 \times 10^{-5}$), a bimodal pattern: the relationship between purpose observability and contemporary persistence is non-monotonic. Guided iterative search converges on the DMT + MAO-I target in centuries; pure random search fails within archaeologically plausible bounds.

Conclusions: Traditional psychoactive ethnobotanical knowledge tracks pharmacological reality where outcome-feedback is observable. Observability offers a principled triage criterion for ethnopharmacological follow-up; small samples and single-author admixture coding warrant replication.

Keywords: psychoactive ethnobotany; ayahuasca; Amazonian admixtures; ethnopharmacological concordance; ceremony duration; traditional pharmacopoeia; observability gradient; cross-cultural ethnobotany

Background

Cross-cultural ethnobotanical research has documented a striking pattern in traditional plant pharmacopoeias: phylogenetically distant cultures independently converge on the same medicinal plant clades, at rates far above chance under any null model of arbitrary cultural choice (Saslis-Lagoudakis *et al.* 2012). Psychoactive plant traditions show the same

convergent pattern at the species level, with cross-cultural selection on neurologically active targets demonstrable across continents (Alrashedy & Molina 2016). For ethnobotanists and ethnopharmacologists, the resulting empirical question is not whether traditional pharmacopoeias track pharmacological reality. They demonstrably do, in aggregate. The question is how, and under what conditions, the tracking arises. Which kinds of traditional pharmacological claim should be treated as empirically grounded prior evidence for ethnopharmacological follow-up, and which should not?

Amazonian psychoactive ethnobotany supplies the paradigm case. The ayahuasca brew, central to dozens of indigenous and syncretic traditions across the western Amazon, requires combining a plant containing *N,N*-dimethyltryptamine (DMT) with a plant containing a reversible monoamine-oxidase inhibitor such as harmine or harmaline; without the MAO-I, orally ingested DMT is degraded in the gut and has no psychoactive effect (Riba *et al.* 2003). The canonical pairing (*Banisteriopsis caapi* (Spruce ex Griseb.) C.V.Morton vine + *Psychotria viridis* Ruiz & Pav. leaves) is one realisation; the ethnobotanical record documents a much wider repertoire of admixture plants alongside the canonical core (Schultes 1957, Luna 1986, Ott 1994, McKenna *et al.* 1986). The two plants are not obviously similar in appearance, taxonomy, or ecology, and the combination produces its characteristic effect only under specific aqueous-decoction protocols. The Amazon basin contains an estimated 14003 taxonomically verified vascular plant species (Cardoso *et al.* 2017). Practitioners were never searching that entire flora, however. Most of it is irrelevant to a search conducted by mouth, because the plants that can realistically be tasted, chewed, or decocted by a medicinal specialist are a modest fraction of the total, and it is that fraction rather than the full species list that sets the size of the search. Assuming an ingestible fraction of 10-30% and varying it as a sensitivity parameter puts roughly 1600-4500 species in play as testable candidates (see Materials and Methods, "Computational search simulation"). How indigenous practitioners arrived at this combination, and at the broader admixture pharmacopoeia surrounding it, is a foundational ethnopharmacological puzzle (Beyer 2009, Schultes *et al.* 2001, Rodd 2002, Ruffell *et al.* 2020).

Comparable pharmacological precision appears across other psychoactive traditions worldwide. Mescaline-containing peyote ceremonies of the Native American Church and Huichol; ibogaine-bearing *Tabernanthe iboga* Baill. preparations in Bwiti initiation; psilocybin-mushroom *velada* in the Mazatec; lysergic-amide ololiuhqui (*Turbina corymbosa* (L.) Raf.) seed divination; smoked *Salvia divinorum* Epling & Játiva in the same Mazatec region; *Virola* and *Anadenanthera* tryptamine snuffs in lowland South America; kavalactone preparations of the Pacific *Piper methysticum* G.Forst.; muscimol-containing *Amanita muscaria* (L.) Lam. in Siberia (Stewart 1987, Myerhoff 1974, Fernandez 1982, Estrada 1981, Wasson *et al.* 1974, MacLean *et al.* 2013, Aporosa 2014, Singh 1992, Aporosa 2022, Seitz 1967, Wasson 1968, Schultes *et al.* 2001, Ott 2001, Torres and Repke 2006, Shulgin and Shulgin 1997). Each tradition pairs a particular plant species with a particular preparation, dose, and ceremonial timing; each was developed without modern pharmacology. The question is the same in every case: what process produces ethnobotanical knowledge that tracks pharmacological reality, given that the practitioners who developed and transmitted that knowledge had no mechanistic access to the underlying chemistry?

The observability gradient framework supplies an analytical tool for evaluating that question (Allan 2026). It parameterises the cross-generational fidelity of a transmitted knowledge item by an observability coefficient *O*, the accessibility of outcome-feedback to practitioners, and predicts a sharp nonlinear relationship between *O* and accuracy: above critical threshold O*, environmental feedback selects for accurate content; below *O**, transmission drifts on cultural attractors. The framework has been applied to a cross-domain compilation of traditional ecological knowledge and to agent-based simulation of transmission under varying observability; that work is in preparation, and its quantitative results are not relied on here. The general theoretical context is cumulative cultural evolution (Boyd and Richerson 1985, Henrich 2016, Mesoudi and Thornton 2018): iterative optimization under outcome-feedback selection across generations of specialists, with structural parallels in terra preta soil chemistry (Glaser & Birk 2012) and Aboriginal Australian fire management (Bliege Bird *et al.* 2012). Within that context, the observability gradient is the framework we apply here as an interpretive tool, not the headline contribution.

We test three quantitative predictions about psychoactive ethnobotanical knowledge:

1. *Does ceremony duration track pharmacokinetic effect duration across psychoactive plant traditions?* Mismatch between ceremony envelope and the pharmacokinetic window of the primary substance is directly observable to practitioners; if ethnobotanical traditions calibrate ceremonies against pharmacological reality, the two durations should covary. 2. *How does admixture-purpose observability relate to a plant's persistence in the contemporary active pharmacopoeia?* Under a strict observability gradient hypothesis, observable-purpose plants would dominate the active set. Under a pure cultural-attractor hypothesis, observability category would be uninformative. The actual contemporary admixture distribution should

distinguish between these. 3. *Can guided iterative search account for ayahuasca discovery within ethnographically plausible exploration bounds?* Pure random trial-and-error on the Amazonian flora is implausible by combinatorial argument; iterative search from a known psychoactive baseline (the kind of search the ethnographic record actually documents) should be tractable.

This is an ethnobotanical synthesis: the question is how indigenous practitioners came to select pharmacologically valid plants and ceremony durations within their documented exploration space, not the chemistry of the plants themselves. Adjacent work addresses neural information theory at the individual brain level (Carhart-Harris *et al.* 2014, Gallimore 2015), evolutionary psychology of psychedelic experience (Winkelman 2017), set-and-setting ethnography (Hartogsohn 2017, Dupuis 2021, Dupuis 2022), and the philosophy of psychedelics (Letheby 2021), but our focus is on cross-cultural ethnobotanical knowledge transmission. The small sample sizes and single-author admixture coding preclude strong general conclusions; we present these results as a structured case study that motivates replication.

Materials and Methods

Tradition selection and independence criteria

Candidate traditions were drawn from English-language secondary ethnographies of indigenous ceremonial psychoactive substance use available as of April 2026, restricted to traditions with (i) at least one published ceremony-duration estimate in the peer-reviewed ethnographic or clinical-pharmacology literature, and (ii) an identifiable primary psychoactive substance whose pharmacokinetic effect duration was either reported in clinical-pharmacology literature or directly extractable from the same ethnographic source. Candidate traditions failing either screen were excluded; candidate traditions meeting both screens were carried forward and filtered against the four independence criteria below. No algorithmic database search was performed: the candidate pool is the universe of cross-cultural psychoactive-ceremony ethnographies with quantifiable ceremony-duration data accessible to the author through standard ethnobotanical and ethnopharmacological reference works. Traditions excluded at the screen step were excluded for lack of a published duration estimate rather than for any substantive judgment about the tradition; the screen is the absence of measurable data, not a quality criterion.

We included eleven independent indigenous psychoactive traditions for the ceremony-pharmacokinetic analysis: (i) Amazonian mestizo and Shipibo ayahuasca; (ii) Santo Daime (Brazilian syncretic); (iii) União do Vegetal (UDV); (iv) peyote Native American Church and Huichol; (v) Bwiti iboga initiation (Gabon, Fang and Mitsogo); (vi) Mazatec *velada* (Oaxaca); (vii) Mazatec salvia *barrida* sessions; (viii) Fijian yaqona (kava); (ix) Yanomami epená (*Virola* snuff); (x) Siberian fly agaric (Koryak / Kamchadal / Khanty composite); and (xi) Mazatec ololiuhqui (*Turbina corymbosa* seed divination). Three modern clinical-pharmacology protocols were included as external calibration: clinical psilocybin (Johns Hopkins protocol), clinical ayahuasca (Brazilian treatment-resistant depression trial), and intravenous clinical DMT (UNM dose-response). Independence was established by four criteria: (a) geographic separation >3000 km between primary tradition origins; (b) distinct language families (Niger-Congo, Uto-Aztecan, Oto-Manguean, Tukanoan/Panoan/Quechuan, Aymaran, Yanomaman, Austronesian, Chukotko-Kamchatkan/Uralic); (c) no documented pre-colonial contact between primary geographic origins; and (d) distinct primary psychoactive molecules and/or distinct administration routes producing distinct pharmacokinetic profiles. The Yanomami epená tradition shares the DMT molecule with ayahuasca but the insufflation route produces a fundamentally different pharmacokinetic profile (~45-minute total duration versus ~4 hours for oral ayahuasca), and we treat it as independent on that basis. The Mazatec ololiuhqui entry shares the Mazatec cultural group with the Mazatec *velada* (psilocybin) entry; we retain it as independent on the strict criterion that plant, alkaloid class, and ritual structure are all distinct, while flagging the cultural overlap in the Discussion limitations.

Pharmacological classes are reported at the receptor-system level (n = 7): (a) DMT-family tryptamines — 5-HT2A agonists administered orally with β-carboline MAO-I (ayahuasca, Santo Daime, UDV — three traditions sharing one substance combination) and insufflated without MAO-I (Yanomami *Virola*); (b) mescaline-type phenethylamines — 5-HT2A agonists (peyote / Native American Church / Huichol); (c) psilocybin / 4-hydroxy tryptamines — 5-HT2A agonists (Mazatec *velada*); (d) ergoline lysergamides — 5-HT2A agonists (Mazatec ololiuhqui (Schultes *et al.* 2001)); (e) salvinorin κ-opioid agonists (Mazatec salvia); (f) ibogaine NMDA / σ / multi-target ligands (Bwiti); and (g) GABA-A-active compounds — kavalactones (positive allosteric modulators, Fijian yaqona (Singh 1992, Aporosa 2022)) and muscimol (direct agonist, Siberian fly agaric (Wasson 1968)). Receptor-system grouping reflects the pharmacokinetic-observability framework's focus on the mechanism producing the ceremonial duration, rather than on chemical taxonomy; the per-substance enumeration with individual molecular identities is retained in Table 1 and electronic supplementary material, table S2.

Ceremony-pharmacokinetic data extraction

For each tradition, we extracted a central estimate of ceremony duration from peer-reviewed ethnographic literature with a plausible minimum-maximum range drawn from reported variability. Ethnographic sources: Amazonian mestizo ayahuasca 5 h (3-8 h) — Beyer (2009), Luna (1986); Santo Daime *hinário* 10 h (8-12 h) — Dawson (2013); UDV 4 h (3.5-5 h) — Callaway *et al.* (1999); peyote NAC/Huichol 10 h (8-14 h) — Stewart (1987), Myerhoff (1974); Bwiti iboga 24 h (18-36 h) — Fernandez (1982); Mazatec *velada* 6 h (4-8 h) — Estrada (1981), Wasson *et al.* (1974); Mazatec salvia 0.17 h (0.08-0.25 h) — MacLean *et al.* (2013); Fijian yaqona 5.5 h (3.0-8.6 h) — Aporosa (2014) pp. 77, 81, 112 (3 h lower bound from earlier Masters work cited on pp. 77, 81; 5.6-8.6 h range and 5.889 h overall mean from Table 7.2, p. 112), Singh (1992), Aporosa (2022); Yanomami epená 1.0 h (0.5-1.5 h) — Seitz (1967) pp. 328, 330, 334 ("after about an hour, the effects of the snuff diminish", p. 334); Siberian fly agaric 10 h (4-16 h) — Wasson (1968) p. 162 ("profound sleep that... comes at the end of ten or twelve hours"), corroborated by the Georgi, Enderli, and Karjalainen accounts in the same volume (pp. 240, 262-263, 282); Mazatec ololiuhqui 3 h (2-5 h) — Schultes, Hofmann and Rätsch (2001) p. 174 ("the natives say that the intoxication lasts three hours… administered to a single individual alone in a quiet, secluded place"). Modern clinical sources: Griffiths *et al.* (2006) and Johnson *et al.* (2008) for clinical psilocybin; Palhano-Fontes *et al.* (2019) and Riba *et al.* (2003) for clinical ayahuasca; Strassman and Qualls (1994) for intravenous DMT.

Pharmacokinetic effect durations were extracted from clinical pharmacology literature where available: Strassman and Qualls (1994) for intravenous DMT; Hasler *et al.* (2004), Brown *et al.* (2017), and Holze *et al.* (2022) for oral psilocybin; Dinis-Oliveira *et al.* (2019) and Ley *et al.* (2023) for mescaline; Riba *et al.* (2003) and Callaway *et al.* (1999) for oral ayahuasca; Mash *et al.* (2000) for ibogaine; MacLean *et al.* (2013) for salvinorin A; Kanumuri *et al.* (2022), Sarris *et al.* (2011), and Teschke *et al.* (2008) for kava; Ott (2001), Torres and Repke (2006), Shulgin and Shulgin (1997) for *Virola* resin snuff, and Shen *et al.* (2010) for 5-methoxy-DMT pharmacokinetics specifically. For muscimol (fly agaric) we use the 4-8 h acute single-dose subjective duration midpoint of 6 h from the Wasson synthesis (Wasson 1968) and the secondary clinical literature; the ~10 h ethnographic ceremony envelope exceeds the single-dose window because of urine-recycling, parallel to Santo Daime's hymn-cycle extension. For lysergic acid amide (ololiuhqui) we use the 3 h subjective duration reported in the same Plants of the Gods source (Schultes *et al.* 2001) as the ceremony duration; Mazatec ololiuhqui ceremony and PK are co-extensive in the source. Full pharmacological sources are in electronic supplementary material.

For all entries except ibogaine, the extracted quantity is the single-dose acute subjective effect duration: the interval from administration until the cited source reports that subjective drug effects have returned to baseline. We did not use a plasma parameter as the endpoint. Terminal half-lives were recorded alongside the subjective windows where the clinical literature reports them (psilocin 180 min, mescaline 216 min, ibogaine 240 min, salvinorin A 75 min, intravenous DMT 9 min), but a clearance parameter is not commensurable with a ceremonial envelope: a ceremony ends when participants have returned to ordinary functioning, not when a compound has been eliminated. Applying one behavioural endpoint across classes is what makes traditions with different metabolic pathways, receptor targets, and administration routes comparable at all, and it is deliberately conservative in that it privileges no single receptor system's kinetics. Concretely, the endpoint is the reported return to baseline for the oral serotonergic preparations (psilocybin 5 h, mescaline 10 h, oral ayahuasca 4 h, lysergic acid amide 3 h), for the rapid insufflated and intravenous tryptamines (*Virola* resin snuff 0.75 h, intravenous DMT 0.5 h), for smoked salvinorin A (0.17 h), and for the GABA-A-active preparations (kavalactones 4 h, muscimol 6 h). Ibogaine is the one entry where the acute and residual windows diverge materially: the acute phase runs to approximately 8 h, while the noribogaine metabolite sustains effects across approximately 24 h (Mash *et al.* 2000). Because the Bwiti initiation spans that residual phase rather than ending with the acute phase, we use the 24 h acute-plus-residual window for that tradition, and we flag it here because it is the single case in which the choice of endpoint materially changes the value entered into the analysis.

Three tradition-specific caveats are relevant. The Mazatec salvia session is the most thinly attested entry in the dataset; unlike the other ten traditions, which have multi-century documented histories, the ethnographic record for smoked *Salvia divinorum* in Mazatec ritual practice is sparse. We include it because it extends the duration range to three orders of magnitude but report sensitivity analyses with and without the salvia data point. The Yanomami epená entry uses the informal single-dose snuffing episode (~1 h); the initiation form of the ceremony (4-5 h with repeated dosing) is a different ceremony type with different pharmacokinetics and is not used in this analysis. The Mazatec ololiuhqui entry shares the Mazatec cultural group with the Mazatec *velada* entry; we treat the two as independent on the basis of distinct plant, alkaloid class, and ritual structure (see Tradition selection and independence criteria above, and the limitations paragraph in the Discussion), and we report both with and without ololiuhqui in the leave-one-out diagnostics.

