

EXPLORING THE ANTIPYRETIC (JWARGHNA) POTENTIAL OF PATHA AND CHIRAYATA: A NARRATIVE REVIEW

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ABSTRACT

Fever, or pyrexia, is a regulated physiological response that commonly accompanies infectious and inflammatory conditions.^[1] Contemporary understanding of fever implicates interactions among exogenous pyrogens, endogenous inflammatory mediators, cyclooxygenase-2 (COX-2), prostaglandin E₂ (PGE₂), and hypothalamic thermoregulatory pathways.^[1] Although conventional antipyretic agents are effective in reducing elevated body temperature, their dose-related limitations and adverse effects continue to stimulate interest in medicinal plants as potential sources of complementary or novel therapeutic agents.^[1] Ayurveda recognizes *Jwara* as a major disease entity and describes numerous medicinal plants with *Jwaraghna* activity.^[4] *Patha* (*Cissampelos pareira* L.) has a longstanding association with

fever and inflammatory disorders.^[2] *Chirayita* (*Swertia chirayita* (Roxb.) H. Karst.) likewise has a longstanding association with fever and inflammatory disorders.^[2] Modern pharmacological investigations have reported antipyretic and related activities for *Patha*.^[3] Modern pharmacological investigations have also reported antipyretic and related activities for *Chirayita*.

The present narrative review examines the Ayurvedic positioning, botanical identity, phytochemical profile, experimental antipyretic evidence and possible mechanisms of *Patha*

and *Chirayita*. Particular attention is given to experimentally induced pyrexia models and to factors that limit direct comparison, including botanical identity, plant part, extraction method, dose, phytochemical variability and experimental design. A comparative synthesis indicates that both drugs have a traditional rationale and preclinical evidence supporting further investigation; however, available evidence does not establish clinical superiority of one drug over the other. Standardized head-to-head experimental studies using authenticated material and chemically characterized extracts are therefore warranted.^[2]

KEYWORDS: *Jwara*, *Jwaraghna*, *Patha*, *Chirayita*, antipyretic, Ayurveda.

1. INTRODUCTION

Fever is one of the most frequently encountered manifestations of infection and inflammation.^[1] It represents a regulated elevation of body temperature resulting from an upward adjustment of the hypothalamic thermoregulatory set point.^[1] This regulated response differs from hyperthermia, in which body temperature rises without a corresponding alteration of the thermoregulatory set point.^[1]

The development of fever involves coordinated interactions between the immune system and the central nervous system.^[1] Microbial components and other exogenous pyrogens can activate innate immune cells and promote the release of endogenous inflammatory mediators, including interleukin-1 β , interleukin-6 and tumour necrosis factor- α .^[1] These mediators contribute to pathways involving cyclooxygenase-2 and prostaglandin E₂.^[1] PGE₂ acts within the preoptic region of the hypothalamus, particularly through EP3 receptor-related signaling, to initiate physiological responses that increase heat production and conserve body heat.^[1]

The central importance of inflammatory mediators and PGE₂ provides a pharmacological basis for understanding the antipyretic action of conventional agents.^[1] However, plant-derived antipyretic activity should not automatically be attributed to direct COX inhibition.^[2] Plant extracts contain multiple constituents and may influence inflammatory cytokines, oxidative stress, prostaglandin synthesis and other biological pathways simultaneously.^[2]

Ayurveda provides a complementary conceptual framework for understanding fever through the broader entity of *Jwara*. Its assessment considers factors such as *Dosha* involvement, *Agni*, *Ama*, *Srotas*, stage and clinical presentation.^[4] The concept of *Jwaraghna* therefore

provides a useful traditional pharmacological starting point for investigating medicinal plants in experimentally established models of pyrexia.^[4]

Patha and *Chirayita* are particularly relevant in this context.^[2] *Cissampelos pareira* L., belonging to Menispermaceae, has been associated with fever and inflammatory conditions and has reported antipyretic, analgesic and anti-inflammatory activities.^[2] *Swertia chirayita* (Roxb.) H. Karst., belonging to Gentianaceae, has a longstanding association with fever management and has been investigated for antipyretic, anti-inflammatory, antioxidant and other pharmacological activities.^[2]

Despite these observations, the available evidence remains heterogeneous.^[2] Differences in botanical identity, plant part, extraction method, dose, experimental model and phytochemical composition make direct comparison difficult.^[2] The present review therefore focuses on the traditional and experimental antipyretic relevance of *Patha* and *Chirayita* while identifying the methodological gaps that should be addressed in future comparative studies.^[2]

