

## Measurable Before Explicable

### Hofmann's Ololiuqui Finding as the Earliest Chemical Detection of a Plant-Fungus Symbiosis

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#### Abstract

Between 1960 and 1963 Albert Hofmann demonstrated lysergic acid amides in the seeds of Mexican morning glories. The finding contradicted the assumption that ergolines are products of fungi in the Clavicipitaceae, and for decades it was filed as a case of chemical convergence in secondary metabolism. Between 2004 and 2011 it emerged that the alkaloids originate in epibiotic fungi of the newly described genus *Periglandula*, which live on the upper leaf surface of the host plants.

This paper argues that Hofmann's measurement thereby acquires, retrospectively, the status of a demonstration of symbiosis — the earliest chemical one in this system. The analysis was correct; the attribution of the producer was systematically wrong. A point in the theory of science follows: measurability and explicability can lie decades apart, and the gap is not an error of the person measuring but a state of the disciplinary landscape.

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#### 1. The Finding

After the Mazatec mushroom rituals were publicised, attention also turned to other plants named in the Mexican tradition. Ololiuqui — seeds of *Rivea corymbosa*, today usually given as *Turbina corymbosa* — and badoh negro (*Ipomoea violacea*) had been described as ritually used agents since the early colonial sources.

Hofmann examined the material at Sandoz and found lysergic acid amide (ergine) and related compounds. The summary account appeared as “Die Zauberdroge «Ololiuqui»” in *Planta Medica* 9 (1963) 354–367. [G]

#### 2. Why the Finding Was Anomalous

The ergolines were well characterised by that point — Hofmann himself had contributed substantially to that characterisation. They were held to be products of the Clavicipitaceae, that is, of ascomycete fungi, known above all from *Claviceps purpurea* on grasses.

Hofmann found them in Convolvulaceae: in dicotyledonous flowering plants, separated from grasses by the full breadth of angiosperm phylogeny, and from fungi by the separation of kingdoms.

The rule this finding violated is a working rule of natural-product chemistry: identical or structurally related secondary metabolites occur in organisms sharing an evolutionary history. [G] The disjunct distribution of ergolines across two unrelated taxa — Clavicipitaceae and Convolvulaceae — contradicted it directly.

### 3. The Auxiliary Hypothesis

The literature responded with the assumption of chemical convergence: two unrelated lineages were supposed to have developed the same complex metabolic pathway independently. Kurt Mothes treated the problem explicitly under this heading. [G]

The assumption is not absurd, but it is expensive. Ergoline biosynthesis is multi-step and enzymatically elaborate; an independent second origin of the entire pathway is improbable. The hypothesis persisted because no better one was available — a textbook case of an auxiliary assumption that manages an anomaly rather than solving it.

Matters were complicated by the heterogeneity of the findings in the Convolvulaceae. All three major ergoline types have been reported from the family — clavines, lysergic acid amides and ergopeptines — along with compounds peculiar to the group such as cycloclavine from *Ipomoea hildebrandtii*. [G] All reports come from the species-rich tribe Ipomoeae and show no clear phylogenetic pattern. [G] A trait without a phylogenetic pattern is an indication that it does not follow the phylogeny of the organism being examined.

### 4. The Resolution, 2004–2011

**2004 — the fungicide experiment.** Kucht and co-workers treated *Ipomoea asarifolia* with two fungicides. The ergoline alkaloids disappeared; the plant's volatile oil remained. Concurrently with the loss of alkaloids, fungal hyphae associated with secretory glands on the upper leaf surface disappeared. [G] The conclusion: accumulation of ergolines in Convolvulaceae depends on a plant-associated fungus.

The design of this experiment is notably economical. With a single intervention it separates two classes of substance — one vanishes, the other does not — and couples the loss to a microscopically visible finding.

**2008 — biosynthesis.** Markert and co-workers demonstrated biosynthesis and accumulation of the ergolines within a mutualistic association between *I. asarifolia* and a clavicipitalean fungus. [G]

**2011 — taxonomy.** Steiner, Leibner, Schardl, Leuchtman and Leistner described the genus *Periglandula* with *P. ipomoeae* (on *I. asarifolia*) and *P. turbiniae* (on *Turbina corymbosa*). The fungi are epibiotic: hyphae were never observed penetrating epidermal cells or stomata; they stand in intimate association with secretory glands on the leaf surface — hence the generic name. [G]

**Afterwards.** Detection in these fungi of the dmaW gene, which catalyses the determining step of ergoline biosynthesis, closes the chain. [G] Later work found *P. ipomoeae* on six of eight examined plant parts of *I. asarifolia* — young folded leaves, mature leaves, flower buds, mature flowers, young and mature seeds — predominantly on external, relatively unexposed surfaces. [G]

The last point bears directly on Hofmann: the fungus sits on the seeds as well. Hofmann had examined seeds.