Statistical analysis — ceremony-pharmacokinetic correlation

Because durations span three orders of magnitude, we report $\log_{10}$-transformed Pearson correlation as the primary estimate, with raw Pearson, Spearman, Fisher z-transform analytical 95% CIs, and nonparametric bootstrap CIs as supporting statistics. The confirmatory test is the log-transformed Pearson correlation on the eleven indigenous traditions (n = 11). Exploratory tests include: the full n = 14 analysis with modern clinical protocols as external calibration; a sensitivity subset restricted to the oral serotonergic traditions (n = 6: ayahuasca, Santo Daime, UDV, peyote, Bwiti iboga, Mazatec *velada*) and the original n = 9 baseline before the 2026-04-11 expansion for direct comparison; leave-one-out diagnostics; Cook's distance at the 4/n threshold; 10000-iteration bootstrap CIs for r and slope; ratio analysis (one-sample t-test of log-ratio against zero); and Monte Carlo sensitivity in which each ceremony duration is varied uniformly across its plausible ethnographic range (Amazonian ayahuasca 3.0-8.0 h; Santo Daime 8.0-12.0; UDV 3.5-5.0; peyote 8.0-14.0; Bwiti iboga 18.0-36.0; *velada* 4.0-8.0; salvia 0.08-0.25; yaqona 3.0-8.6; epená 0.5-1.5; fly agaric 4.0-16.0; ololiuhqui 2.0-5.0) while pharmacokinetic durations are held fixed, for 10000 iterations.

Nonparametric bootstrap is near the edge of its reliable regime at the sample sizes available here; the 95% interval is typically well calibrated only from about n = 12 upward. Bootstrap intervals (10000 iterations) were computed for the n = 9 indigenous baseline and for the n = 12 pre-expansion set that included the three clinical protocols, and the indigenous-only interval is reported in the electronic supplementary material for transparency. No bootstrap was run on the n = 11 confirmatory sample. We therefore rely on the Fisher z-transform analytical CI as the primary interval estimate throughout, reporting it alongside each correlation in the Results.

Literature search and source selection

The 118-plant admixture catalogue was assembled by exhaustive mining of four canonical primary sources selected to span four time slices of documented Amazonian admixture practice: Schultes (1957), the founding systematic taxonomic treatment of the malpighiaceous narcotics drawn from mid-twentieth-century botanical surveys in the Colombian Amazon; Luna (1986), the canonical single-source ethnography of mestizo vegetalismo from extended fieldwork with four vegetalista lineages in the Peruvian Amazon; Ott (1994), the canonical pharmacological-review compendium of ayahuasca analogues and their ethnographically documented or pharmacologically plausible substitutes; and Allan (2026, Track 1), the contemporary-practice synthesis listing the twelve most widely documented admixture plants in present-day mestizo practice. This is a design built on targeted canonical sources rather than a database systematic review: no PubMed, Scopus, Web of Science, or Google Scholar query was performed, because canonical standing in Amazonian ethnobotany, rather than database indexing, is the relevant inclusion criterion for sources of this kind, and the temporal-contraction analysis (Figure 4) requires anchor sources the field treats as authoritative for their respective decades. Beyer (2009), *Singing to the plants*, is acknowledged as a canonical secondary ethnographic work; it was not used as a primary source because because Allan (2026) provides a contemporary-practice synthesis with a more recent observation window, and because Beyer's ethnographic plant list overlaps substantively with Luna's prior published list.

Source materials were obtained from peer-reviewed publishers and academic libraries between January and April 2026. The four primary sources were extracted into JSON via the pypdf library (extraction files: _schultes1957_extracted.json, _luna1986_extracted_text.json, _ott1994_extracted.json; the Allan 2026 contemporary list is included as a hand-curated Track 1 reference in bibliography_A.json of the public deposit). The systematic-inventory sections of each primary source were the targeted extraction scope: Schultes 1957 §SUMMARY (pp. 41-42) plus the detailed species treatments; Luna 1986 §3.7 plant-teachers, §3.4 vegetalista cosmology, and §6.4-§6.9 healing-practice descriptions; Ott 1994 Table I (pp. 25-26), Chapter 3 (pp. 53-54), and the liberal-Malpighiaceae list (p. 17). Three corroborating sources contributed single additional plants identified by citation-chase: Schultes (1960) supplied one taxon not in the 1957 inventory; Rodd (2002) supplied one toxic-candidate plant flagged in its pharmacological-systematic review; and Ruffell *et al.* (2020) supplied one additional ergoline-bearing candidate. Date range of substantively used sources: 1957-2026. Languages: English (all four primary and three corroborating sources), plus Latin botanical nomenclature for species identification. The McKenna *et al.* (1986) *América Indígena* paper, originally in Spanish, was consulted via its subsequent English-language book-chapter restatement (cited in the same McKenna *et al.* 1986 reference entry per the published-record convention); no other non-English ethnographies were used. Grey literature, conference abstracts, popular compendia, and non-peer-reviewed websites were excluded.

Admixture plant catalogue construction

The admixture plant catalogue was assembled by merging four primary source lists: (1) the contemporary active list from the Track 1 paper (Allan 2026), comprising the 12 most widely documented admixture plants in present Amazonian mestizo

practice; (2) the 41 admixture plants documented ethnographically by Luna (1986) from fieldwork with four mestizo vegetalista lineages in the Peruvian Amazon; (3) the 15 admixture plants recorded by Schultes (1957) from mid-twentieth-century botanical surveys in the Colombian Amazon; and (4) the 83 plants listed by Ott (1994) in his pharmacological review of ayahuasca analogues, including ethnographically documented admixtures plus pharmacologically relevant candidate substitutes. Additional legacy sources (Schultes 1960, Rodd 2002, Ruffell *et al.* 2020) contributed 4 plants not present in the primary four. After deduplication by canonical Latin binomial, the merged catalogue contains 118 unique plant entries.

Inclusion rule. A plant entered the catalogue if and only if at least one of the four primary source lists named it as an admixture, ingredient, source-species, or rejected source-species in the ayahuasca / caapi / yajé complex; plants mentioned only in passing without a stated admixture role were excluded. No external taxonomic gatekeeping was applied beyond what the four primary sources themselves enforced: plants from non-Amazonian floras named by Ott (1994) as pharmacologically plausible analogues (e.g., *Acacia phlebophylla* F.Muell. ex H.B.Will.) were retained because Ott identifies them as candidate substitutes, and their retention is what makes the 'analogue candidate' subcategory of the temporal classification informative.

Deduplication. Plants were merged on a canonical Latin binomial constructed by stripping parenthetical author citations and infraspecific qualifiers (var. / subsp. / ssp. / f.) and lowercasing the resulting genus-species string (the canonical() function in build_full_catalogue.py of the public deposit). Where historical and modern names differed — for example, Schultes 1957's *Banisteriopsis Rusbyana* corresponds to the current *Diplopterys cabrerana* (Cuatrec.) B.Gates under contemporary Malpighiaceae taxonomy — the modern accepted name is recorded in the compound_notes field of the catalogue JSON, but the canonical key followed the original source name and the two were not collapsed into a single entry. Where two sources coded the same plant with different pharmacological-validation values, the higher-severity value was retained (priority order: toxic > validated > not_validated > not_tested). Observability disagreements between sources were preserved as flagged fields in the catalogue JSON; the manuscript reports the first-loaded source's classification, with the disagreement recorded in the supplementary catalogue file.

Taxonomic authorities. Botanical authorities for all determined taxa in the catalogue were verified against World Flora Online at final proof stage, with Index Fungorum used for the single fungal taxon, which lies outside World Flora Online's scope. Names as used in the primary sources are retained as catalogue keys, per the source-name convention adopted throughout: where World Flora Online treats a name as a synonym the authority is applied to the name as used and the accepted name is recorded in the proof-stage resolution record rather than substituted. The 118-plant count and the source-coverage matrix therefore remain conservative against synonymy collapse, since a reconciliation that merged any two currently-separate entries would reduce, not inflate, the catalogue size. Genus-level entries (*sp.*, *spp.*) carry no authority, by botanical convention: with no species epithet there is nothing to attribute. Two historical binomials are retained as sourced: *Lippia odorata*, which could not be resolved in the nomenclatural databases reachable at the time of verification, and *Dutaillyea oreophila*, a combination with no nomenclatural record in either World Flora Online or IPNI, footnoted as such in the catalogue. The full per-plant × per-source binary matrix is provided in full_source_coverage_matrix.csv of the public deposit so that any further reconciliation can be performed downstream without re-extraction.

Plants were classified as *active* if present in the contemporary active list (n = 12) and as *candidate* otherwise (plants documented in one or more historical or analogue sources but absent from the contemporary active pharmacopeia, n = 106). The candidate category subdivides into: abandoned since Schultes 1957 (9 plants), historically persistent then later abandoned (6), Luna-era variants (29), Ott analogue candidates (60), and ambiguous (2).

Each plant was coded for (a) purpose observability, (b) pharmacological validation status, (c) toxic flag, and (d) source coverage. All observability coding in this study was performed by a single researcher against the explicit criteria defined in Allan (2026); a blinded multi-rater validation is in preparation but not yet complete, and until it is reported the admixture results below should be treated as preliminary. The observability coding rules follow the protocol in Allan (2026). *Observable* purposes refer to physical, directly perceptible effects: purging, warming, stimulation, sedation, analgesia, intensification of visual experience. *Non-observable* purposes refer to metaphysical or spiritual effects that cannot be directly verified: protection from evil spirits, soul communication, spiritual cleansing, divination without testable output. *Mixed* purposes claim both aspects. Pharmacological validation was recorded as *validated* when peer-reviewed pharmacological evidence supports the traditional claim; *not validated* when the available studies do not support the claim, or when no compound with a plausible relationship to the stated purpose has been characterized in the species; *not tested* when insufficient studies exist; and *toxic* when the plant is known to cause acute toxicity, organ damage, or dermatitis at typical ceremonial doses.

Full sources for every coding decision are in the catalogue JSON and electronic supplementary material, table S1. Two points about this scheme should be stated plainly. The *not validated* and *not tested* categories record the absence of identified pharmacological support for the stated purpose; neither demonstrates that a species is pharmacologically inert, and both are contingent on what happens to have been screened. Nor does the scheme grade the plant as a whole: a species coded *not validated* against one stated purpose may carry characterized activity of another kind entirely.

Source coverage was recorded per plant. Six plants appear in three or more independent sources (*Brugmansia suaveolens* (Willd.) Sweet, *Brunfelsia grandiflora* D.Don, *Mansoa alliacea* (Lam.) A.H.Gentry, *Couroupita guianensis* Aubl., *Hura crepitans* L., *Diplopterys cabrerana*); these are the most extensively documented admixture plants and serve as an internal consistency check. One active plant, *Hura crepitans*, is coded as observable by Luna's purgative classification but would be flagged as toxic on phytochemistry (phorbol esters); we retained Luna's coding in the active column but note the discrepancy in electronic supplementary material.

Statistical analysis — admixture

The primary admixture test is a 3 × 2 chi-square on the observability × active-vs-candidate contingency table, with observability coded as observable / mixed / non-observable. We also report two 2 × 2 variants: (i) collapsing mixed into observable (observable + mixed vs non-observable) and (ii) excluding mixed entirely (strict observable vs non-observable). For robustness, we report coding-sensitivity variants in which specific contestable coding decisions are flipped (recoding copal incense as mixed; recoding cimora *mishas herbáceas* as mixed; reclassifying vision-intensification plants as mixed; including cannabis in the Bwiti case as observable-validated; including soma under the *Ephedra* identification as observable-validated).

The bimodality finding in the active-admixture purpose-clarity distribution (7 observable, 0 mixed, 5 non-observable) was not pre-specified; it emerged from the expanded 118-plant catalogue and is reported as an exploratory observation requiring replication.

The toxic candidate analysis compares the toxic-plant count in the active pharmacopeia (1 plant: *Hura crepitans*, noting the coding discrepancy above) against the toxic-plant count in the candidate pool (9 plants: *Aristolochia*, *Malouetia tamaquarina* (Aubl.) A.DC., *Chorisia/lupuna*, *Dieffenbachia*, *Pilocarpus organensis* Occhioni & Rizzini, *Desmodium*, *Dutaillyea*, *Melicope*, *Vepris*). This is a descriptive comparison, not a formal statistical test, because the candidate pool is not a randomised sample.

Computational search simulation

We implemented a Python agent-based simulation of the ayahuasca discovery process, parameterised by values traced to specific sources in search_space_parameters.json (electronic supplementary material, table S3). Search-space parameters: N = 14003 taxonomically verified Amazonian vascular plants (Cardoso *et al.* 2017), with 1600-4500 as the ingestible candidate subset (10-30% of the flora under an assumed ingestible fraction, varied as a sensitivity parameter); D = 8-20 DMT-containing species (Ott 1994, McKenna *et al.* 1986); M = 3-10 MAO-I-containing species on the same sources; $V = D \times M$ = 24-200 valid target combinations; K = 5-200 trials per generation per specialist community; generation time = 25 years; G_max = 400-800 generations. Each parameter combination was run for 10000 iterations. Success criterion: the specialist community tests at least one valid DMT + MAO-I combination before the generation budget expires.

Six strategies were simulated: (1) **pure random trial** — K species drawn uniformly at random each generation; (2) **random with memory** — as (1) but previously tested plants are excluded; (3) **cue-guided** — plants displaying observable cues (bitter taste, unusual latex, bark morphology) tested with higher probability, cue-hit rates 0.1-0.5 and testing-bias multipliers 3-10 varied in sensitivity analyses; (4) **iterative from baseline** — practitioners start from *Banisteriopsis caapi* used alone (which has documented mild β-carboline psychoactivity) and test additional plants against that baseline, with the effective search space reduced to D DMT-containing candidates; (5) **ecological co-occurrence** — search restricted to plants in the same forest habitat as *B. caapi* (N_hab = 100-500, D_hab = 1-5); (6) **pharmacological null** — per-trial success probability drawn from the same pharmacological prior without any search strategy.

Archaeological calibration: Miller *et al.* (2019) report chemical evidence for DMT + harmine combinations in a Bolivian ritual bundle at approximately 1000 years before present, which we use as the minimum empirical constraint on the discovery timeline.

Cross-cultural predictions: for peyote (*Lophophora williamsii* (Lem. ex Salm-Dyck) J.M.Coult., single target, Chihuahuan Desert flora ~3500 species) and iboga (*Tabernanthe iboga*, single target, West African Apocynaceae subset), we ran Strategy 4 simulations with reduced search-space parameters and report the median convergence times in the Results.

The simulation is a plausibility demonstration, not a historical reconstruction: it rules out the strong "astronomical improbability" claim under reasonable parameters but does not establish which specific plants were tested in what order by any particular community.

The ingestible fraction is an assumption rather than a measured quantity, and we treat it as one. No published estimate specifies what proportion of the Amazonian flora a medicinal specialist would plausibly test by mouth, and the quantity depends on how testability is defined: the low end corresponds to plants regularly consumed as food, the high end to any plant a specialist might prepare as a decoction. We therefore did not fit this parameter to a source. We ran the simulation across the full assumed range instead, at N = 1600, 3000, and 4500 candidate species, so that the conclusion can be checked against the assumption rather than resting on it. The qualitative result is invariant across that range: guided iterative search from the *B. caapi* baseline reaches a valid combination in 100% of iterations at every candidate-pool size tested, while pure random-search success remains low, falling from 26% at N = 1600 to 3.8% at N = 4500 at 20 trials per generation. Varying the ingestible fraction changes the median discovery time but not the ordering of the strategies or the inference drawn from it.

Data and code availability

All JSON data files, Python analysis scripts, simulation code, source-extraction data, and the 118-plant admixture catalogue are publicly deposited at the Zenodo preprint record doi: 10.5281/zenodo.19521104 (concept DOI; always resolves to the latest version). The primary analysis scripts are compute_convergence_analysis.py, compute_revision_analyses.py, compute_expansion_revision_analyses.py, ayahuasca_search_simulation.py, build_full_catalogue.py, and compute_full_analyses.py. All analyses are reproducible by running these scripts against the committed JSON inputs.

Ethics statement

This paper is a retrospective analysis of published ethnographic and pharmacological literature. No new human data were collected. No ethics approval was required.

Results

Ceremony-pharmacokinetic calibration across eleven independent traditions

We compiled ceremony duration and pharmacokinetic effect duration for eleven independent indigenous traditions (Amazonian ayahuasca (Beyer 2009, Luna 1986), Santo Daime (Dawson 2013), União do Vegetal (Callaway *et al.* 1999), peyote Native American Church / Huichol (Stewart 1987, Myerhoff 1974), Bwiti iboga (Fernandez 1982), Mazatec *velada* (Estrada 1981, Wasson *et al.* 1974), Mazatec salvia (MacLean *et al.* 2013), Fijian yaqona [kava] (Aporosa 2014, Singh 1992, Aporosa 2022), Yanomami epená [*Virola* snuff] (Seitz 1967), Siberian fly agaric (Wasson 1968), Mazatec ololiuhqui (Schultes *et al.* 2001)), plus three modern clinical protocols as external calibration (clinical psilocybin (Griffiths *et al.* 2006, Johnson *et al.* 2008), clinical ayahuasca (Palhano-Fontes *et al.* 2019, Riba *et al.* 2003), intravenous clinical DMT (Strassman & Qualls 1994)). The eleven indigenous traditions span five continents (Eurasia added by the fly agaric tradition), seven pharmacological classes at the receptor-system level (DMT-family tryptamines — oral with β-carboline MAO-I and insufflated; mescaline-type phenethylamines; psilocybin / 4-hydroxy tryptamines; ergoline lysergamides; salvinorin κ-opioid; ibogaine NMDA/σ/multi-target; and GABA-A-active compounds — kavalactones and muscimol), and three orders of magnitude in ceremony duration — from ~10-minute Mazatec salvia sessions to 24-hour Bwiti iboga initiations. Independence was established by geographic separation >3000 km between primary tradition origins, distinct language families, no documented pre-colonial contact, and distinct primary psychoactive molecules. Per-tradition ceremony durations, pharmacokinetic windows, and ceremony/pharmacokinetic ratios are in Table 1; full sourcing is in Methods and electronic supplementary material, table S2.

