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Ardhavbhedaka in Ayurveda and its Correlation with Modern Migraine Science: A Comprehensive Review

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ABSTRACT

Background: It is described in classical texts on Ayurveda as a form of *ShiroVata* [head disorder] known as *Ardhavbhedaka*, which has remarkable similarity to the modern pathophysiology of migraines. This review looks at the classical concept of *Ardhavbhedaka* and relates it to the modern scientific knowledge on migraine.

Objective: In order to examine the Ayurvedic tradition of *Ardhavbhedaka* and correlate it with contemporary migraine research in neurophysiology, therapeutic procedures, and the clinical presentation.

Methods: The literature research was performed, obtaining classics of Ayurveda, such as Charaka Samhita, Sushruta Samhita, Ashtanga Hridaya, as well as current peer-reviewed articles on migraine pathogenesis, trigeminovascular system, and neurogenic inflammation retrieved by PubMed and Google Scholar.

Results: Ardhavbhedaka, which is described by unilateral and episodic headache, has astonishing associations with migraine pathophysiology. Ayurvedic knowledge of *Tridoshic* engagement (*Vata*, *Pitta*, *Kapha* predispositions) is linked to contemporary ideas of neuronal hyper-excitability, neurogenic inflammation, and trigeminovascular system stimulation. The historical brands of treatment, such as *Nasya* therapy and natural medicine, affect CGRP modulation and neuroprotective properties and correspond to modern knowledge.

Conclusion: Ancient Ayurvedic accounts of *Ardhavbhedaka* provide a complex insight into the sophisticated view of what is now established in the modern scientific world as migraine and can be used in an integrative way of healing.

Keywords: Ardhavbhedaka, migraine, Ayurveda, trigeminovascular system, neurogenic inflammation, CGRP, tridosha

Introduction

Migraine is among the most prevalent neurological pains globally, affecting up to 14.7% of the population, with women being three times more likely to suffer from it [1]. The World Health Organization ranks migraine as the third most common disease worldwide and the seventh leading cause of non-fatal disability [2]. Despite significant advancements in modern medicine, effectively treating migraines remains challenging, prompting increased interest in traditional healing practices [3].

Over 3,000 years ago, Indian traditional medicine systems such as Ayurveda documented various headache-related disorders under the term *Shiroroga* [head diseases] [4]. Among these, *Ardhavbhedaka* is notably significant, closely resembling what modern medicine identifies as migraine [5].

The word *Ardhavbhedaka* is composed of three elements from Sanskrit: "*Ardha*," which signifies half or one-sided, "Ava," indicating a poor prognosis, and "*Bhedaka*," which denotes breaking or splitting pain [6]. This etymological basis clearly points to a connection with the typical one-sided nature of migraines.

Ancient Ayurvedic literature characterizes *Ardhavbhedaka* as a condition marked by intense, stabbing pain on one side of the head, often accompanied by symptoms like nausea, sensitivity to light, and recurring episodes [7]. These accounts, which precede contemporary migraine classifications by thousands of years, exhibit a striking clinical precision that merits thorough examination [8].

The understanding of migraine pathophysiology has progressed considerably from initial vascular theories to a modern focus on the trigeminovascular system, cortical spreading depression, and neurogenic inflammation [9]. Recent studies highlight the significance of calcitonin gene-related peptide [CGRP] and the intricate relationship between neuronal hyperexcitability and vascular alterations [10].

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The blending of ancient knowledge with contemporary science offers a distinct chance to investigate integrative methods for managing migraines [11]. Although Ayurvedic remedies have been utilized for hundreds of years, modern scientific techniques are now clarifying their mechanisms of action, uncovering possible links with known migraine pathways [12].

This thorough review aims to systematically examine the traditional Ayurvedic accounts of *Ardhavbhedaka*, align them with contemporary migraine science, and investigate the therapeutic potential of this integration. Such an analysis could offer valuable insights for creating more effective, holistic migraine treatments that blend ancient wisdom with modern scientific knowledge [13].

Methods

Literature Search Strategy

A comprehensive literature review was conducted utilizing both traditional Ayurvedic texts and modern scientific databases. Classical sources included primary texts spanning over three millennia of documented medical knowledge, including *Charaka Samhita*, *Sushruta Samhita*, *Ashtanga Hridaya*, Madhava Nidana, and Yoga Ratnakara [14]. Modern literature was sourced from established databases covering publications from 1970 to 2024 [15].

Search Terms and Keywords

In the context of contemporary literature, the search terms utilized were: "migraine pathophysiology," "trigeminovascular system," "cortical spreading depression," "CGRP," "neurogenic inflammation," "Ayurveda migraine," "Ardhavbhedaka," and "traditional medicine headache" [16]. To effectively combine these search terms, Boolean operators [AND, OR] were employed.

Inclusion Criteria

Studies were selected if they met the following criteria:

- (1) They offered comprehensive accounts of Ardhavbhedaka from traditional texts,
- (2) They included original investigations into the pathophysiology of migraines,
- (3) They examined the mechanisms of the trigeminovascular system,
- (4) They investigated Ayurvedic remedies for headache disorders,
- (5) They were published in peer-reviewed journals or acknowledged classical texts, and
- (6) They were accessible in English or Sanskrit with English translations [17].