2. FEVER: A MODERN PHARMACOLOGICAL PERSPECTIVE

Fever develops when infectious or inflammatory stimuli activate endogenous pyrogenic pathways.^[1] Exogenous pyrogens, including microbial products, can stimulate innate immune cells and promote cytokine production.^[1] IL-1 β , IL-6 and TNF- α participate in signaling pathways that ultimately influence central thermoregulation.^[1]

A major event in this process is induction of COX-2 and subsequent formation of PGE₂.^[1] PGE₂ acts on receptors in the preoptic hypothalamus and modifies neuronal activity responsible for maintaining body temperature.^[1] The resulting physiological responses include peripheral vasoconstriction, altered heat dissipation and increased thermogenesis.^[1]

This pathway provides a mechanistic basis for antipyretic research.^[1] Nevertheless, reduction in experimentally induced body temperature should be interpreted as evidence of pharmacological antipyretic activity under the tested conditions, rather than as proof of a particular molecular mechanism or clinical efficacy.^[1] For medicinal plants, a multi-target interpretation may be more appropriate unless constituent-level mechanistic evidence is available.^[1]

3. AYURVEDIC UNDERSTANDING OF JWARA AND THE JWARAGHNA CONCEPT

In Ayurveda, *Jwara* occupies an important position among disease conditions and is discussed in relation to diverse etiological and pathological factors.^[4] Its presentation is not restricted to elevation of body temperature but may include systemic manifestations affecting multiple physiological functions.^[4] Ayurvedic assessment considers *Dosha*, *Agni*, *Ama*, *Srotas*, disease stage and type; consequently, management is traditionally individualized rather than being based exclusively on lowering body temperature.^[4]

The term *Jwaraghna* broadly refers to drugs or therapeutic substances traditionally used in the management of *Jwara*.^[4] This concept provides an important bridge for pharmacological investigation because plants recognized for fever-related indications can be evaluated using experimentally established models of pyrexia.^[4]

Patha has been described in classical Ayurvedic literature in association with *Jwara* and is included in formulations used for various therapeutic indications.^[4] *Chirayita* likewise has a longstanding traditional association with fever management.^[3] The traditional positioning of both drugs therefore provides a rationale for examining whether their historical therapeutic use correlates with experimentally measurable antipyretic activity.^[4]

4. PATHA — *Cissampelos pareira* L.

4.1 Botanical identity

Cissampelos pareira L. belongs to the family Menispermaceae and is a perennial climbing medicinal plant distributed in tropical and subtropical regions. In Ayurvedic literature, the name *Patha* is associated with more than one botanical identity in different contexts.^[4] *C. pareira* is generally recognized as an important source of *Laghu Patha*, whereas *Cyclea peltata* has also been associated with *Raj Patha* in certain regions as mentioned in different Ayurvedic texts.



Figure 1: Morphological features of *Patha* (*Cissampelos pareira* L.): field photographs showing plant habit, leaves and inflorescence.

This botanical variation has direct implications for pharmacological research. Different species may differ in phytochemical composition and biological activity.^[7] Accurate botanical authentication and documentation of the plant material are therefore essential for reproducible evaluation of *Patha*.^[7]

4.2 Ayurvedic profile

Classical reviews describe *Patha* with pharmacological attributes including *Katu* and *Tikta Rasa*, *Ushna Virya*, and *Laghu* and *Tikshna Guna*, although individual classical sources may show variations.^[4] *Patha* is traditionally associated with therapeutic applications including *Jwara* and *Atisara*.^[4]

4.3 Phytochemistry

The phytochemistry of *C. pareira* is dominated by structurally diverse isoquinoline alkaloids.^[2] Published reviews describe bisbenzylisoquinoline, benzylisoquinoline, aporphine, protoberberine and related alkaloid classes, together with flavonoids, flavonoid glycosides and fatty acids.^[2]

Analytical investigations have employed techniques such as HPTLC, HPLC, UPLC, LC-MS and GC-MS for characterization and chemical fingerprinting.^[2] Geographical origin, plant part, extraction solvent and processing can influence the chemical composition of an extract.^[2]

4.4 Experimental evidence for antipyretic activity

Experimental investigations have evaluated *C. pareira* in animal models of pyrexia.^[6] An ethanolic extract has been reported to show antipyretic activity in Brewer's yeast-induced pyrexia, with accompanying analgesic and anti-inflammatory effects.^[6] A comparative study also evaluated *C. pareira* alongside *Cyclea peltata*, highlighting the importance of botanical identity when interpreting evidence associated with the traditional drug name *Patha*.^[7]