Primary confirmatory test (n = 11 indigenous): log Pearson r = 0.977, $p = 2.5 \times 10^{-7}$, 95% CI [0.910, 0.994]; log-log slope 1.010. Full-dataset (n = 14): log Pearson r = 0.971, $p = 8.1 \times 10^{-9}$. Sources and per-row ethnography/pharmacology citations are in Materials and Methods, Ceremony-pharmacokinetic data extraction, and electronic supplementary material, table S2.

Table 1. Ceremony duration versus pharmacokinetic effect duration across 14 tradition-substance pairs. Rows 1-11: indigenous traditions (confirmatory, n = 11). Rows 12-14: modern clinical-pharmacology protocols (external calibration).

Tradition	Substance	Route	Ceremony (h)	Range (h)	PK effect (h)	Ratio
Amazonian mestizo / Shipibo ayahuasca	DMT + β-carbolines	oral	5.0	3.0-8.0	4.0	1.25
Santo Daime	ayahuasca ("Daime")	oral	10.0	8.0-12.0	4.0	2.50
União do Vegetal (UDV)	hoasca	oral	4.0	3.5-5.0	4.0	1.00
Peyote / NAC / Huichol	mescaline	oral	10.0	8.0-14.0	10.0	1.00
Bwiti iboga initiation	ibogaine	oral	24.0	18.0-36.0	24.0	1.00
Mazatec *velada*	psilocybin	oral	6.0	4.0-8.0	5.0	1.20
Mazatec salvia *barrida*	salvinorin A	smoked	0.17	0.08-0.25	0.17	1.00
Fijian yaqona (kava)	kavalactones	oral	5.5	3.0-8.6	4.0	1.38
Yanomami epená (*Virola* snuff)	DMT + 5-MeO-DMT	insufflated	1.0	0.5-1.5	0.75	1.33
Siberian fly agaric (Koryak)	muscimol	oral	10.0	4.0-16.0	6.0	1.67
Mazatec ololiuhqui	LSA (ergine)	oral	3.0	2.0-5.0	3.0	1.00
Clinical psilocybin (Hopkins)	psilocybin	oral	6.0	6.0-8.0	5.0	1.20
Clinical ayahuasca (RCT)	ayahuasca	oral	4.0	4.0-4.0	4.0	1.00
Clinical DMT i.v. (UNM)	DMT	i.v.	0.25	0.1-0.5	0.5	0.50

On $\log_{10}$-transformed durations across the eleven indigenous traditions, the Pearson correlation between ceremony and pharmacokinetic effect duration was $r = 0.977$, $p = 2.5 \times 10^{-7}$, 95% CI [0.910, 0.994] (Fisher z-transform); Spearman $\rho = 0.920$, $p = 6.0 \times 10^{-5}$. The log-log regression slope was 1.010, even closer to perfect unity than the $n = 9$ baseline (0.998), and consistent with an unbiased 1:1 calibration of ceremony duration to drug effect duration. The two added traditions both fall on the regression line: the Siberian fly agaric ratio is 1.67 (10 h ceremony / 6 h single-dose pharmacological window; the gap is consistent with the documented urine-recycling extension method, structurally parallel to Santo Daime's hymn-cycle extension of ayahuasca), and the Mazatec ololiuhqui ratio is 1.00 (3 h ceremony / 3 h subjective intoxication, co-extensive in the source). Nine of eleven ratios fall within ±0.5 of unity; the mean ratio is 1.30 ± 0.45. For comparison, the $n = 9$ baseline before the 2026-04-11 expansion gave log $r = 0.980$, essentially unchanged, indicating that adding two new traditions (extending receptor-system coverage to the ergoline lysergamide class with ololiuhqui and the GABA-A-active class with muscimol, and continental coverage to Eurasia with fly agaric) does not perturb the calibration. Including the three modern clinical protocols as external calibration ($n = 14$) gave log Pearson $r = 0.971$, $p = 8.1 \times 10^{-9}$. The clinical protocols were designed by researchers with access to plasma pharmacokinetic data and sit on the regression line defined by the indigenous traditions. This is an independent convergence on the same pattern, not a test of the framework.

The association is robust to leave-one-out exclusion (Pearson $r = 0.943$-0.991 across all eleven traditions) and to rank-based estimation (Spearman $\rho = 0.920$, $p = 6.0 \times 10^{-5}$). Influence diagnostics identify the Mazatec salvia session — the shortest ceremony in the sample, as noted above — as the single observation exceeding the Cook's distance threshold $4/n = 0.36$; excluding it leaves $n = 10$, $r = 0.943$ (electronic supplementary material, table S4). The two new traditions (fly agaric, ololiuhqui) each removed individually returned r values of 0.978 and 0.978 respectively. The dataset is robust to single-point exclusion of any of the new entries. Monte Carlo sensitivity varied each ceremony duration uniformly across its plausible ethnographic range in 10000 iterations; the resulting Pearson r had mean 0.968 (SD 0.009), 95% range [0.950, 0.983], and the correlation was significant at $p < 0.05$ in 100% of iterations and exceeded 0.90 in 100%. We continue to rely on the Fisher

z-transform analytical CI [0.910, 0.994] as the primary interval estimate rather than on a nonparametric bootstrap, which is not well calibrated at this sample size.

Santo Daime *hinário* ceremonies (10 hours) are 2.5× longer than the pharmacokinetic effect window of oral ayahuasca (~4 hours). Three interpretations are compatible with the data. The Santo Daime church may represent genuine counterevidence against ceremony-pharmacokinetic calibration; the extended duration may reflect liturgical structure (hymn cycles, formal phases) layered on top of a pharmacologically calibrated core; or the 10-hour duration may reflect a different optimization target in which pharmacological timing is one input among several. We cannot distinguish between these with present data. We note that União do Vegetal, the other Brazilian syncretic ayahuasca church, maintains a 4-hour ceremony matching pharmacokinetic duration exactly. Figure 1 presents the log-log scatter with indigenous-only and full regression lines. This temporal accuracy prompts the second test: whether similar empirical accuracy exists in the selection of admixture plants.

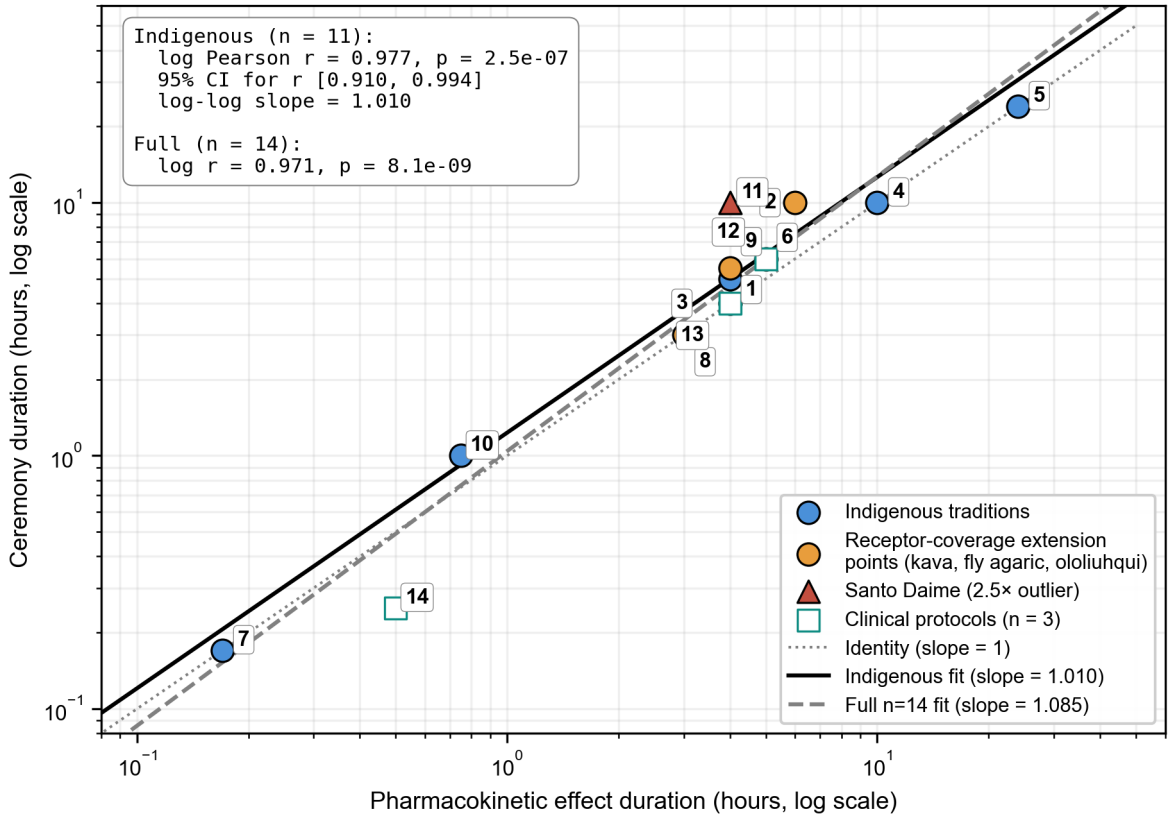

Figure 1. Ceremony duration tracks pharmacokinetic effect duration across independent traditions. Log-log scatter of ceremony duration (hours) versus pharmacokinetic effect duration (hours) for n = 11 indigenous traditions (numbered 1-11; blue circles for the remaining indigenous traditions, orange circles for the three receptor-coverage extension points kava/fly agaric/ololiuhqui, red triangle for the Santo Daime 2.5× outlier) plus three modern clinical-pharmacology protocols (numbered 12-14; open squares). Tradition assignments are given in the table immediately below. Solid line: log-log ordinary-least-squares fit to indigenous-only data (Pearson r = 0.977, 95% CI for r [0.910, 0.994] from Fisher z-transform, p = 2.5 × 10^{-7}; slope = 1.010). Dashed line: fit to full n = 14 dataset (r = 0.971, p = 8.1 × 10^{-9}). Dotted line: identity (slope = 1). The added GABAergic, muscimol, and ergoline test points (numbers 8, 9, 11) all fall on the regression line, extending the calibration beyond serotonergic psychedelics to seven distinct pharmacological mechanisms across five continents.

#	Tradition	Marker group	Ceremony (h)	PK (h)	Ratio
1	Amazonian ayahuasca	Indigenous	5.0	4.0	1.25
2	Santo Daime	Indigenous (outlier)	10.0	4.0	2.50
3	UDV	Indigenous	4.0	4.0	1.00
4	Peyote NAC / Huichol	Indigenous	10.0	10.0	1.00
5	Bwiti iboga	Indigenous	24.0	24.0	1.00
6	Mazatec velada	Indigenous	6.0	5.0	1.20
7	Mazatec salvia	Indigenous	0.17	0.17	1.00
8	Mazatec ololiuhqui	Extension point (LSA)	3.0	3.0	1.00

9	Fijian yaqona (kava)	Extension point (GABAergic)	5.5	4.0	1.38
10	Yanomami epená (*Virola*)	Indigenous	1.0	0.75	1.33
11	Siberian fly agaric	Extension point (muscimol)	10.0	6.0	1.67
12	Clinical psilocybin	Clinical control	6.0	5.0	1.20
13	Clinical ayahuasca	Clinical control	4.0	4.0	1.00
14	Clinical DMT (i.v.)	Clinical control	0.25	0.5	0.50

Admixture concordance gradient across 118 plants

We assembled a merged admixture plant catalogue from Schultes' 1957 botanical survey (Schultes 1957), Luna's 1986 ethnographic fieldwork in the Peruvian Amazon (Luna 1986), Ott's 1994 *Ayahuasca Analogues* chemical and ethnobotanical review (Ott 1994), and the contemporary active list from Allan (2026), plus additional legacy sources (Schultes 1960, Rodd 2002, Ruffell *et al.* 2020). After deduplication by Latin binomial, the catalogue contains 118 unique plants: 12 active in contemporary practice and 106 candidates (plants documented in one or more historical or analogue sources but absent from the contemporary active pharmacopeia; Table 2 summaries catalogue composition by purpose-observability category). This is, to our knowledge, the largest cross-temporal admixture-plant catalogue assembled for any psychoactive tradition.

Table 2. Admixture plant catalogue summary: 118 plants across 70 years of ethnobotanical documentation.

Category	**Observable**	**Mixed**	**Non-observable**	**Total**
Active pharmacopeia (contemporary)	7	**0**	5	12
Candidate pool (historical or analogue)	43	56	7	106
Total	**50**	**56**	**12**	**118**

Primary confirmatory test: 3 × 2 chi-square on observability × active/candidate, $\chi^2(2) = 20.2$, $p = 4.2 \times 10^{-5}$. Collapsed 2 × 2 (mixed into observable): OR = 0.10, $p = 2.5 \times 10^{-3}$. Strict 2 × 2 (mixed excluded): OR = 0.23, $p = 0.044$. Bimodality observation (exploratory, post hoc): the active pharmacopeia is bimodally distributed with zero mixed-purpose plants, while the candidate pool's largest subgroup is mixed-purpose. Replication on non-ayahuasca pharmacopeias is required before the bimodality can be treated as a confirmed structural prediction. Full catalogue in electronic supplementary material, table S1; toxic candidates (9 plants) in table S1b.

Each plant was coded for purpose observability (observable / non-observable / mixed) by the explicit rules reported in Methods. The key confirmatory test is a 3 × 2 chi-square on the observability × active/candidate contingency. The table is [[7 observable, 0 mixed, 5 non-observable], [43 observable, 56 mixed, 7 non-observable]] for [active, candidate]; $\chi^2(2) = 20.2$, $p = 4.2 \times 10^{-5}$. The 2 × 2 test collapsing mixed into observable yields odds ratio 0.10, $p = 2.5 \times 10^{-3}$; the strict 2 × 2 test excluding mixed yields OR = 0.23, $p = 0.044$. All variants are significant (electronic supplementary material, table S1a).

An unexpected pattern in the data is that active admixture plants cluster at the extremes of the observability distribution (7 observable, 0 mixed, 5 non-observable), while candidate plants show the opposite distribution (43 observable, 56 mixed, 7 non-observable; Figure 2). We did not predict this pattern in advance. One interpretation, consistent with the observability framework, is that cultural selection acts against purpose ambiguity — retaining only plants with clearly defined, testable roles — because plants whose stated purposes are heterogeneous generate divergent transmission lineages under environmental feedback. However, the pattern could equally reflect documentation-density differences: active plants have richer ethnographic records that allow cleaner classification. We present this as an exploratory observation requiring replication in independent pharmacopeias (e.g., peyote admixtures, iboga adjuncts) before theoretical weight is placed on it.

Nine toxic plants appear in the candidate pool but not in current active practice: *Aristolochia*, *Malouetia tamaquarina*, *Chorisia/lupuna*, *Dieffenbachia*, *Pilocarpus organensis*, *Desmodium*, *Dutaillyea*, *Melicope*, and *Vepris*. These are plants Amazonian practitioners tried and appear to have rejected, most plausibly through observable negative feedback (acute toxicity, nephrotoxicity, dermatitis, or cardiac effects). One toxic plant, *Hura crepitans*, is coded as active in Luna's Peruvian fieldwork as a non-observable spirit-protection admixture; Luna's coding resolves an apparent discrepancy with the toxicity signal. The candidate pool thus contains a suggestive "failed experiments" signal: plants tried, observed to harm, and abandoned. We cannot, however, distinguish rejection from documentation attrition without a systematic survival analysis. The full toxic catalogue with sources is in electronic supplementary material, table S1b.

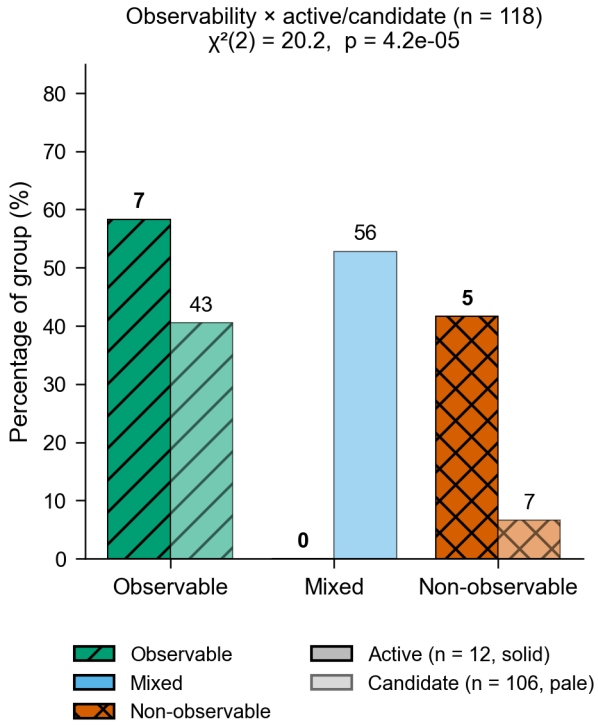

Figure 2. Admixture plant concordance gradient. Grouped-bar chart of 118 admixture plants, normalised within each group so the active (*n* = 12, solid bars) and candidate (*n* = 106, pale bars) distributions can be compared directly. Raw counts are labelled above each bar. Active: 7 observable, 0 mixed, 5 non-observable; the mixed-purpose category is empty. Candidate: 43 observable, 56 mixed, 7 non-observable; the mixed category is the largest candidate subgroup. $\chi^2(2) = 20.2$, $p = 4.2 \times 10^{-5}$. Active pharmacopeias are bimodally distributed in purpose clarity while candidate pools span all three classes. The bimodality finding is exploratory, potentially confounded by documentation-density differences between groups, and requires replication in independent pharmacopeias.