## 5. What Hofmann Measured

The reinterpretation can be stated precisely.

| Level            | Hofmann's reading, 1963                                | Reading after 2011                                                                    |
|------------------|--------------------------------------------------------|---------------------------------------------------------------------------------------|
| Analyte          | lysergic acid amide in seeds of <i>Rivea corymbosa</i> | identical                                                                             |
| Producer         | the plant                                              | epibiotic fungus <i>Periglandula turbinae</i>                                         |
| Systemic unit    | plant                                                  | symbiotum of plant and fungus                                                         |
| Taxonomic status | anomaly, chemical convergence                          | rule-conforming — the ergolines here too originate in a fungus of the Clavicipitaceae |
| Significance     | ethnopharmacological curiosity                         | first chemical detection in this symbiotic system                                     |

The decisive point in the bottom row: after the resolution, the rule the finding appeared to violate is not violated at all. In both cases the ergolines originate in Clavicipitaceae. What was violated was an assumption about the boundaries of the organism under examination — the tacit premise that a seed one extracts contains only what the plant produced.

## 6. Consequence for the Theory of Science

Three points generalise.

**Measurability can precede explicability by decades.** Hofmann's analysis was correct in 1963 and has remained so. What was missing was not precision but a discipline — endophyte and symbiosis research, which emerged as a field only in the following decades. Roughly fifty years separated the correct measurement from the correct attribution.

**The boundary of the organism is a methodological stipulation, not a fact of nature.**

Every extraction presupposes an answer to the question of where the organism under examination ends. In the case of epibiotic associations that answer is wrong, without anything being wrong with the procedure. For natural-product chemistry this is a systematic risk, not an isolated case: the holobiont view entered the discipline only in retrospect.

**Auxiliary hypotheses persist as long as they are unopposed.** The convergence assumption was improbable and held for over forty years. The criterion of its fall was not an argument but an experiment with an intervention — the fungicide treatment of 2004.

## 6a. Relation to the existing literature

Frank Petersen’s *The Mystery in the Rye* (Springer 2025) treats the same subject in chapter 10, pp. 181–200. Checking that chapter’s 48 references shows: from the *Periglandula* complex it cites only Steiner & Leistner 2012 and Steiner et al. 2006. **Not cited** are Kucht et al. 2004, Markert et al. 2008 and the 2011 description of the genus. No literature in the theory of science appears. [G]

The demarcation of this paper follows. Petersen narrates the overthrow of the “only fungi” dogma as a discovery story. This paper is not a first account of that story but its evaluation: the full chain of evidence from 2004 to 2011, and the conclusion drawn in section 6 — measurability before explicability, the organism boundary as a methodological stipulation.

**Reservation:** the judgement rests on the table of contents, abstract and reference list; chapter 10 is paywalled. The full text is to be checked before publication; German edition *Das Mysterium im Roggen* (Springer). [V]

## 7. Follow-On Questions

| #  | Question                                                                                 | Status                                  |
|----|------------------------------------------------------------------------------------------|-----------------------------------------|
| Q1 | Does the archive indicate that Hofmann himself considered fungal involvement?            | [O] — Bern correspondence to be checked |
| Q2 | How is the finding treated across the editions of <i>Plants of the Gods</i> ?            | [O]                                     |
| Q3 | Can historical seed samples be tested for <i>Periglandula</i> DNA?                       | [O] — herbarium material, aDNA methods  |
| Q4 | Are there comparable cases of delayed producer attribution in natural-product chemistry? | [W] — systematic survey outstanding     |
| Q5 | What follows from the symbiosis reading for ethnobotanical attributions?                 | [O]                                     |

Q4 is the most load-bearing extension: if several cases are found, an episode becomes a pattern, and the paper carries a more general thesis about the organism boundary in natural-product chemistry.

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## Maturity of this version

v1.0 means: complete in substance, readable on its own, references given, reservations named. It does not mean every reservation is resolved. What remains open is in section 7 and, as far as the quality of references goes, in Appendix W section 2 of the parent work FORSCH-0331.

## Sources

Full details in the source register of the parent work FORSCH-0331, section D. Core references:

- Hofmann A. (1963): Die Zauberdroge «Ololiuqui». *Planta Medica* 9:354–367.
  - Kucht S., Gross J., Hussein Y., Grothe T., Keller U., Basar S., König W. A., Steiner U., Leistner E. (2004): Elimination of ergoline alkaloids following treatment of *Ipomoea asarifolia* (Convolvulaceae) with fungicides. *Planta* 219:619–625.
  - Markert A., Steffan N., Ploss K., Hellwig S., Steiner U., Drewke C., Li S.-M., Boland W., Leistner E. (2008): Biosynthesis and accumulation of ergoline alkaloids in a mutualistic association between *Ipomoea asarifolia* (Convolvulaceae) and a clavicipitalean fungus. *Plant Physiology* 147:296–305.
  - Leistner E., Steiner U. (2009): Fungal origin of ergoline alkaloids present in dicotyledonous plants (Convolvulaceae). In: Anke T., Weber D. (eds): *The Mycota XV*. Springer, 197–208.
  - Steiner U., Leibner S., Schardl C. L., Leuchtmann A., Leistner E. (2011): *Periglandula*, a new fungal genus within the Clavicipitaceae and its association with Convolvulaceae. *Mycologia*.
  - Steiner U., Leistner E. (2018): The genus *Periglandula* and its symbiotum with morning glory plants (Convolvulaceae). In: *The Mycota*. Springer. DOI 10.1007/978-3-319-71740-1\_5.
  - Panaccione D. G. et al. (2014): Bioactive alkaloids in vertically transmitted fungal endophytes. *Functional Ecology*. DOI 10.1111/1365-2435.12076.
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