The available evidence supports further investigation of *Patha* as a potential antipyretic drug.^[6] However, existing studies do not establish a single definitive molecular mechanism or identify one constituent as solely responsible for the antipyretic effect.^[6] Experimental reduction of pyrexia under a defined model should therefore not be equated with established clinical efficacy.^[6]

5. CHIRAYITA — *Swertia chirayita* (Roxb.) H. Karst.

5.1 Botanical identity and traditional relevance

Swertia chirayita (Roxb.) H. Karst. belongs to the family Gentianaceae and is one of the extensively investigated medicinal species of the genus *Swertia*.^[3] It has a longstanding history of traditional medicinal use in the Indian subcontinent. Reported traditional indications include fever, digestive disorders, jaundice, diabetes, malaria and inflammatory conditions.^[3]



Figure 2: Morphological features of Chirayata (*Swertia chirayita* (Roxb.) H. Karst.): field photographs showing plant habit and characteristic leaves.

The traditional association of *Chirayita* with fever is particularly relevant to pharmacological research because the historical indication provides a testable hypothesis for experimental evaluation.^[3] Modern reviews have documented antipyretic activity among its reported pharmacological properties.^[3]

5.2 Phytochemistry

The phytochemistry of *S. chirayita* is chemically diverse. Reported constituents include xanthones, secoiridoid glycosides, terpenoids, flavonoids, alkaloids and other secondary metabolites. Important compounds reported from the plant include amarogentin, swertiamarin, sweroside, gentiopicroin, mangiferin and swerchirin.^[3]

HPTLC, HPLC, UPLC and LC-MS have been used for chemical characterization and quality assessment.^[3] Such standardization is particularly important because phytochemical composition may vary according to geographical origin, developmental stage, processing and other factors.^[3]

5.3 Experimental evidence for antipyretic activity

Experimental evidence supporting the antipyretic potential of *Chirayata* is available from animal studies.^[8] Bhargava and colleagues evaluated an aqueous root extract of *Swertia chirayita* using Brewer's yeast-induced pyrexia in rats and vaccine-induced hyperpyrexia in rabbits and reported a dose-related reduction in elevated body temperature, with activity compared with paracetamol.^[8]

Another experimental investigation evaluated a water-soluble portion of an alcoholic extract in rats using Brewer's yeast-induced pyrexia and reported significant activity at the tested doses.^[9] The investigators proposed that inhibition of prostaglandin synthesis and/or modulation of other chemical mediators might contribute to the observed effect, while recognizing the need for further investigation.^[9]

Taken together, these findings provide experimental support for the traditional antipyretic use of *Chirayita*.^[8] Nevertheless, the precise molecular mechanisms and the contribution of individual phytoconstituents remain incompletely defined.^[8]

6. MECHANISTIC PERSPECTIVE OF ANTYPYRETIC ACTIVITY

The antipyretic activity of medicinal plants may arise through more than one biological pathway. The best-established pathway in fever involves inflammatory cytokines, COX-2 and

PGE₂.^[1] Consequently, suppression of cytokine production, reduction of COX-2 activity, modulation of PGE₂ synthesis or broader anti-inflammatory effects may contribute to reduction of fever.^[1] For *Patha*, experimentally demonstrated antipyretic activity has been accompanied by anti-inflammatory and analgesic effects in some studies.^[6] However, direct attribution of the antipyretic response to a specific alkaloid or molecular pathway remains insufficiently established.^[6]

For *Chirayita*, experimental literature has suggested a possible relationship between antipyretic effects and prostaglandin-related pathways, while its broader anti-inflammatory and antioxidant activities provide additional biological context.^[10] A multi-target interpretation is therefore more appropriate than assuming a single mechanism without constituent-level evidence.^[10]

7. COMPARATIVE SYNTHESIS OF *PATHA* AND *CHIRAYITA*

Patha is traditionally associated with *Jwara* and belongs to the family Menispermaceae.^[4]

Chirayita is traditionally associated with *Jwara* and belongs to the family Gentianaceae.^[3]

The two drugs differ in phytochemical profile and in the nature of the available experimental evidence.^[7] These differences are important when designing a direct comparative study.^[7]