The candidate pool also contains 26 plants with partial psychoactive effects (stepping stones in the search landscape). These include alternative DMT sources (*Psychotria viridis* itself in source records predating its identification as the canonical admixture; *Diplopterys cabrerana*; *Virola* resins; *Anadenanthera* snuffs), alternative β-carboline sources (*Banisteriopsis muricata* (Cav.) Cuatrec.), and plants with distinct psychoactive profiles (*Tabernaemontana* species, *Erythrina* alkaloids). The existence of this graded middle, plants that "almost work" or work via different mechanisms, is what makes iterative search tractable. The search landscape is not a binary lookup over species; it is a graded topology in which partial-hit plants guide further exploration.

The temporal trajectory reveals an informative, non-linear shape. Schultes (1957) documented 15 distinct admixture plants; Luna (1986) documented 41 (expansion); the contemporary active core is 12 (Allan 2026) (contraction). Luna's ethnography actually expanded the documented pharmacopeia relative to Schultes, followed by contraction to the active core. Nine of the 15 plants Schultes recorded were already abandoned by Luna's time and six persisted into Luna's inventory; none of the Schultes plants is retained in the contemporary active core, while six of the 12 contemporary actives were documented by Luna. This is an exploration-then-convergence pattern consistent with cumulative cultural search. Figure 4 shows the per-period plant counts. We note a documentation caveat: Luna's fieldwork was more intensive than Schultes' survey, so part of the 1957 → 1986 increase reflects documentation density rather than genuine pharmacopeia growth. The 1986 → present contraction is less exposed to this bias because both periods draw on sustained contemporary ethnographic contact. Whether iterative search on such a graded landscape could plausibly have discovered the canonical DMT + MAO-I combination within the documented time depth is a computational question, and the third analysis addresses it directly.

Computational plausibility of guided iterative search

The iterative-search account of the ayahuasca discovery requires that the mechanism be computationally plausible over archaeologically available timeframes. The earliest chemically confirmed ayahuasca-type combination (harmine + DMT residues in a ritual bundle) dates to approximately 1000 years before present (Miller *et al.* 2019); linguistic evidence suggests substantially greater time depth. The question is whether any plausible search strategy, given the search space, trial budget, and observable cues available to Amazonian practitioners, can discover the MAO-I + DMT combination in <5000 years.

We simulated six search strategies on the Amazonian admixture search space, parameterised by values traced to specific sources (electronic supplementary material, table S3): 14003 taxonomically verified Amazonian vascular plants (Cardoso *et al.* 2017) as the upper bound on the raw flora; 1600-4500 as the ingestible candidate subset (10-30% of the flora under an assumed ingestible fraction, varied as a sensitivity parameter); 8-20 DMT-containing species based on McKenna *et al.* (1986) and Ott (1994); 3-10 MAO-I-containing species on the same sources; 5-200 trials per generation per specialist community; 25-year generation time; 400 generations (10000 years) as the base time budget, extended to 800 generations in the sensitivity runs. Each parameter combination was simulated 10000 times. The six strategies were (1) pure random trial; (2) random with memory of previously tested plants; (3) search guided by observable cues (taste, smell, latex, morphology); (4) iterative search from a known psychoactive baseline (*Banisteriopsis caapi* used alone as the starting point, with additive trials against that baseline); (5) ecological co-occurrence constraint (testing only plants encountered in the same forest patch as *B. caapi*); and (6) a pharmacological null model.

At representative parameter values (N = 1600 candidate species, V = 24 valid combinations, K = 20 trials per generation), pure random search produced discovery in only 26% of 10000 iterations within 800 generations, with a median of 9050 years when successful. At larger candidate pools (N = 3000), pure random search succeeded in 8% of iterations. Pure random search cannot discover ayahuasca in archaeologically plausible timeframes under any reasonable parameter set. In contrast, iterative search from the *B. caapi* baseline (Strategy 4) produced 100% discovery at all tested parameter values; across the full grid of DMT-source counts (D = 8-20) median discovery times ranged from 25 years (N = 1600, K = 200) to 1875 years (N = 4500, D = 8, K = 5), and from 25 to 1075 years for the D = 14 midpoint. Ecological co-occurrence (Strategy 5) gave median discovery times of 25-1225 years across parameter combinations.

The ethnographic record is consistent with Strategy 4 as the mechanism Amazonian practitioners describe. Luna (1986, p. 65) reports that the vegetalistas of Iquitos use ayahuasca itself as a tool for studying the properties of other plants: "by perceiving the changes caused by the additive to the basic preparation... the properties and application of the plants are studied". Luna further notes (p. 158) that "the number of additives is unlimited, simply because ayahuasca is a means of exploring the properties of new plants and substances", and records a specific episode in which Don Fidel tested the properties of aspirin as a candidate admixture. The search is ongoing, and extends to industrial pharmaceuticals. Ott (1994, p. 18) reinforces the same picture: "the ayahuasca plant and potion is itself the teacher of the aspiring shaman". Schultes (1957, 1960) provides the independent 40-years-earlier botanical observation of the same pattern. Three independent sources across 40 years document the same iterative-search mechanism in which the already-active baseline serves as the sensory instrument for testing additional plants.

Figure 3 compares median discovery time across all six strategies at a representative parameter set. The gap between random and iterative search is several orders of magnitude. The simulation's contribution is not to prove how ayahuasca was discovered, which is unknowable, but to rule out the strong form of the "astronomically improbable" claim that is sometimes invoked to argue for non-trial-and-error explanations. Under realistic parameters, guided search converges in centuries rather than millennia. The substantive observation is not that ayahuasca was eventually found, but that the search strategy the ethnographic record documents (using the brew as a plant-testing instrument) is exactly the approach of searching iteratively from an active baseline that the observability framework predicts. Cross-cultural prediction: smaller search spaces and fewer target species should yield faster discovery. Peyote (*Lophophora williamsii* in the Chihuahuan Desert flora of ~3500 species, target = 1) should converge roughly 3× faster than ayahuasca; our simulation gave median 400 years for peyote and 1250 years for iboga, consistent with the single-target/smaller-flora expectation. The simulation is not intended to reconstruct the historical sequence by which ayahuasca arose. It tests a narrower question: whether the learning mechanism the ethnographic record documents is sufficient to make pharmacologically complementary combinations discoverable on plausible cultural timescales. Full simulation results and sensitivity heatmaps are in the electronic supplementary material. Taken together, the duration calibration, the admixture gradient, and the search simulation supply three independent lines of evidence; the Discussion evaluates what they jointly do and do not establish.

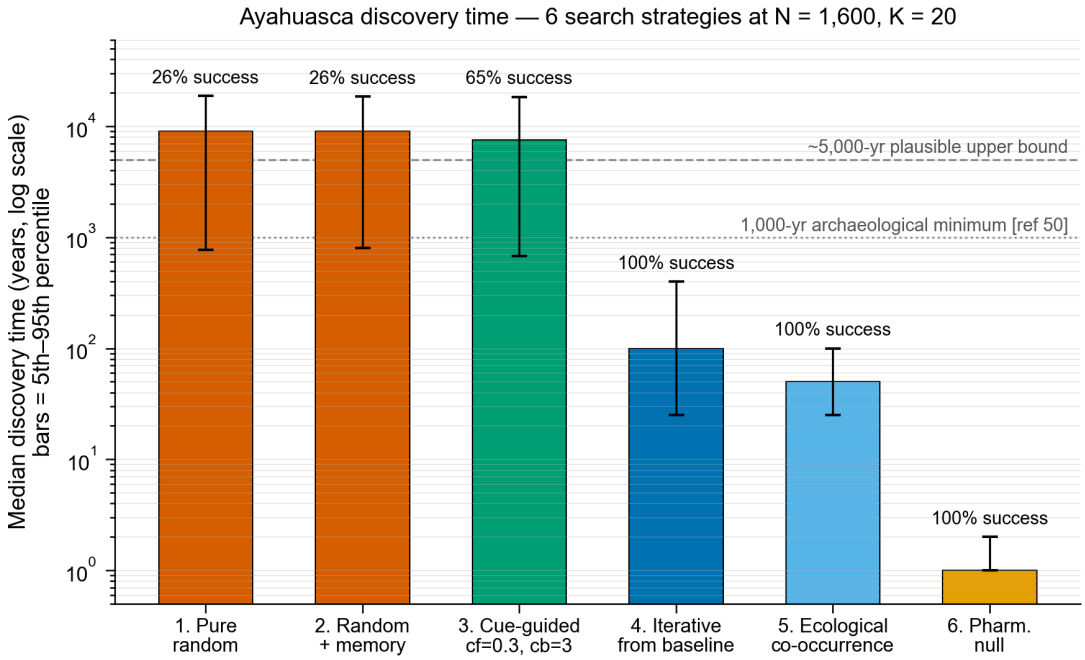

Figure 3. Pure random search fails; guided iterative search succeeds. Bar chart of median ayahuasca discovery time (log scale) for each of the six simulated search strategies at a representative parameter set (*N* = 1600 candidate species, *V* = 24 valid combinations, *K* = 20 trials per generation; cue-guided strategy uses cue-hit fraction *cf* = 0.3 and cue bias *cb* = 3; iterative-baseline strategy uses *D* = 14 DMT-containing candidates; ecological co-occurrence uses *N*_hab = 100, *D*_hab = 3; pharmacological null uses *N* = 1000, *D* = 14, *K*_yr = 100). Error bars span the 5th-95th percentile of successful iterations. Success rates are annotated above each bar. Strategies 1 and 2 (random, orange/vermillion) achieve only 26% success and median discovery times around 9000 years, exceeding the plausible archaeological window. Strategies 4 and 5 (iterative/ecological, blue) achieve 100% success with median discovery times of 50-100 years; strategy 3 (cue-guided) is intermediate. Dashed line: ~5000-year plausible upper bound; dotted line: 1000-year archaeological minimum (Miller *et al.* 2019). All cells are 10000 iterations. Full parameter grid and sensitivity heatmaps are in electronic supplementary material, table S3.

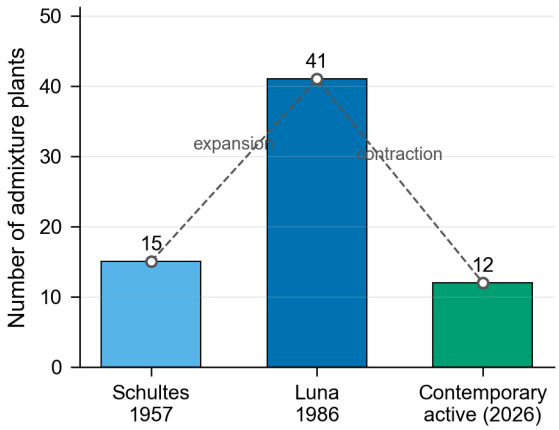

Figure 4. Temporal trajectory of the admixture pharmacopeia — exploration then contraction. Plant counts for three documentation eras: Schultes 1957 (*n* = 15), Luna 1986 (*n* = 41), and the contemporary active core (*n* = 12). The shape is exploration (1957 → 1986, expansion from 15 to 41 plants) followed by contraction (1986 → present, 41 back down to 12 retained as canonical active admixtures). Of the 15 Schultes plants, nine were already abandoned by Luna's time and six persisted into Luna's inventory, but none is retained in the contemporary active core; of the 41 Luna plants, six remain in contemporary active practice, accounting for half of the 12 active admixtures. The nine toxic candidates listed in the Results are plants that entered one of the historical catalogues and were later dropped. The apparent 1957 → 1986 expansion should be interpreted with caution: Luna's fieldwork was more intensive than Schultes' survey, so part of the increase reflects documentation density rather than genuine pharmacopeia growth. The 1986 → present contraction is less exposed to this bias because both periods draw on sustained contemporary ethnographic contact.

Discussion

Three quantitative findings, drawn from independent evidence types, jointly support an empirical reading of psychoactive ethnobotanical knowledge. First, ceremony duration tracks pharmacokinetic effect duration across eleven independent traditions on three orders of magnitude, with a 1.010 log-log slope consistent with unbiased 1:1 calibration: indigenous practitioners have, in aggregate, fitted ceremonial timing to the pharmacological window of the substance they administer. Second, in a 118-plant Amazonian admixture catalogue spanning 70 years of ethnobotanical documentation, observability category and contemporary-pharmacopoeia status are non-independent ($\chi^2(2) = 20.2$, $p = 4.2 \times 10^{-5}$), with active admixtures clustering at both extremes of the observability distribution (7 observable + 5 non-observable + 0 mixed in active; $n = 12$) while the broader candidate pool concentrates in the mixed-observability middle (43 + 56 + 7 in candidate; $n = 106$). The active distribution differs from the candidate distribution in shape, not in average observability. This is a bimodal rather than monotonic pattern, and it warrants closer empirical examination of mid-observability candidates currently under-represented in the active set. Third, agent-based simulation shows that guided iterative search from a known psychoactive baseline — the kind of search the ethnographic record actually documents (Luna 1986, p. 158) — converges on the DMT + MAO-I combination in centuries to millennia under realistic Amazonian search-space parameters, while pure random trial-and-error fails within archaeologically plausible budgets. Three convergent lines, three independent methods, one ethnobotanical conclusion: traditional psychoactive plant knowledge contains structured pharmacological signal that ethnopharmacologists can use, where the signal correlates with observability of practitioner-accessible feedback.

An ethnobotanist might reasonably question whether a nightly kava session, a ~10-minute *Virola* snuff episode, and a multi-hour ayahuasca ceremony — embedded in distinct ritual structures, social meanings, and ethnographic contexts — are comparable units of analysis. We argue that the comparability question is what the test addresses: the prediction concerns a structural property (ceremony envelope calibrating to pharmacokinetic window) that is independent of ritual content, social meaning, or cultural framing. The prediction is that wherever a psychoactive substance is used in a culturally structured temporal frame, that frame will calibrate to the substance's effect duration — regardless of pharmacological class, administration route, or ritual formality. If the prediction held only for oral serotonergic psychedelics, it would be a narrow pharmacological observation; the inclusion of GABAergic kava and fly agaric, the ergoline ololiuhqui, the κ-opioid salvia, and insufflated *Virola* is what tests cross-class generalization. That all eleven traditions — spanning three orders of magnitude, seven pharmacological classes, and three administration routes (with oral DMT distinguished by co-administered MAO-I as a pharmacokinetically distinct mode) — are described by the same near-1:1 overall relationship, with the Santo Daime outlier discussed below, is the finding. We therefore report both the full $n = 11$ and a subset restricted to the oral serotonergic traditions ($n = 6$: ayahuasca, Santo Daime, UDV, peyote, Bwiti iboga, Mazatec *velada*; log Pearson $r = 0.874$, $p = 0.023$, 95% CI [0.21, 0.99]) to let readers evaluate each. The subset correlation is materially weaker than the full-sample value, which is the point: the heterogeneous sample is what supports the generalization claim. Readers unconvinced by the inclusion of kava, fly agaric, or ololiuhqui may evaluate the oral-serotonergic subset as the primary result; our interpretation does not depend on any single tradition.

These results extend the cross-cultural ethnobotanical literature on traditional medicine in two directions. The Saslis-Lagoudakis *et al.* (2012) phylogenetic-bioprospecting result, that phylogenetically distant cultures converge on the same medicinal plant clades, establishes that traditional pharmacopoeias track pharmacological reality in aggregate. The present results specify a feedback condition under which the convergence arises: where outcome-feedback is observable to practitioners, the cross-cultural signal is strongest; where it is not, the signal vanishes. The Cardoso *et al.* (2017) Amazonian flora census defines the search space within which the ayahuasca search took place; we show that the documented practitioner search strategy (iterative additive trials against the *Banisteriopsis caapi* baseline) is sufficient to render that search space tractable. The Alrashedy and Molina (2016) phylogenetic analysis of psychoactive plant use across cultures shows the same convergent pattern at the level of psychoactive species; we provide a quantitative test of why the convergence is distributed unevenly across observable versus non-observable purpose categories within a single tradition. The contribution sits within the ethnobotanical research tradition rather than imported from outside it.

The practical implication for ethnopharmacological prioritization is nuanced rather than monotonic. Observable-purpose admixtures, those referring to physically verifiable effects like purging, stimulation, analgesia, and intensification of subjective state, represent 58% of the active pharmacopeia (7 of 12) despite being only 41% of the candidate pool (43 of 106), reflecting empirical-feedback selection in the expected direction. But the non-observable category is also enriched in the active set (5 of 12 active versus 7 of 106 candidate; 42% within-column active rate). The bimodal structure has two implications for ethnobotanical practice. First, observable-purpose claims constitute reliable prior evidence for empirical follow-up. Ethnobotanists evaluating traditional pharmacological literature have an empirical justification for weighting

observable-purpose plants when designing bioprospecting studies. Second, admixtures retained despite a non-observable stated purpose (the active set's non-observable contingent) merit closer empirical investigation: their stable transmission despite the absence of practitioner-accessible outcome-feedback suggests either pharmacological activity that has not yet been characterized through the lens of the stated purpose, or cultural-attractor stability whose biological correlates merit follow-up. The under-investigated category is the mid-observability set. These are plants with mixed observable and non-observable purposes, and they are over-represented in the candidate pool. This is not a stance against traditional knowledge; it is a stance taken from within it, using the structure of the tradition itself (observable versus non-observable purpose categories) to triage the empirical content. The 9-plant toxic discard pile in the candidate pool — *Aristolochia*, *Malouetia*, *Dieffenbachia*, *Pilocarpus*, and others — is consistent with observable-feedback selection operating in the negative direction: plants observed to harm were rejected, even where some had been historically documented.

The five non-observable admixtures retained in contemporary practice are the sharpest test case the catalogue offers, and the hypothesis they generate is worth stating explicitly. They are *Mansoa alliacea*, *Couroupita guianensis*, *Hura crepitans*, *Cavanillesia umbellata* Ruiz & Pav., and *Calycophyllum* spp., documented for spirit protection, soul work, and metaphysical cleansing rather than for any physically verifiable effect. On the framework's own logic these should be the least stable elements of the pharmacopoeia, because their stated purposes generate no practitioner-accessible outcome feedback, so their persistence requires an explanation. One possibility is cultural-attractor stability alone. A second, which we regard as directly testable, is that these species contain uncharacterized secondary metabolites, or produce synergistic effects in combination with the β-carboline-containing base, that exert genuine biological activity outside the indigenous stated purpose. On that reading the plants are retained because they do something, even though what they do is not what the stated purpose claims, and the stated purpose is then a culturally transmitted label attached to a real but unnamed effect. The two hypotheses make different predictions. Under cultural-attractor stability, phytochemical screening of these five species should return no consistent bioactivity beyond that of the base brew; under the secondary-metabolite hypothesis it should return detectable activity that the ethnographic purpose does not name. Two of the five already show biological activity of some kind: *Mansoa alliacea* is coded as pharmacologically validated in the catalogue, and *Hura crepitans* carries a toxicity signal from its phorbol-ester content. Targeted screening of the remaining three, with the base brew as the comparison condition, would weigh directly on the question on a sample small enough to be tractable: detected activity would support the secondary-metabolite account, while non-detection would weigh against it without excluding it. The two accounts are not mutually exclusive, and we offer this as the most direct empirical follow-up the present dataset supports.

The interpretive mechanism we apply is the observability gradient framework (Allan 2026), which parameterizes traditional knowledge transmission by the accessibility of outcome-feedback to practitioners and predicts a sharp non-linear relationship between observability and accuracy. The framework operates on the observable layer only: selection pressure on accuracy cannot operate where the feedback is not there. A tradition that preserves "the river spirit is benevolent" is not making a falsifiable empirical claim; it is maintaining a cultural resource whose function is something other than prediction. We emphasise what the result does and does not imply. It does imply that observability of a claimed mechanism predicts pharmacological concordance within these traditions. It does not imply that practitioners understand pharmacology, that they can reliably generate new pharmacological knowledge on demand, or that the entire content of any tradition is accurate. The framework neither requires nor supports any causal role for psychoactives in the evolution of human cognition or language (cf. McKenna 1992); the claim is that ethnobotanical transmission systems can optimize psychoactive technology once it exists, not that psychoactive technology originated cognition.

A scope note on what concordance means here is necessary. We do not treat correspondence with characterized pharmacology as a criterion for the validity of Indigenous knowledge systems as wholes. Those systems encode ecological, medical, social, and cosmological knowledge whose purposes extend well beyond the narrow pharmacological questions this analysis can address, and nothing in the design licenses a judgment about them. Where a traditional claim is discordant with currently characterized pharmacology, the discordance does not establish that the claim is erroneous: the pharmacological record is partial, screening has been uneven across taxa, and the stated purpose need not be the dimension along which a preparation was selected in the first place. Throughout this paper the words accurate and calibrated therefore carry a deliberately restricted meaning. They refer to correspondence with the specific external measurements we name (published pharmacokinetic effect durations, and published phytochemical and pharmacological findings), and to nothing beyond them.

The cross-class generalization is the substantive finding for ethnopharmacology. The seven receptor-system classes represented in the n = 11 sample — DMT-family tryptamines (5-HT2A; oral and insufflated routes), mescaline-type phenethylamines (5-HT2A), psilocybin / 4-hydroxy tryptamines (5-HT2A), ergoline lysergamides (5-HT2A), salvinorin κ-opioid

agonists, ibogaine NMDA/σ/multi-target ligands, and GABA-A-active compounds (kavalactones and muscimol) — cover most of the major receptor systems implicated in traditional psychoactive use, across five continents (the Siberian fly agaric tradition extends the sample to Eurasia). The absence of a systematic mismatch in any of them, including the non-psychedelic GABAergic kava, the sub-hour insufflated *Virola*, the GABA-A muscimol of fly agaric, and the ergoline ololiuhqui, is the pattern consistent with modality-independent calibration. Restricting the sample to any single class would collapse the test to a pharmacological observation.

Set and setting is the proximate mechanism through which outcome-feedback selection operates on ceremony structure (Hartogsohn 2017, Dupuis 2021, Dupuis 2022): the ritual is the selective environment in which ceremony parameters are tested, practitioners observe whether participants enter the expected state on schedule and whether they return to baseline as the ceremony concludes, and variants producing mismatched experiences are abandoned. Indigenous ceremony durations should therefore be treated not as arbitrary cultural choices but as the output of a multi-generational ethnobotanical optimization process. Modern clinical protocols for psilocybin, ayahuasca, and related substances have independently converged on session durations that match the indigenous values (Griffiths *et al.* 2006, Johnson *et al.* 2008, Palhano-Fontes *et al.* 2019); ethnobotanical calibration and clinical pharmacology appear to be solving the same optimization problem with different inputs.

The exploratory bimodality finding, if it replicates, would add a second structural prediction to the framework: that ethnobotanical selection acts against purpose ambiguity at the species level, not merely against non-observability. A plant whose stated purpose is "it produces clarity and spiritual protection" is unstable under environmental feedback because the observable half can be tested while the non-observable half cannot, and practitioners who disagree about which component is primary produce divergent transmission lineages. Plants with unambiguous purposes transmit stably either because they are selected for accuracy (observable) or because they are selected for cultural coherence (non-observable). We flag this as a post-hoc interpretation requiring blinded multi-rater replication on independent pharmacopeias (peyote and iboga admixtures are the natural targets) before theoretical weight is placed on it; alternative explanations remain live: documentation-density artefacts, author-coding idiosyncrasy, and historical sampling bias.

The limitations are substantial and must be stated directly. The indigenous-only ceremony-pharmacokinetic analysis has n = 11. Bootstrap confidence intervals remain wide at this sample size and nonparametric bootstrap is unreliable below $n \approx 20$; we rely on analytical Fisher z-transform CIs and Monte Carlo duration sensitivity as the robust estimates. The heterogeneity of practices in the sample is both the main strength of the generalization claim and the main limitation of the calibration analysis: a narrower, more homogeneous sample yields a materially weaker result (oral serotonergic traditions only, n = 6: r = 0.874). Two of the eleven traditions raise specific independence concerns. The Mazatec ololiuhqui entry shares a cultural group with the Mazatec *velada* entry; leave-one-out diagnostics show that excluding ololiuhqui changes the r by less than 0.001. The Siberian fly agaric ceremony envelope (~10 h) exceeds the single-dose pharmacological window (~6 h) because of urine-recycling extension; we treat this as parallel to Santo Daime's hymn-cycle extension of ayahuasca, and excluding fly agaric likewise leaves r essentially unchanged. The admixture observability coding was performed by a single researcher; a blinded multi-rater validation is in preparation, and until completed the chi-square result should be treated as preliminary and the bimodality as exploratory. The toxic discard pile is inferred from absence in later sources and could reflect documentation bias. The simulation uses simplified feedback models; it rules out the strong "astronomical improbability" claim but does not reconstruct any specific historical process. The Santo Daime outlier has three interpretations we cannot distinguish with present data.

Several empirical patterns would speak against the framework's predictions. The strongest a priori prediction was a monotonic decline in active-set membership across the observability gradient (observable > mixed > non-observable). What the data show is partially counter to that strong prediction: within-column active rates are 14% (observable), 0% (mixed), and 42% (non-observable). The bimodal pattern is consistent with the framework's general claim that observability shapes cultural transmission of pharmacological knowledge — both extremes are stably transmitted, for different reasons (observable purposes through empirical feedback; non-observable but persistent admixtures as cultural attractors whose biological correlates merit follow-up) — but it falsifies a strict monotonic reading. A reviewer evaluating the framework should treat the present results as constraining the form of the observability-accuracy relationship to bimodal rather than monotonic. If indigenous ceremony durations showed no systematic relationship to pharmacokinetic effect durations — or if the relationship held only for traditions with documented contact with Western pharmacology — the ethnobotanical-calibration interpretation would be undermined. If simulation showed that pure random search was sufficient to discover ayahuasca in archaeologically plausible timeframes, iterative search would not be a necessary explanation. If continuous

observability scoring revealed a non-monotonic or inverted relationship between observability and pharmacological concordance, the gradient prediction would fail. The present data are consistent with the framework but do not exclude all alternative explanations.

Conclusion

Three quantitative tests on psychoactive ethnobotanical knowledge — cross-cultural ceremony-pharmacokinetic calibration across eleven traditions, purpose-observability versus pharmacological-validity in a 118-plant Amazonian admixture catalogue, and agent-based simulation of guided iterative search — converge on a single result: traditional psychoactive plant knowledge contains structured pharmacological signal where outcome-feedback is observable to practitioners. The observability gradient framework supplies a principled interpretive account of the structure: ethnobotanical transmission is selected for accuracy where feedback is observable, and drifts on cultural attractors where it is not. For ethnopharmacological practice, the implication is a triage criterion: observable-purpose claims constitute prior evidence for empirical follow-up, while claims based on non-observable purposes should be treated as cultural resources. The small samples and single-author admixture coding warrant replication on independent pharmacopeias before strong conclusions are drawn. As an ethnobotanical synthesis, the work shows that traditional psychoactive plant traditions track pharmacological reality unevenly and predictably, and that the unevenness is itself ethnographic data worth attending to.

Declarations

List of abbreviations: DMT = *N,N*-dimethyltryptamine; MAO = monoamine oxidase; MAO-I = monoamine oxidase inhibitor; PK = pharmacokinetic / pharmacokinetics; LSA = lysergic acid amide; UDV = União do Vegetal (Brazilian syncretic ayahuasca church); NAC = Native American Church; ISE = International Society for Ethnobiology.

Ethics approval and consent to participate: This study is a meta-analysis of previously published ethnobotanical, ethnographic, and pharmacological literature. No new fieldwork, primary ethnographic data collection, or human-subjects research was conducted. The research methodology followed the principles of the International Society for Ethnobiology (ISE) Code of Ethics insofar as the cited primary studies attested to those principles in their own publications. The Convention on Biological Diversity and the Nagoya Protocol on Access and Benefit Sharing did not apply directly because no new genetic or biological resources were accessed; we acknowledge these instruments as binding on the original primary studies cited.

Consent for publication: Not applicable.

Availability of data and materials: All JSON data files, Python analysis scripts, simulation code, source-extraction data, and the 118-plant admixture catalogue used in this study are deposited at the Zenodo preprint record doi: 10.5281/zenodo.19521104 (concept DOI; always resolves to the latest version). The primary analysis scripts are compute_convergence_analysis.py, compute_revision_analyses.py, compute_expansion_revision_analyses.py, ayahuasca_search_simulation.py, build_full_catalogue.py, and compute_full_analyses.py. All results reported in the manuscript are reproducible by running these scripts against the committed JSON inputs. All plant taxa cited in this analysis derive from published ethnobotanical sources; no new field collections or voucher specimens were generated for this study, and voucher specimen documentation for individual plant taxa is the responsibility of the cited primary sources, which we identify by Latin binomial throughout.

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Literature cited

Allan E. 2026. Data and pre-registered predictions for: Emergent precision in oral traditions [data set]. Zenodo. doi: 10.5281/zenodo.19342595

Alrashedy NA, Molina J. 2016. The ethnobotany of psychoactive plant use: a phylogenetic perspective. PeerJ 4:e2546. doi: 10.7717/peerj.2546

Aporosa SA. 2014. Yaqona (Kava) and Education in Fiji. VDM Verlag, Saarbrücken, Germany.

Aporosa SA. 2022. Yaqona (kava) and the school campus: Regulation versus facilitation. The Australian Journal of Indigenous Education 51(1). doi: 10.55146/ajie.2022.6

Beyer SV. 2009. Singing to the Plants: A Guide to Mestizo Shamanism in the Upper Amazon. University of New Mexico Press, Albuquerque, U.S.A.

Bliege Bird R, Codding BF, Kauhanen PG, Bird DW. 2012. Aboriginal hunting buffers climate-driven fire-size variability in Australia's spinifex grasslands. Proceedings of the National Academy of Sciences USA 109:10287-10292. doi: 10.1073/pnas.1204585109

Boyd R, Richerson PJ. 1985. Culture and the Evolutionary Process. University of Chicago Press, Chicago, U.S.A.

Brown RT, Nicholas CR, Cozzi NV, Gassman MC, Cooper KM, Muller D, Thomas CD, Hetzel SJ, Henriquez KM, Ribaudo AS, Hutson PR. 2017. Pharmacokinetics of escalating doses of oral psilocybin in healthy adults. Clinical Pharmacokinetics 56:1543-1554. doi: 10.1007/s40262-017-0540-6

Callaway JC, McKenna DJ, Grob CS, Brito GS, Raymon LP, Poland RE, Andrade EN, Andrade EO, Mash DC. 1999. Pharmacokinetics of hoasca alkaloids in healthy humans. Journal of Ethnopharmacology 65:243-256. doi: 10.1016/S0378-8741(98)00168-8

Cardoso D, Särkinen T, Alexander S, Amorim AM, Bittrich V, Celis M, Daly DC, Fiaschi P, Funk VA, Giacomin LL, Goldenberg R, Heiden G, Iganci J, Kelloff CL, Knapp S, Cavalcante de Lima H, Machado AFP, dos Santos RM, Mello-Silva R, Michelangeli FA, Mitchell J, Moonlight P, de Moraes PLR, Mori SA, Nunes TS, Pennington TD, Pirani JR, Prance GT, de Queiroz LP, Rapini A, Riina R, Rincon CAV, Roque N, Shimizu G, Sobral M, Stehmann JR, Stevens WD, Taylor CM, Trovó M, van den Berg C, van der Werff H, Viana PL, Zartman CE, Forzza RC. 2017. Amazon plant diversity revealed by a taxonomically verified species list. Proceedings of the National Academy of Sciences USA 114:10695-10700. doi: 10.1073/pnas.1706756114

Carhart-Harris RL, Leech R, Hellyer PJ, Shanahan M, Feilding A, Tagliazucchi E, Chialvo DR, Nutt D. 2014. The entropic brain: a theory of conscious states informed by neuroimaging research with psychedelic drugs. Frontiers in Human Neuroscience 8:20. doi: 10.3389/fnhum.2014.00020

Dawson A. 2013. Santo Daime: A New World Religion. Bloomsbury Academic, London, U.K.

Dinis-Oliveira RJ, Pereira CL, da Silva DD. 2019. Pharmacokinetic and pharmacodynamic aspects of peyote and mescaline: clinical and forensic repercussions. Current Molecular Pharmacology 12:184-194. doi: 10.2174/1874467211666181010154139

Dupuis D. 2021. Psychedelics as tools for belief transmission: set, setting, suggestibility, and persuasion in the ritual use of hallucinogens. Frontiers in Psychology 12:730031. doi: 10.3389/fpsyg.2021.730031

Dupuis D. 2022. The socialization of hallucinations: cultural priors, social interactions, and contextual factors in the use of psychedelics. Transcultural Psychiatry 59:625-637. doi: 10.1177/13634615211036388

Estrada A. 1981. María Sabina: Her Life and Chants. Ross-Erikson, Santa Barbara, U.S.A.

Fernandez JW. 1982. Bwiti: An Ethnography of the Religious Imagination in Africa. Princeton University Press, Princeton, U.S.A.

Gallimore AR. 2015. Restructuring consciousness — the psychedelic state in light of integrated information theory. Frontiers in Human Neuroscience 9:346. doi: 10.3389/fnhum.2015.00346

Gentry AH. 1988. Tree species richness of upper Amazonian forests. Proceedings of the National Academy of Sciences USA 85:156-159. doi: 10.1073/pnas.85.1.156

Glaser B, Birk JJ. 2012. State of the scientific knowledge on properties and genesis of Anthropogenic Dark Earths in Central Amazonia (terra preta de Índio). Geochimica et Cosmochimica Acta 82:39-51. doi: 10.1016/j.gca.2010.11.029

Griffiths RR, Richards WA, McCann U, Jesse R. 2006. Psilocybin can occasion mystical-type experiences having substantial and sustained personal meaning and spiritual significance. Psychopharmacology 187:268-283. doi: 10.1007/s00213-006-0457-5

Hartogsohn I. 2017. Constructing drug effects: a history of set and setting. Drug Science, Policy and Law 3:1-17. doi: 10.1177/2050324516683325

Hasler F, Grimberg U, Benz MA, Huber T, Vollenweider FX. 2004. Acute psychological and physiological effects of psilocybin in healthy humans: a double-blind, placebo-controlled dose-effect study. Psychopharmacology 172:145-156. doi: 10.1007/s00213-003-1640-6

Henrich J. 2016. The Secret of Our Success: How Culture Is Driving Human Evolution, Domesticating Our Species, and Making Us Smarter. Princeton University Press, Princeton, U.S.A.