Parameter	<i>Patha</i>	<i>Chirayita</i>	Interpretive significance
Ayurvedic name	<i>Patha</i> / <i>Laghu Patha</i>	Chirayata / <i>Kirātatikta</i>	<i>Patha</i> and <i>Chirayita</i> are traditionally associated with <i>Jwara</i> / <i>Jwaraghna</i> use acc. to ancient ayurvedic textx.
Botanical identity	<i>Cissampelos pareira</i> L.	<i>Swertia chirayita</i> (Roxb.) H. Karst.	Authentication is essential before pharmacological comparison.
Family	Menispermaceae	Gentianaceae	The two drugs have distinct taxonomic backgrounds. ^[2]
Useful part reported in reviewed literature	Root / plant material varies by study ^[7]	Root and whole-plant material are represented in the reviewed literature ^[3]	Plant part must be explicitly documented in comparative experiments. ^[7]
Major phytochemical groups	Isoquinoline alkaloids, flavonoids, fatty acids ^[2]	Secoiridoids, xanthones, flavonoids, terpenoids,	Different phytochemical profiles may influence pharmacological responses. ^[2]

		alkaloids ^[3]	
Traditional association	Jwara, Atisara and inflammatory conditions ^[4]	Jwara, digestive disorders, malaria and inflammatory conditions ^[3]	These traditional indications provide a rationale for experimental investigation. ^[4]
Reported antipyretic evidence	Experimental antipyretic evidence is available. ^[7]	Experimental antipyretic evidence is available. ^[8]	Both drugs have preclinical antipyretic support; direct equivalence of evidence cannot be assumed. ^[7]
Major experimental models reported	Brewer's yeast-induced pyrexia ^[7]	Brewer's yeast-induced pyrexia; vaccine-induced hyperpyrexia ^[8]	Different experimental models limit direct quantitative comparison. ^[7]
Mechanistic evidence	Limited/incompletely characterized ^[7]	Suggestive, including prostaglandin-related pathways; requires validation ^[10]	Common-biomarker mechanistic studies are needed for direct comparison. ^[10]
Key standardization concern	Botanical identity, plant part and extraction variation ^[2]	Geographical, chemotypic and processing variation ^[3]	Standardized material is necessary for reproducibility. ^[2]
Current comparative evidence	Limited head-to-head evidence ^[7]	Limited direct comparative evidence with <i>Patha</i> ^[3]	A standardized direct comparison represents a clear research opportunity. ^[2]
Priority for future research	Active constituent identification, mechanism and safety ^[2]	Constituent-level mechanism, standardization and safety ^[3]	Both require chemically characterized preparations and validated models. ^[2]

The comparison indicates that both plants possess a traditional and experimental basis for further investigation. However, the existing literature cannot be interpreted as demonstrating that one plant is clinically superior to the other. Differences in botanical identity, extraction procedure, dose, experimental model and phytochemical composition make direct comparison difficult.^[7] A head-to-head study using authenticated plant material, identical experimental conditions and appropriately standardized extracts would provide substantially stronger evidence.^[7]

Evidence domain	What the present literature supports	What remains unresolved
Traditional use	<i>Patha</i> has a longstanding association with Jwara. ^[4] <i>Chirayita</i> has a	The correspondence between traditional indications and

	longstanding association with fever/ <i>Jwara</i> . ^[3]	standardized pharmacological outcomes remains to be established. ^[3]
Animal antipyretic activity	<i>Patha</i> has demonstrated antipyretic activity in experimental pyrexia. ^[7] <i>Chirayita</i> has demonstrated antipyretic activity in experimental pyrexia. ^[8]	Relative potency under identical experimental conditions remains unresolved. ^[7]
Phytochemistry	<i>Patha</i> contains multiple classes of secondary metabolites. ^[2] <i>Chirayita</i> contains multiple classes of secondary metabolites. ^[3]	The constituents or fractions contributing most strongly to antipyretic activity remain unresolved. ^[2]
Mechanism	Inflammatory and prostaglandin-related pathways are biologically plausible in fever. ^[1] Amarogentin has been investigated in relation to COX-2/prostaglandin biosynthesis. ^[10]	Direct biomarker-level evidence linking whole extracts or individual constituents with cytokines, COX-2 and PGE ^[2] remains limited. ^[10]
Standardization	Analytical methods are available for chemical characterization of <i>Patha</i> . ^[2] Analytical methods are available for chemical characterization of <i>Chirayita</i> . ^[3]	A common validated standardization strategy for comparative experiments remains to be established. ^[2]
Translation	Evidence for <i>Patha</i> is predominantly preclinical. ^[7] Evidence for <i>Chirayita</i> is predominantly preclinical. ^[8]	Clinical relevance, safety and therapeutic applicability in human fever remain unresolved. ^[8]

8. RESEARCH GAPS

9.1 Lack of standardized extracts

Different studies have employed aqueous, alcoholic and other extract preparations.^[2] Extraction solvent influences the phytochemical composition of the final preparation; therefore, results obtained from different extracts cannot automatically be considered equivalent.^[2]