Holze F, Becker AM, Kolaczynska KE, Duthaler U, Liechti ME. 2022. Pharmacokinetics and pharmacodynamics of oral psilocybin administration in healthy participants. Clinical Pharmacology and Therapeutics 113:822-831. doi: 10.1002/cpt.2821

Johnson MW, Richards WA, Griffiths RR. 2008. Human hallucinogen research: guidelines for safety. Journal of Psychopharmacology 22:603-620. doi: 10.1177/0269881108093587

Kanumuri SRR, Mamallapalli J, Nelson R, McCurdy CR, Mathews CA, Xing C, Sharma A. 2022. Clinical pharmacokinetics of kavalactones after oral dosing of standardized kava extract in healthy volunteers. Journal of Ethnopharmacology 297:115514. doi: 10.1016/j.jep.2022.115514

Letheby C. 2021. Philosophy of Psychedelics. Oxford University Press, Oxford, U.K. doi: 10.1093/med/9780198843122.001.0001

Ley L, Holze F, Arikci D, Becker AM, Straumann I, Klaiber A, Coviello F, Dierbach S, Thomann J, Duthaler U, Luethi D, Varghese N, Eckert A, Liechti ME. 2023. Comparative acute effects of mescaline, lysergic acid diethylamide, and psilocybin in a randomized, double-blind, placebo-controlled cross-over study in healthy participants. Neuropsychopharmacology 48:1659-1667. doi: 10.1038/s41386-023-01607-2

Luna LE. 1986. Vegetalismo: Shamanism Among the Mestizo Population of the Peruvian Amazon. Almqvist & Wiksell International, Stockholm, Sweden.

MacLean KA, Johnson MW, Reissig CJ, Prisinzano TE, Griffiths RR. 2013. Dose-related effects of salvinorin A in humans: dissociative, hallucinogenic, and memory effects. Psychopharmacology 226:381-392. doi: 10.1007/s00213-012-2912-9

Mash DC, Kovera CA, Pablo J, Tyndale RF, Ervin FD, Williams IC, Singleton EG, Mayor M. 2000. Ibogaine: complex pharmacokinetics, concerns for safety, and preliminary efficacy measures. Annals of the New York Academy of Sciences 914:394-401. doi: 10.1111/j.1749-6632.2000.tb05213.x

McKenna DJ, Luna LE, Towers GHN. 1986. Biodynamic constituents in ayahuasca admixture plants: an uninvestigated folk pharmacopoeia. América Indígena 46:73-101. [Originally published in Spanish as "Ingredientes biodinámicos en las plantas que se mezclan al ayahuasca: una farmacopea popular no investigada"; an English-language revision of this work appeared as a chapter in Schultes RE, von Reis S (eds.) 1995. Ethnobotany: Evolution of a Discipline. Portland, Oregon: Dioscorides Press, pp. 349-361.]

McKenna T. 1992. Food of the Gods: The Search for the Original Tree of Knowledge. Bantam, New York, U.S.A.

Mesoudi A, Thornton A. 2018. What is cumulative cultural evolution. Proceedings of the Royal Society B 285:20180712. doi: 10.1098/rspb.2018.0712

Miller MJ, Albarracin-Jordan J, Moore C, Capriles JM. 2019. Chemical evidence for the use of multiple psychotropic plants in a 1000-year-old ritual bundle from South America. Proceedings of the National Academy of Sciences USA 116:11207-11212. doi: 10.1073/pnas.1902174116

Myerhoff BG. 1974. Peyote Hunt: The Sacred Journey of the Huichol Indians. Cornell University Press, Ithaca, U.S.A.

Ott J. 1994. Ayahuasca Analogues: Pangaean Entheogens. Natural Products Company, Kennewick, U.S.A.

Ott J. 2001. Pharmañopo—psychonautics: Human intranasal, sublingual, intrarectal, pulmonary and oral pharmacology of bufotenine. Journal of Psychoactive Drugs 33:273-281. doi: 10.1080/02791072.2001.10400574

Palhano-Fontes F, Barreto D, Onias H, Andrade KC, Novaes MM, Pessoa JA, Mota-Rolim SA, Osório FL, Sanches R, dos Santos RG, Tófoli LF, de Oliveira Silveira G, Yonamine M, Riba J, Santos FR, Silva-Junior AA, Alchieri JC, Galvão-Coelho NL, Lobão-Soares B, Hallak JEC, Arcoverde E, Maia-de-Oliveira JP, Araújo DB. 2019. Rapid antidepressant effects of the psychedelic

ayahuasca in treatment-resistant depression: a randomized placebo-controlled trial. Psychological Medicine 49:655-663. doi: 10.1017/S0033291718001356

Peltoniemi MA, Hagelberg NM, Olkkola KT, Saari TI. 2016. Ketamine: a review of clinical pharmacokinetics and pharmacodynamics in anesthesia and pain therapy. Clinical Pharmacokinetics 55:1059-1077. doi: 10.1007/s40262-016-0383-6

Riba J, Valle M, Urbano G, Yritia M, Morte A, Barbanoj MJ. 2003. Human pharmacology of ayahuasca: subjective and cardiovascular effects, monoamine metabolite excretion, and pharmacokinetics. Journal of Pharmacology and Experimental Therapeutics 306:73-83. doi: 10.1124/jpet.103.049882

Rodd R. 2002. Snuff synergy: preparation, use and pharmacology of yopo and *Banisteriopsis caapi* among the Piaroa of southern Venezuela. Journal of Psychoactive Drugs 34:273-279. doi: 10.1080/02791072.2002.10399963

Ruffell S, Netzband N, Bird C, Young AH, Juruena MF. 2020. The pharmacological interaction of compounds in ayahuasca: a systematic review. Brazilian Journal of Psychiatry 42:646-656. doi: 10.1590/1516-4446-2020-0884

Sarris J, LaPorte E, Schweitzer I. 2011. Kava: a comprehensive review of efficacy, safety, and psychopharmacology. Australian and New Zealand Journal of Psychiatry 45:27-35. doi: 10.3109/00048674.2010.522554

Saslis-Lagoudakis CH, Savolainen V, Williamson EM, Forest F, Wagstaff SJ, Baral SR, Watson MF, Pendry CA, Hawkins JA. 2012. Phylogenies reveal predictive power of traditional medicine in bioprospecting. Proceedings of the National Academy of Sciences USA 109:15835-15840. doi: 10.1073/pnas.1202242109

Schultes RE, Hofmann A, Rätsch C. 2001. Plants of the Gods: Their Sacred, Healing and Hallucinogenic Powers. Healing Arts Press, Rochester, U.S.A.

Schultes RE. 1957. The identity of the malpighiaceous narcotics of South America. Botanical Museum Leaflets, Harvard University 18:1-56.

Schultes RE. 1960. Native narcotics of the New World. Texas Journal of Pharmacy 2:141-167.

Seitz GJ. 1967. Epená, the intoxicating snuff powder of the Waika Indians and the Tucano medicine man, Agostino. In: Efron DH, Holmstedt B, Kline NS. (eds). Ethnopharmacologic Search for Psychoactive Drugs. US Government Printing Office, Washington, DC, U.S.A., Pp. 315-338.

Shen H-W, Jiang X-L, Winter JC, Yu A-M. 2010. Psychedelic 5-Methoxy-*N,N*-dimethyltryptamine: metabolism, pharmacokinetics, drug interactions, and pharmacological actions. Current Drug Metabolism 11:659-666. doi: 10.2174/138920010794233495

Shulgin AT, Shulgin A. 1997. TIHKAL: The Continuation. Transform Press, Berkeley, U.S.A.

Singh YN. 1992. Kava: an overview. Journal of Ethnopharmacology 37:13-45. doi: 10.1016/0378-8741(92)90003-A

Stewart OC. 1987. Peyote Religion: A History. University of Oklahoma Press, Norman, U.S.A.

Strassman RJ, Qualls CR. 1994. Dose-response study of *N,N*-dimethyltryptamine in humans. I. Neuroendocrine, autonomic, and cardiovascular effects. Archives of General Psychiatry 51:85-97. doi: 10.1001/archpsyc.1994.03950020009001

Teschke R, Schwarzenboeck A, Hennermann K-H. 2008. Kava hepatotoxicity — a clinical survey and critical analysis of 26 suspected cases. European Journal of Gastroenterology and Hepatology 20:1182-1193. doi: 10.1097/MEG.0b013e3283036768

Torres CM, Repke DB. 2006. *Anadenanthera*: Visionary Plant of Ancient South America. Haworth Herbal Press, Binghamton, U.S.A.

Wasson RG, Cowan G, Cowan F, Rhodes W. 1974. María Sabina and Her Mazatec Mushroom Velada. Harcourt Brace Jovanovich, New York, U.S.A.

Wasson RG. 1968. Soma: Divine Mushroom of Immortality. Harcourt Brace Jovanovich, New York, U.S.A.

Winkelman MJ. 2017. The mechanisms of psychedelic visionary experiences: hypotheses from evolutionary psychology. Frontiers in Neuroscience 11:539. doi: 10.3389/fnins.2017.00539

Electronic supplementary material

Observability and pharmacological calibration in psychoactive ethnobotany: ceremony duration, admixture selection, and the discovery of ayahuasca

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This document accompanies the main manuscript. Tables S1, S1a, S1b, S2, S3 and the narrative ESM sections N1-N3 are referenced inline in the main text. All numerical values are derived from the canonical data artifacts in the public Zenodo deposit (concept DOI 10.5281/zenodo.19521104), reproducible via the scripts listed therein. Source citations in the ESM tables are the same Literature cited references as the main manuscript; no new references are introduced here.

Table S1. Full admixture plant catalogue (n = 118). Columns: canonical binomial; common name(s); primary source citation(s); purpose-observability coding (observable / mixed / non-observable); pharmacological validation status (validated / not validated / not tested / toxic); toxic flag (Y/N); source-coverage count (number of independent primary sources naming this plant). Sorted by current status (active first) then alphabetically by canonical binomial. Compiled from full_admixture_catalogue.json and full_source_coverage_matrix.csv (Zenodo v7 deposit).

Canonical binomial	Common name(s)	Primary source(s)	Observability	Pharmacological validation	Toxic	# sources
Brugmansia insignis (Barb.Rodr.) Lockwood ex R.E.Schult.	toe	Allan 2026 Track 1; Ott 1994	observable	validated	N	2
Brugmansia suaveolens (Willd.) Sweet	toe, white angel's trumpet	Allan 2026 Track 1; Luna 1986; Ott 1994	observable	validated	N	3
Brunfelsia grandiflora D.Don	chiricsanango	Allan 2026 Track 1; Luna 1986; Ott 1994	observable	validated	N	3
Calycophyllum spp.	capirona	Allan 2026 Track 1	non-observable	not_validated	N	1
Cavanillesia umbellata Ruiz & Pav.	pretino	Allan 2026 Track 1	non-observable	not_validated	N	1
Couroupita guianensis Aubl.	cannonball tree, ayahuma	Allan 2026 Track 1; Luna 1986; Ott 1994	non-observable	not_validated	N	3
Erythroxylum coca Lam.	coca	Allan 2026 Track 1; Ott 1994	observable	validated	N	2
Hura crepitans L.	catahua, sandbox tree	Allan 2026 Track 1; Luna 1986; Ott 1994	non-observable	toxic	Y	3
Ilex guayusa Loes.	guayusa	Allan 2026 Track 1; Ott 1994	observable	validated	N	2
Mansoa alliacea (Lam.) A.H.Gentry	ajo sacha, wild garlic	Allan 2026 Track 1; Luna 1986; Ott 1994	non-observable	validated	N	3
Nicotiana rustica L.	mapacho, sacred tobacco	Allan 2026 Track 1; Ott 1994	observable	validated	N	2
Petiveria alliacea L.	mucura, anamu	Luna 1986; Allan 2026 Track 1	observable	validated	N	2
Abuta grandifolia (Mart.) Sandwith	abuta	Luna 1986; Ott 1994	observable	validated	N	2
Acacia maidenii F.Muell.	—	Ott 1994	observable	validated	N	1
Acacia phlebophylla F.Muell. ex H.B.Will.	—	Ott 1994	observable	validated	N	1
Acacia simplicifolia Druce	—	Ott 1994	observable	validated	N	1

Alchornea castaneifolia (Humb. & Bonpl. ex Willd.) A.Juss.	hiporuru	Luna 1986; Ott 1994	mixed	validated	N	2
Alternanthera sp.	—	Ott 1994	mixed	not_tested	N	1
Alternanthera Lehmanii Hieron.	borrachera, chicha	Schultes 1957	observable	not_tested	N	1
Anadenanthera peregrina (L.) Speg. / A. colubrina (Vell.) Brenan	yopo, cebil, vilca	Rodd 2002	observable	validated	N	1
Aristolochia sp. (proposed by Fischer)	yajé (wrongly)	Schultes 1957	mixed	toxic	Y	1
Banisteriopsis caapi (Spruce ex Griseb.) C.V.Morton	caapi, yajé, ayahuasca, natema, nepe, pinde	Luna 1986; Schultes 1957	observable	validated	N	2
Banisteriopsis inebrians C.V.Morton	yajé, ayahuasca	Luna 1986; Schultes 1957	observable	validated	N	2
Banisteriopsis longialata (Nied.) B.Gates	—	Schultes 1957	mixed	not_tested	N	1
Banisteriopsis lutea (Griseb.) Cuatrec.	—	Ott 1994	mixed	validated	N	1
Banisteriopsis martiniana (Juss.) Cuatrec. var. subenervia (= var. laevis Cuatrec.)	—	Ott 1994	mixed	not_tested	N	1
Banisteriopsis muricata (Cav.) Cuatrec.	mii (Waorani)	Luna 1986; Schultes 1957	observable	validated	N	2
Banisteriopsis quitensis (Nied.) C.V.Morton	yajé, ayawasca, hayawasca	Luna 1986; Schultes 1957	observable	validated	N	2
Banisteriopsis Rusbyana (Nied.) C.V.Morton	chagropanga, yajé	Schultes 1957	observable	validated	N	1
Bauhinia guianensis Aubl.	—	Ott 1994	mixed	not_tested	N	1
Brugmansia versicolor Lagerh.	—	Ott 1994	observable	validated	N	1
Brunfelsia chiricaspi Plowman	chiricaspi	Ott 1994	observable	validated	N	1
Caesalpinia echinata Lam.	Brazilwood	Ott 1994	mixed	not_tested	N	1
Calathea sp.	—	Ott 1994	mixed	not_tested	N	1
Calathea veitchiana Veitch ex Hook.f.	—	Ott 1994	mixed	not_tested	N	1
Callaeum antifebrile (Griseb.) D.M.Johnson	cabi	Luna 1986	mixed	not_tested	N	1
Calliandra angustifolia Spruce ex Benth.	bobinzana	Luna 1986; Ott 1994	non-observable	not_validated	N	2
Campsiandra laurifolia Benth.	acapú do igapó	Ott 1994	mixed	not_tested	N	1
Capirona decorticans Spruce	capirona negra	Luna 1986	mixed	not_tested	N	1
Capsicum sp.	aji, chili pepper	Ott 1994	observable	validated	N	1
Carludovica divergens Drude	—	Ott 1994	mixed	not_tested	N	1
Cedrelinga catanaeformis (Ducke) Ducke	huairacaspi	Luna 1986	non-observable	not_validated	N	1
Cedrelinga catenaeformis (Ducke) Ducke	huairacaspi	Ott 1994	non-observable	not_validated	N	1
Chorisia speciosa A.St.-Hil., A.Juss. & Cambess. (Luna notes: before *Ceiba pentandra* L.)	lupuna	Luna 1986	mixed	toxic	Y	1

Clusia sp.	—	Ott 1994	mixed	not_tested	N	1
Coussapoa tessmannii Mildbr.	—	Ott 1994	mixed	not_tested	N	1
Cyperus sp.	—	Ott 1994	mixed	not_tested	N	1
Cyperus digitatus Roxb.	piripiri	Ott 1994	mixed	not_tested	N	1
Cyperus prolixus Kunth	piripiri	Ott 1994	mixed	not_tested	N	1
Datura sp. (= *Brugmansia* in modern nomenclature)	guanto, maicoma, maikoa	Schultes 1957	observable	validated	N	1
Desmanthus illinoensis (Michx.) MacMill. ex B.L.Rob. & Fernald	prairie bundleflower	Ott 1994	observable	validated	N	1
Desmodium gangeticum (L.) DC.	—	Ott 1994	observable	toxic	Y	1
Dieffenbachia sp.	patiquina, patuquina negra	Luna 1986	mixed	toxic	Y	1
Diplopterys cabrerana (Cuatrec.) B.Gates	chaliponga, chagrupanga, ocó yagé	Luna 1986; Ott 1994; Schultes 1957	observable	validated	N	3
Diplopterys involuta (Turcz.) Nied. = Mezia includens (Benth.) Cuatrec.	ayahuasca negro	Ott 1994	mixed	not_tested	N	1
Dutaillyea oreophila †	—	Ott 1994	observable	toxic	Y	1
Erythrina glauca Willd.	—	Ott 1994	mixed	validated	N	1
Erythrina poeppigiana (Walp.) O.F.Cook	amaciza	Luna 1986; Ott 1994	mixed	validated	N	2
Ficus sp.	renaco	Luna 1986	non-observable	not_validated	N	1
Ficus insipida Willd.	doctor ojé, ojé	Luna 1986; Ott 1994	observable	validated	N	2
Ficus ruiziana Standl.	—	Ott 1994	mixed	not_tested	N	1
Gnetum nodiflorum Brongn.	—	Ott 1994	mixed	not_tested	N	1
Guettarda ferox Standl.	—	Ott 1994	mixed	not_tested	N	1
Himatanthus sucuuba (Spruce ex Müll.Arg.) Woodson	bellaco caspi	Luna 1986	non-observable	not_validated	N	1
Huancavisacha sp. unidentified	huancavisacha	Luna 1986	mixed	not_tested	N	1
Iochroma fuchsioides (Bonpl.) Miers	—	Ott 1994	mixed	validated	N	1
Iryanthera ulei Warb.	—	Ott 1994	observable	validated	N	1
Jatropha gossipifolia L.	piñón rojo	Luna 1986	non-observable	not_validated	N	1
Juanulloa ochracea Cuatrec.	—	Ott 1994	mixed	not_tested	N	1
Lippia odorata (Poepp. & Endl.) Poepp.	—	Ott 1994	mixed	not_tested	N	1
Lomariopsis japurensis (C.Martius) J.Sm.	—	Ott 1994	mixed	not_tested	N	1
Lophanthera lactescens Ducke	—	Ott 1994	mixed	not_tested	N	1