9.2 Botanical authentication

Patha presents a particularly important pharmacognostical challenge because more than one species has historically been associated with the Ayurvedic drug.^[4] Accurate botanical authentication is essential for reproducible pharmacological research.^[7]

9.3 Limited constituent-level evidence

Although numerous phytoconstituents have been identified from both plants, the specific molecules responsible for antipyretic activity have not been conclusively established.^[2]

9.4 Mechanistic limitations

Reduction in experimentally induced body temperature demonstrates an antipyretic response under the tested conditions but does not by itself establish a molecular mechanism.^[1] Future investigations should incorporate appropriate inflammatory biomarkers, including cytokines, COX-2 and PGE₂, where scientifically justified.^[1]

9.5 Limited comparative evidence

Although individual experimental studies exist for both plants, standardized head-to-head comparisons remain limited.^[7] Comparative studies using identical experimental conditions, equivalent extraction procedures and validated analytical methods could provide stronger evidence.^[7]

9.6 Translation to clinical use

Most available evidence remains preclinical.^[2] Further pharmacological, toxicological and clinical investigations are required before definitive therapeutic conclusions can be drawn.^[3]

Based on the limitations identified in the reviewed literature, a scientifically stronger comparative evaluation should minimize methodological heterogeneity. The following framework is proposed as a research-oriented synthesis rather than as evidence already established by the reviewed studies:^[2,3,7,10] Botanically authenticate both drugs and preserve voucher/specimen documentation.^[7] Clearly define the plant part, collection source, processing procedure and storage conditions.^[2] Prepare extracts using a predefined and identical extraction strategy where scientifically appropriate, with extraction yield recorded.^[6]

Characterize and, where feasible, standardize the extracts using validated chromatographic or other appropriate analytical methods.^[3] Use the same animal species, sex/selection criteria, experimental conditions and validated pyrexia model for both test drugs.^[7] Include an appropriate vehicle/control group and a standard antipyretic comparator, with randomization and blinded outcome assessment where feasible.^[7,8,9] Record baseline and post-induction temperatures at predefined time points and report the magnitude and time course of temperature reduction.^[8] Where feasible, investigate relevant inflammatory mediators or mechanistic biomarkers to move beyond simple temperature reduction.^[10] Document acute/subacute safety or toxicity parameters appropriate to the study design. Report the study in sufficient detail to allow replication and meaningful comparison with previous literature.^[7,8,9]

Future research on *Patha* and *Chirayita* should move beyond simple demonstration of antipyretic activity and focus on standardized, mechanism-oriented pharmacological evaluation. Botanical authentication, pharmacognostical standardization, chemically characterized extracts and quantitative estimation of relevant marker compounds should precede or accompany biological evaluation.^[2,3,6,7,8,9]

Mechanistic investigations may explore inflammatory cytokines, COX-2/PGE₂ signaling and oxidative-stress-related pathways where appropriate.^[1] Correlating phytochemical composition with pharmacological activity may help identify active fractions or candidate constituents.^[10] Validated chromatographic fingerprints could improve reproducibility between laboratories.^[10]

For *Patha*, resolution of botanical identity is particularly important. For *Chirayita*, geographical and phytochemical variability warrants attention during standardization.^[3] Ultimately, appropriately designed clinical research will be required to determine whether preclinical antipyretic activity translates into clinically meaningful effects.^[3]

11. CONCLUSION

The current evidence therefore supports further comparative pharmacological investigation rather than definitive claims of therapeutic superiority.^[7] A well-standardized, authenticated and mechanism-oriented head-to-head evaluation of *Patha* and *Chirayita* may provide a stronger bridge between the Ayurvedic concept of *Jwaraghna* Dravyas and contemporary evidence-based pharmacology.

Modern experimental studies provide evidence of antipyretic activity for both plants in models of experimentally induced pyrexia. *Patha* is characterized by a phytochemical profile rich in isoquinoline alkaloids, whereas *Chirayita* contains diverse secoiridoids, xanthonoids, flavonoids, terpenoids and other secondary metabolites.^[3] However, the available studies differ considerably in plant material, extraction procedures, dosage, experimental models and phytochemical characterization.^[3]

Patha (*Cissampelos pareira* L.) has a longstanding traditional association with fever management.^[2] *Chirayita* (*Swertia chirayita* (Roxb.) H. Karst.) also has a longstanding traditional association with fever management.^[3] Their positioning within the broader

Ayurvedic concept of *Jwaraghna* therapy provides a valuable starting point for contemporary pharmacological investigation.^[4]

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