Lygodium venustum Sw.	—	Ott 1994	mixed	not_tested	N	1
Malouetia Tamaquarina (Aubl.) A.DC.	gway-ee-ga-mo-yoo-he-re (Makuna), tree of the gill of fishes	Schultes 1957; Schultes 1960	mixed	toxic	Y	2
Mascagnia psilophylla (A.Juss.) Griseb. var. antifebrilis Ndz.	—	Schultes 1957	mixed	not_tested	N	1
Maytenus ebenifolia Reissek	chuchuhuasi	Luna 1986; Ott 1994	observable	validated	N	2
Melicope leptococca Guillaumin	—	Ott 1994	observable	toxic	Y	1
Mimosa hostilis Benth. (= *Mimosa tenuiflora* (Willd.) Poir.)	jurema	Ott 1994	observable	validated	N	1
Mimosa nigra Huber	—	Ott 1994	mixed	not_tested	N	1
Mimosa verrucosa Benth.	—	Ott 1994	mixed	not_tested	N	1
Montrichardia arborescens (L.) Schott	raya-balsa	Luna 1986	non-observable	not_validated	N	1
Nicotiana Tabacum L.	tobacco	Ott 1994; Schultes 1957	observable	validated	N	2
Ocimum micranthum Willd.	albahaca	Ott 1994	mixed	validated	N	1
Osteophloeum platyspermum (Spruce ex A.DC.) Warb.	—	Ott 1994	observable	validated	N	1
Paullinia yoco R.E.Schult. & Killip	yoco	Ott 1994	observable	validated	N	1
Peganum harmala L.	Syrian rue	Ott 1994	observable	validated	N	1
Phalaris tuberosa L.	—	Ott 1994	observable	validated	N	1
Phrygilanthus eugenioides (Kunth) Eichler	—	Ott 1994	mixed	not_tested	N	1
Phthirusa pyrifolia Eichler	suelda con suelda	Ott 1994	observable	not_tested	N	1
Phtirusa pyrifolia Eichler	suelda con suelda	Luna 1986	observable	not_tested	N	1
Pilocarpus organensis Occhioni & Rizzini	—	Ott 1994	observable	toxic	Y	1
Pithecellobium laetum Benth.	remo caspi	Luna 1986; Ott 1994	mixed	not_tested	N	2
Prestonia amazonica J.F.Macbr.	caapi-pinima, painted caapi, yajé (incorrectly)	Schultes 1957	mixed	not_validated	N	1
Psychotria carthagenensis Jacq.	amyruca, sameruka	Ruffell 2020	observable	validated	N	1
Psychotria carthaginensis Jacq.	amyruca	Luna 1986; Ott 1994	observable	validated	N	2
Psychotria poeppigiana Müll.Arg.	—	Ott 1994	mixed	not_tested	N	1
Psychotria psychotriaefolia (Seem.) Standl.	—	Ott 1994	observable	not_tested	N	1
Psychotria viridis Ruiz & Pav.	chacruna	Luna 1986; Ott 1994	observable	validated	N	2
Rinorea viridiflora (Tul.) Baill.	—	Ott 1994	mixed	not_tested	N	1
Rudgea retifolia Standl.	—	Ott 1994	mixed	not_tested	N	1

Sabicea amazonensis Wernham	—	Ott 1994	mixed	not_tested	N	1
Sclerolobium setiferum Ducke	—	Ott 1994	mixed	not_tested	N	1
Scoparia dulcis L.	ñuc-ñuc pichana	Luna 1986; Ott 1994	mixed	validated	N	2
Stigmaphyllon fulgens A.Juss.	—	Ott 1994	mixed	not_tested	N	1
Tabebuia heteropoda (DC.) Sandwith	tahuarí	Luna 1986	mixed	validated	N	1
Tabernaemontana sp.	uchu-sanango	Luna 1986	mixed	validated	N	1
Tabernaemontana sananho Ruiz & Pav.	sananho, uchu-sanango	Ott 1994	observable	validated	N	1
Tetrapterys methystica R.E.Schult.	caapi-pinima, painted caapi	Luna 1986; Schultes 1957	observable	validated	N	2
Tetrapterys mucronata Cav.	—	Ott 1994	mixed	not_tested	N	1
Tovomita sp.	chullachaqui-caspi	Luna 1986; Ott 1994	mixed	not_validated	N	2
Triplaris surinamensis Cham. var. chamissoana Meisn.	tangarana	Luna 1986	observable	not_validated	N	1
Tynanthus panurensis (Bureau) Sandwith	clavohuasca	Luna 1986	mixed	not_tested	N	1
Uncaria guianensis (Aubl.) J.F.Gmel.	uña de gato, cat's claw	Ott 1994	observable	validated	N	1
Vepris ampody H.Perrier	—	Ott 1994	observable	toxic	Y	1
Virola sp. Aubl.	cumala	Luna 1986; Rodd 2002	observable	validated	N	2
Virola surinamensis (Rol. ex Rottb.) Warb.	caupuri	Luna 1986	observable	validated	N	1
Vitex triflora Vahl	—	Ott 1994	mixed	not_tested	N	1
Vouacapoua americana Aubl.	huacapú	Luna 1986; Ott 1994	mixed	not_tested	N	2

† Name as used in the phytochemical source literature (Baudouin *et al.* 1981). The combination *Dutaillyea oreophila* has no nomenclatural record in World Flora Online or IPNI: the IPNI treatment of *Dutaillyea* Baill. (Rutaceae; urn:lsid:ipni.org:names:35698-1) holds nine records, none carrying this epithet. Retained as sourced.

Table S1a. Statistical-test sensitivity on the observability × active/candidate contingency table. Computed from full_admixture_catalogue.json. The 3×2 full test uses Pearson chi-square; the 2×2 variants report BOTH Fisher's exact test (two-sided) AND Pearson chi-square with Yates continuity correction, as a transparency / robustness pairing. The two methods agree on directionality and rank-order significance for both 2×2 variants; the magnitude differs modestly because Fisher exact is the conservative reference for small, expected cell counts (the strict-2×2 cell [5, 7] has expected count below 5 under independence). Main-text p-values are the Fisher exact values; the chi-square values are reported here for sensitivity. All variants remain significant at $\alpha = 0.05$ under either test, and the 2×2 collapsed variant remains significant at $\alpha = 0.001$ under either test.

Test	Contingency table (active / candidate)	Method	Statistic	df	p	OR (95% CI)
3×2 full (observable / mixed / non-observable)	[[7, 0, 5], [43, 56, 7]]	Pearson χ^2	$\chi^2 = 20.17$	2	4.16×10^{-5}	—
2×2 collapsed (mixed → observable)	[[7, 5], [99, 7]]	Fisher exact (two-sided)	—	—	2.46×10^{-3}	OR = 0.099 (95% CI 0.025-0.394)
2×2 collapsed (mixed → observable)	[[7, 5], [99, 7]]	Pearson χ^2 (Yates corr.)	$\chi^2 = 10.92$	1	9.50×10^{-4}	—
2×2 strict (mixed excluded)	[[7, 5], [43, 7]]	Fisher exact (two-sided)	—	—	4.43×10^{-2}	OR = 0.228 (95% CI 0.056-0.923)
2×2 strict (mixed excluded)	[[7, 5], [43, 7]]	Pearson χ^2 (Yates corr.)	$\chi^2 = 3.14$	1	7.65×10^{-2}	—

Counts from full_admixture_catalogue.json (n = 118): active (n = 12) = 7 observable + 0 mixed + 5 non-observable; candidate (n = 106) = 43 observable + 56 mixed + 7 non-observable. Pearson χ^2 implemented in scipy.stats.chi2_contingency (correction=True for the 2×2 variants); Fisher exact in scipy.stats.fisher_exact with two-sided alternative.

Table S1b. Nine toxic plants in the candidate pool absent from contemporary active practice. Toxic flag derived from pharmacological-validation = 'toxic' in full_admixture_catalogue.json. Phytochemistry source is the active-compound field of the catalogue, with the rejected toxic mechanism named per row. *Hura crepitans* (the tenth toxic-flagged plant in the catalogue) is in the active set under Luna's purgative classification — discussed in narrative section N2 below.

Genus/species	Family	Active toxic compound(s)	Toxic mechanism / outcome	Primary source
Aristolochia sp. (proposed by Fischer)	Aristolochiaceae	Aristolochic acids are nephrotoxic and carcinogenic; genus-level hazard	Documented in Schultes 1957 but absent from Luna 1986 AND Track 1 2026 — clean 'abandoned by 1986' signal	Schultes 1957
Malouetia Tamaquarina (Aubl.) A.DC.	Apocynaceae	Steroid alkaloids (malouphylline); latex is toxic	Documented in Schultes 1957 but absent from Luna 1986 AND Track 1 2026 — clean 'abandoned by 1986' signal	Schultes 1957; Schultes 1960
Chorisia speciosa A.St.-Hil., A.Juss. & Cambess. (Luna notes: before *Ceiba pentandra* L.)	Malvaceae (formerly Bombacaceae)	Ceiba-family plants contain toxic saponins; Luna notes 'might kill' and 'sap used in magical art of wizard' (p. 70)	Documented in Luna 1986 but not Track 1 2026; specialist-use or regionally-partitioned admixture	Luna 1986
Dieffenbachia sp.	Araceae	Calcium oxalate raphides, proteolytic enzymes; irritant/toxic but no CNS or anti-spirit validation	Documented in Luna 1986 but not Track 1 2026; specialist-use or regionally-partitioned admixture	Luna 1986
Pilocarpus organensis Occhioni & Rizzini	Rutaceae	Pilocarpine (imidazole alkaloid) in several Pilocarpus species; potentially lethal; explicit TOXIC WARNING for ayahuasca analogue experimenters	Mentioned only by Ott 1994 as analogue candidate; not part of traditional Amazonian practice	Ott 1994
Desmodium gangeticum (L.) DC.	Fabaceae	Hordenine (toxic psychoactive)	Mentioned only by Ott 1994 as analogue candidate; not part of traditional Amazonian practice	Ott 1994
Dutaillyea oreophila †	Rutaceae	Hordenine	Mentioned only by Ott 1994 as analogue candidate; not part of traditional Amazonian practice	Ott 1994
Melicope leptococca Guillaumin	Rutaceae	5-MeO-DMT + 8 other alkaloids of obscure toxicity	Mentioned only by Ott 1994 as analogue candidate; not part of traditional Amazonian practice	Ott 1994
Vepris ampody H.Perrier	Rutaceae	DMT + 7 other alkaloids of obscure toxicity	Mentioned only by Ott 1994 as analogue candidate; not part of traditional Amazonian practice	Ott 1994

† Name as used in the phytochemical source literature (Baudouin *et al.* 1981). The combination *Dutaillyea oreophila* has no nomenclatural record in World Flora Online or IPNI: the IPNI treatment of *Dutaillyea* Baill. (Rutaceae; urn:lsid:ipni.org:names:35698-1) holds nine records, none carrying this epithet. Retained as sourced.

Table S2. Per-tradition ceremony duration, pharmacokinetic effect duration, and ceremony-to-PK ratio for the eleven independent indigenous traditions (rows 1-11) plus three modern clinical-pharmacology protocols (rows 12-14). Central-estimate values are those used in the log-Pearson confirmatory test. Receptor-system class reflects the pharmacological-class enumeration in Methods §Tradition selection (n = 7 receptor systems). Source columns name the ethnographic and clinical-pharmacology references for ceremony and PK values respectively; full citations are in the main manuscript's Literature cited section.

Tradition	Region	Substance	Receptor class	Ceremony (h)	PK (h)	Ratio	Ethnographic source	Pharmacology source
Amazonian ayahuasca	South America	ayahuasca (DMT + harmala β-carbolines)	5-HT2A (oral with MAO-I)	5	4	1.25	Beyer 2009; Luna 1986	Callaway *et al.* 1999; Riba *et al.* 2003
Santo Daime hinário	South America	ayahuasca (Daime)	5-HT2A (oral with MAO-I)	10	4	2.50	Dawson 2013	Callaway *et al.* 1999
União do Vegetal (UDV)	South America	ayahuasca (hoasca)	5-HT2A (oral with MAO-I)	4	4	1.00	Callaway *et al.* 1999	Callaway *et al.* 1999
Peyote NAC/Huichol	North America	mescaline	5-HT2A	10	10	1.00	Stewart 1987; Myerhoff 1974	Dinis-Oliveira *et al.* 2019; Ley *et al.* 2023
Bwiti iboga	Africa	ibogaine	NMDA / σ / multi-target	24	24	1.00	Fernandez 1982	Mash *et al.* 2000
Mazatec velada	North America	psilocybin (psilocin active)	5-HT2A	6	5	1.20	Estrada 1981; Wasson *et al.* 1974	Hasler *et al.* 2004; Brown *et al.* 2017
Mazatec salvia barrida	North America	salvinorin A	κ-opioid	0.17	0.17	1.00	MacLean *et al.* 2013	MacLean *et al.* 2013
Fijian yaqona (kava)	Oceania	kavalactones	GABA-A positive allosteric modulator	5.5	4	1.38	Aporosa 2014; Singh 1992; Aporosa 2022	Singh 1992; Kanumuri *et al.* 2022; Sarris *et al.* 2011; Teschke *et al.* 2008
Yanomami epená (*Virola* snuff)	South America	DMT + 5-MeO-DMT insufflated	5-HT2A (insufflated)	1	0.75	1.33	Seitz 1967	Ott 2001; Torres & Repke 2006; Shulgin & Shulgin 1997
Siberian fly agaric (Koryak)	Eurasia	muscimol	GABA-A direct agonist	10	6	1.67	Wasson 1968	Wasson 1968 (synthesis +

								secondary clinical)
Mazatec ololiuhqui	North America	lysergic acid amide (ergine, LSA)	5-HT2A ergoline	3	3	1.00	Schultes, Hofmann & Rätsch 2001	Schultes, Hofmann & Rätsch 2001
Modern clinical psilocybin (Johns Hopkins)	Clinical	psilocybin	5-HT2A	6	5	1.20	Griffiths *et al.* 2006; Johnson *et al.* 2008	Hasler *et al.* 2004; Brown *et al.* 2017
Modern clinical ayahuasca	Clinical	ayahuasca (DMT + harmala)	5-HT2A (oral with MAO-I)	4	4	1.00	Palhano-Fontes *et al.* 2019	Riba *et al.* 2003
Modern clinical DMT iv (UNM)	Clinical	DMT (intravenous)	5-HT2A (intravenous)	0.25	0.5	0.50	Strassman & Qualls 1994	Strassman & Qualls 1994

Confirmatory test on rows 1-11 (indigenous n = 11): log-Pearson r = 0.977, $p = 2.5 \times 10^{-7}$; slope = 1.010; 95% CI Fisher z = [0.910, 0.994]. Exploratory full test (rows 1-14, n = 14): log-Pearson r = 0.971, $p = 8.1 \times 10^{-9}$. Computed via compute_revision_analyses.py + compute_expansion_revision_analyses.py from the central ceremony and PK values listed above.

Table S3 — Search-space parameter trace, sensitivity heatmaps, and full simulation results

Table S3-i. Search-space parameter trace. Each row names a simulation parameter, the value (or range) used, and the primary source from which the value was drawn. Values reproduce ayahuasca_search_simulation.py + search_space_parameters.json. Page-level references retained where available in the source citation.

Parameter	Value or range	Unit	Source
Amazonian vascular flora (verified)	14003	species	Cardoso D *et al.* 2017, An updated, taxonomically verified checklist of Amazonian vascular plants, PNAS 114(40):10695-10700
Amazonian vascular flora (upper estimate)	14,003-16,000	species	Cardoso *et al.* 2017 PNAS, noting that ferns, lycophytes and fungi would add to the vascular count
Ingestible-fraction estimate	10.0%-30.0%	fraction	Documented in search_space_parameters.json (ingestible_fraction_estimate.source field) of the public Zenodo deposit. Supported by broader ethnobotanical screening literature.
Candidate ingestible species (low)	1600	species	Cardoso 2017 base x 0.10 ingestible fraction; rounded
Candidate ingestible species (mid)	3000	species	Cardoso 2017 base x 0.20 ingestible fraction (midpoint)
Candidate ingestible species (high)	4500	species	Cardoso 2017 base x 0.30 ingestible fraction
DMT-containing species (confirmed Amazonian)	8	species	*Psychotria viridis*, *Diplopterys cabrerana*, *Virola surinamensis*, *Virola theiodora*, *Virola calophylla*, *Anadenanthera peregrina*, *Anadenanthera colubrina*, *Mimosa tenuiflora*
DMT-containing species (extended)	20	species	Includes lower-concentration DMT sources and phytochemically screened species that contain detectable tryptamines even if not traditionally used. Upper bound for sensitivity analysis.
MAO-I-containing species (confirmed Amazonian)	3	species	*Banisteriopsis caapi*, *Banisteriopsis muricata*, *Diplopterys cabrerana* (minor beta-carboline content)
MAO-I-containing species (extended)	10	species	Includes additional Malpighiaceae and other families with trace beta-carbolines, and plants with alternative MAO-I compounds. Upper bound for sensitivity.
Valid combinations V = D × M (low)	24	ordered pairs of species	8 DMT x 3 MAO-I = 24
Valid combinations V = D × M (high)	200	ordered pairs of species	20 DMT x 10 MAO-I = 200
Cue hit rate — conservative	0.1	fraction	Strict interpretation: only plants with highly distinctive cues (e.g., B. caapi's corkscrew vine morphology) count
Cue hit rate — moderate	0.3	fraction	Includes plants with notable-but-not-unique features
Cue hit rate — generous	0.5	fraction	Includes any plant with a detectable taste/smell/latex cue

Cue testing-bias multiplier	—	×	How much more likely a cued plant is to be tested vs a random plant, per generation
Habitat species estimate (low)	100	species	Local species diversity in a single Amazonian forest patch can exceed 300 tree species per hectare (Gentry 1988), but the subset that co-occurs with B. caapi specifically is smaller. This is a bounded estimate.
Habitat species estimate (mid)	250	species	—
Habitat species estimate (high)	500	species	—
Generations available	400	generations	10,000 years of habitation / 25 years per generation
Trials per generation (range)	5-200	trials/gen	How many distinct plant trials a specialist community conducts per generation. Low: one specialist doing one trial every 5 years. High: multiple specialists across villages, several per year.
Generation time	25	years	Anthropological convention
Archaeological minimum (earliest documented use)	1000	years BP	Miller MJ, Albarracin-Jordan J, Moore C, Capriles JM 2019, Chemical evidence for the use of multiple psychotropic plants in a 1,000-year-old ritual bundle from South America, PNAS 116(23):11207-11212
Linguistic depth estimate	1,500-5,000	years BP	Multiple unrelated language families have distinct terms for ayahuasca - suggesting deep time depth; upper bound is a conservative guess consistent with linguistic reconstruction
Specialists concurrent (estimate)	1,000-10,000	specialists	Pre-Columbian Amazonian populations ~1-10 million; specialists/shamans ~0.1-0.5% of population

Figures S3a-S3b. Sensitivity heatmaps for Strategy 4 (iterative search from *Banisteriopsis caapi* baseline). Both figures generated by ayahuasca_search_simulation.py (RNG seed 20260410, 10,000 iterations per parameter cell). Source PNG files in zenodo_v7/bundle/ancillary/process_archaeology/figures/.

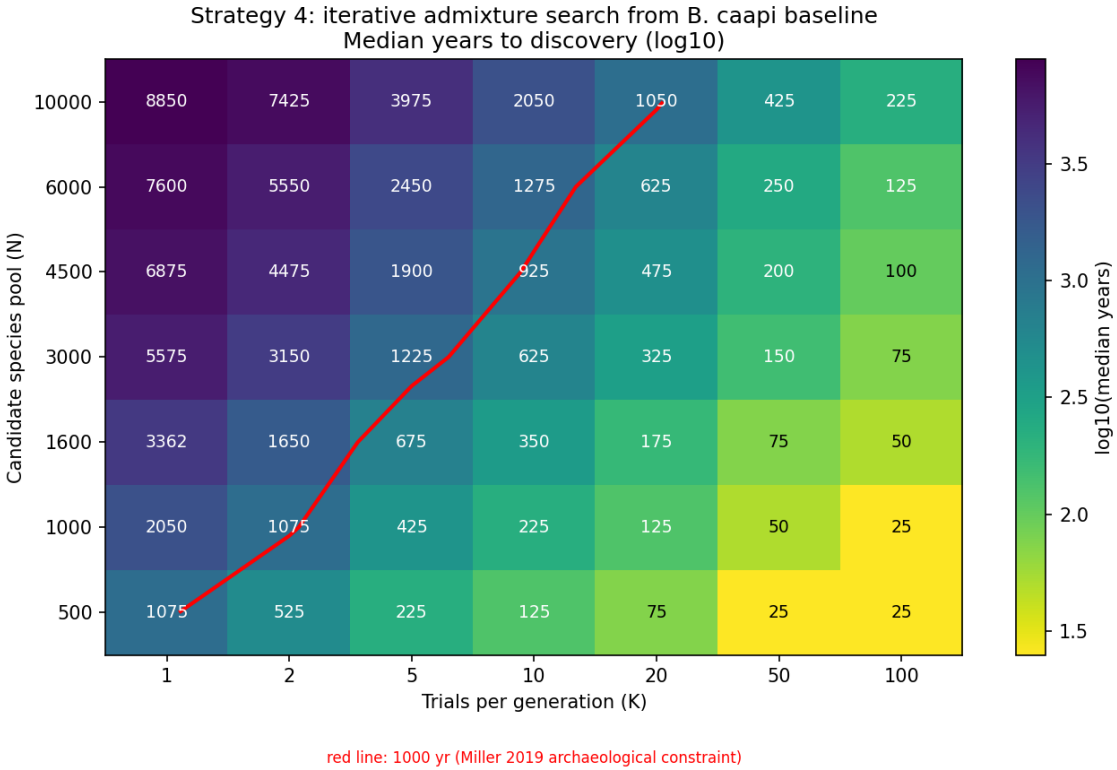

Figure S3a. Heatmap of median years to discovery for Strategy 4 across N (candidate-flora size) and K (trials per generation) parameter grid. 100% success rate across all tested cells; median years ranges from 25 (N=500, K=100) to >6,000 (N=4,500, K=1). The parameter region compatible with the 1,000-year archaeological constraint (Miller *et al.* 2019) covers the majority of the tested space.

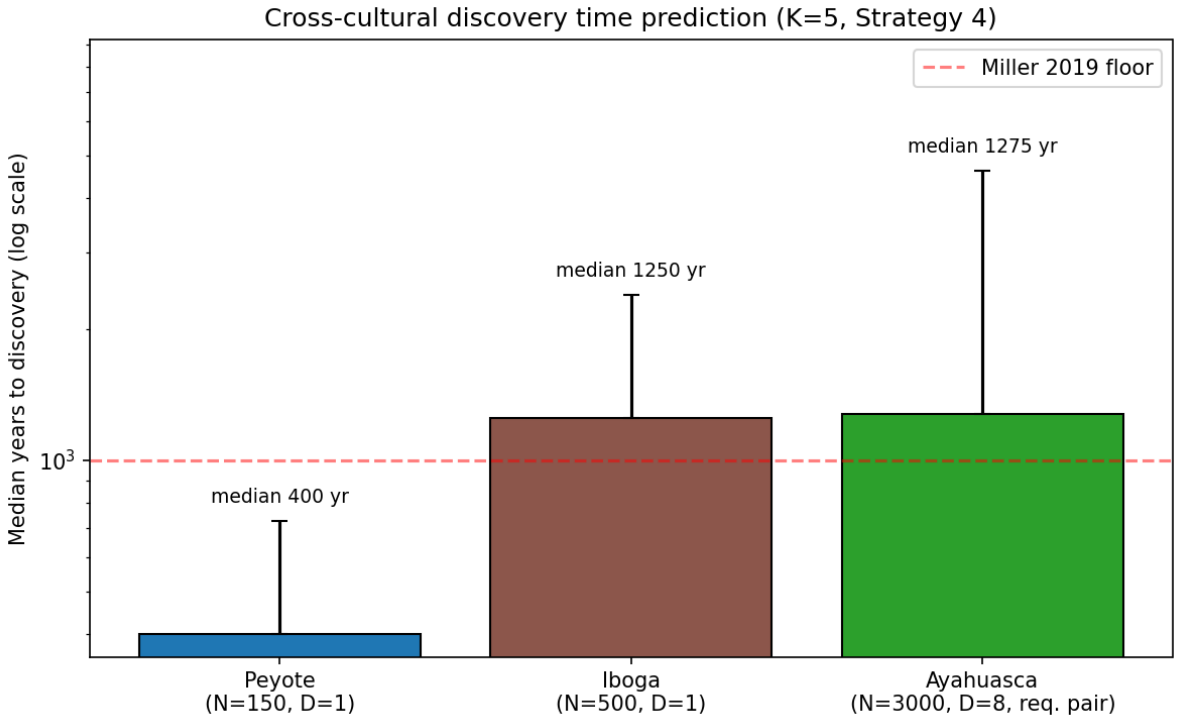

Figure S3b. Cross-cultural prediction — peyote (*Lophophora williamsii* in the Chihuahuan Desert flora, single target) and iboga (*Tabernanthe iboga* in the West African Apocynaceae subset, single target) under Strategy 4 with reduced search-space parameters. Peyote median 400 years (95th percentile 725); iboga median 1,250 years (95th percentile 2,400). Smaller-flora / single-target case converges ~3× faster than ayahuasca, consistent with the analytical expectation.

Table S3-iii. Full simulation results — representative parameter cell per strategy. Each row reports median years to discovery, 5th and 95th percentiles of successful iterations, and success rate (fraction of iterations that reached a valid DMT + MAO-I combination before the 10,000-year budget expired). Strategies 1-2 (pure random / random with memory) fail to reach the archaeological window in the majority of iterations; strategies 4-5 (iterative-from-baseline / ecological co-occurrence) succeed in 100% of iterations with median discovery times of 50-150 years. Full parameter-grid results in search_simulation_results.json.

Strategy	Cell	Median years	5th %ile	95th %ile	Success rate
1. Pure random	N1600_V24_K20	9,050	775	18,692	26%
2. Random + memory	N1600_V24_K20	9,025	800	18,650	26%
3. Cue-guided	N1600_V24_K20_cf0.3_cb3	7,525	675	18,425	65%
4. Iterative from B. caapi	N1600_D14_K20	100	25	400	100%
5. Ecological co-occurrence	Nhab100_Dhab3_K20	50	25	100	100%
6. Pharmacological null	N1000_D14_Kyr100	1	1	2	100%

Table S4. Robustness diagnostics for the ceremony-pharmacokinetic correlation (n = 11 indigenous traditions). Leave-one-out Pearson r is computed on log10-transformed durations; Cook's distance and leverage are computed on the published regression direction, log10(ceremony) ~ log10(pk). Values recomputed from the frozen arrays in expansion_revision_analyses.json; no input data was modified and no previously reported statistic changed. Full-sample values: log-Pearson r = 0.9768 (p = 2.51e-07); Spearman rho = 0.9203 (p = 5.95e-05).

Excluded tradition	n remaining	Pearson r (log10)	p	Cook's D	Leverage h
Amazonian ayahuasca	10	0.9767	1.24e-06	0.0000	0.0925
Santo Daime hinário	10	0.9913	2.44e-08	0.2939	0.0925
UDV	10	0.9783	9.39e-07	0.0305	0.0925
Peyote NAC/Huichol	10	0.9776	1.07e-06	0.0666	0.1600
Bwiti iboga	10	0.9745	1.81e-06	0.2151	0.3177
Mazatec velada	10	0.9767	1.26e-06	0.0012	0.0997
Mazatec salvia	10	0.9433	4.22e-05	0.8966	0.6241
Fijian yaqona (kava)	10	0.9770	1.20e-06	0.0055	0.0925
Yanomami epená (*Virola* snuff)	10	0.9736	2.06e-06	0.0134	0.2267
Siberian fly agaric (Koryak)	10	0.9784	9.33e-07	0.0609	0.1100
Mazatec ololiuhqui	10	0.9781	9.73e-07	0.0295	0.0918

Leave-one-out range: r = 0.9433 (excluding Mazatec salvia) to 0.9913 (excluding Santo Daime hinário). Cook's distance threshold 4/n = 0.3636; observations exceeding it: Mazatec salvia. The salvia session is the shortest ceremony in the sample by an order of magnitude and therefore sits at the extreme of the predictor range, so its high leverage is expected by construction; excluding it leaves r = 0.9433.

Narrative ESM sections

N1. Nonparametric bootstrap CI at n = 9

At n = 9 the indigenous-only nonparametric bootstrap is near the edge of its reliable regime (the minimum sample size at which the 95% CI is well-calibrated is typically n ≈ 12). For transparency we report the bootstrap CIs here, but rely on the Fisher z-transform analytical CI as the primary interval estimate in the main text. Bootstrap (10,000 iterations, RNG seed 20260410): log-Pearson r 95% CI [0.799, 0.998]; log-log slope 95% CI [0.675, 1.116]. Computed via compute_revision_analyses.py.

N2. *Hura crepitans* phorbol-ester discrepancy

Hura crepitans L. (Euphorbiaceae) is in the contemporary active admixture set per Luna (1986), where it is coded as *observable* on its documented purgative function. The phytochemistry, however, would warrant a toxic flag: *Hura* latex is rich in phorbol-ester diterpenoids (huratoxin family) that are vesicant and irritant; the same diterpene class is responsible for the ichthyotoxic (piscicide) use of *Hura crepitans* wood and bark in Amazonian fishing practice. We retain Luna's observable-active coding on the basis that the purgative effect itself is verifiable and was the basis for the traditional inclusion; the phorbol-ester toxicity is a real concern that an ethnopharmacological evaluation of the plant would need to address. This is the one plant in the active set for which our observability coding rule and the phytochemistry would assign different validation labels.

N3. Full per-tradition pharmacological sources

Pharmacology-source column of Table S2 lists the principal references; this section extends those entries with secondary citations where the PK central estimate is drawn from a synthesis rather than a single study.

Substance	Route	Half-life / duration	Source(s)
DMT	intravenous	total duration 0.5 h; half-life 9 min	Strassman & Qualls 1994 Arch Gen Psychiatry 51:85-97
5-MeO-DMT	inhaled / vaporized	total duration 0.33 h	Shen *et al.* 2010 Drug Metab Dispos (preclinical)
psilocybin (psilocin active)	oral	total duration 5 h; half-life 180 min	Hasler 2004 Psychopharmacology 172:145-156; Brown 2017 Clin Pharmacokinet; Holze 2022 Clin Pharmacol Ther
mescaline	oral	total duration 10 h; half-life 216 min	Dinis-Oliveira 2019 Curr Mol Pharmacol 12(3):184-194; Ley 2023 Transl Psychiatry
ayahuasca (DMT + β-carbolines)	oral	total duration 4 h; half-life not_extracted_precise min	Riba 2003 J Pharmacol Exp Ther 306:73-83
ibogaine	oral	total duration 8 h; half-life 240 min	Mash 2000 Ann NY Acad Sci
ketamine	intravenous	total duration 0.25 h; half-life 150 min	Peltoniemi 2016 Clin Pharmacokinet
salvinorin A	smoked / inhaled	total duration 0.17 h; half-life 75 min	MacLean 2013 Psychopharmacology 226(2):381-392 human dose-response
kavalactones (kavain, dihydrokavain, methysticin, yangonin, desmethoxyyangonin, dihydromethysticin)	oral (pounded or masticated root infusion)	total duration 4.0 h	Kanumuri SR *et al.* 2022 J Ethnopharmacol 297:115514 DOI 10.1016/j.jep.2022.115514 (Tmax 1-3h for kavain); Sarris J *et al.* 2011 Aust NZ J Psychiatry 45(1):27-35 DOI 10.3109/00048674.2010.522554 (clinical review); Teschke R 2008 Eur J Gastroenterol Hepatol 20(12):1182-1188 DOI 10.1097/MEG.0b013e3283036768

DMT + 5-MeO-DMT insufflated (*Virola* resin snuff)	nasal insufflation	total duration 0.75 h	Ott J 2001 'Pharmanopo-Psychonautics: Human Intranasal, Sublingual, Intrarectal, Pulmonary and Oral Pharmacology of Bufotenine' J Psychoactive Drugs 33(3):273-281 DOI 10.1080/02791072.2001.10400574; Torres CM & Repke DB 2006 *Anadenanthera*: Visionary Plant of Ancient South America (Haworth Press); Shulgin A & Shulgin A 1997 TiHKAL (Transform Press)
muscimol (*Amanita muscaria*)	oral	total duration 6.0 h	Wasson 1968 'Soma' p. 162 narrative synthesis; muscimol clinical pharmacology onset 30-120 min, peak 1-3h, total 4-8h. Secondary clinical pharmacology parameters (onset, peak, total duration) documented in ceremony_pharmacokinetics.json (pharmacokinetics field) of the public Zenodo deposit.
lysergic acid amide (ergine, LSA) — Ololiuhqui	oral	total duration 3.0 h	Schultes, Hofmann & Rätsch 2001 'Plants of the Gods' p. 174 (verbatim above); see also p. 171 on LSA chemistry (2-5 mg hallucinogenic dose, ~100x less potent than LSD).