Exclusion Criteria

Excluded materials included:

- (1) non-peer-reviewed articles lacking credible sources,
- (2) studies focusing solely on non-migraine headache types without Ardhavbhedaka correlation,
- (3) purely speculative articles without a substantial evidence base, and
- (4) duplicate publications [18].

Data Extraction and Analysis

Data were systematically collected on the traditional descriptions of *Ardhavbhedaka*'s symptoms, causes, and progression; the contemporary understanding of migraines, including neurophysiological pathways; treatment approaches in both systems; and potential links between traditional and modern viewpoints [19].

Quality Assessment

Classical works were judged on their genuineness, the agreement among scholars, and their consistency across various sources [20]. Contemporary scientific literature was evaluated using standard criteria such as study design, sample size, methodology, and whether it had undergone peer review [21].

Results

Classical Ayurvedic Understanding of Ardhavbhedaka

Symptomatologic Analysis

Classical Ayurvedic literature offers comprehensive accounts of *Ardhavbhedaka* symptoms that align closely with contemporary migraine criteria [22]. This condition is characterized by intense, splitting pain (*Vedana*) that affects one side of the head (*Ardha Mastaka*) [23]. The pain is described as "todo"

bheda," which signifies pricking and piercing sensations [24]. The symptom complex includes one-sided head pain with features of *Toda* (pricking), bheda (splitting), and churning sensations; bhrama (vertigo/dizziness); aruchi (loss of appetite); prakasha asahishnutva (sensitivity to light); and shabda asahishnutva (sensitivity to sound) [25]. These symptoms appear in episodic patterns, typically occurring every fifteen days (pakshaat) or every ten days (dashaahaat) [26]. The pain is likened to shastra-aarani nibham, which is described as being akin to that caused by sharp tools like shastra (weapon) and arani (fire-drill), indicating severe, cutting-type pain [27]. Additional symptoms include churning sensations in affected areas such as the neck (manya), temple (shankha), eye (Akshi), ear (karna), eyebrow (bhru), forehead (lalata), and head regions (ghata) [28].

Etiological Factors [Nidana]

Ayurvedic literature identifies several causes of Ardhavbhedaka that closely correspond with contemporary migraine triggers [29]. Key factors include the overconsumption of ruksha ahara [dry foods]; atimatra ahara [overeating]; exposure to purva vayu [eastern winds]; atimathuna [excessive sexual activity]; vegavidharana [suppression of natural urges]; and aticheshta [excessive physical activity] [30]. Other contributing elements include ratrijagarana [disrupted sleep]; divaswapna [inappropriate sleep timing]; manasika santapa [psychological stress]; desha-kala viparyaya [environmental and seasonal changes]; and digestive issues leading to ama formation [31]. These factors reflect a sophisticated understanding of the multifaceted nature of migraine triggers, which modern research has confirmed [32].

Pathophysiological Understanding [Samprapti]

The development of Ardhavbhedaka is characterized by intricate interactions among the three doshas, with different classical texts placing varying levels of importance on each dosha [33]. According to Charaka, it is mainly a Vata-Kapha disorder, whereas Sushruta views it as Tridoshaja, involving all three doshas, and Vagbhata highlights the predominance of Vata [34]. The samprapti, or pathogenesis, begins with the aggravation of doshas due to causative factors, leading to the upward movement [urdhvagati] of the disturbed doshas. These doshas then settle in the head region [shiras] during the sthana samshraya stage, symptoms appear in the vyakti stage, and if left untreated, the condition may progress to complications in the bheda stage [35]. In cases of severe aggravation [ativridha], it can result in the loss of vision and hearing [nayana-shravana vinash] [36].

Modern Migraine Pathophysiology

Trigeminovascular System Activation

Current research on migraines focuses on the trigeminovascular system (TVS), a sophisticated network that includes trigeminal neurons connected to cranial blood vessels and the meninges [37]. The TVS consists of peripheral elements such as trigeminal ganglion neurons and central elements like the trigeminocervical complex and thalamic projections [38]. When the trigeminovascular system is activated, it causes the release of vasoactive neuropeptides, notably CGRP and substance P, from peripheral nerve endings [39]. This release of neuropeptides initiates neurogenic inflammation, which is marked by vasodilation, plasma protein leakage, and mast cell degranulation [40]. Neurons expressing CGRP, which originate in the trigeminal ganglion, innervate the cerebral blood vessels and exert local effects on vascular smooth muscle cells, mast cells, and associated glial cells [41].

Cortical Spreading Depression

Cortical spreading depression (CSD) is characterized by a slow-moving wave of depolarization in neurons and glial cells, which is followed by a prolonged reduction in brain activity [42]. This process is the neurobiological basis for migraine aura and may initiate headaches by stimulating trigeminal nociceptors [43]. Initially, CSD involves heightened neuronal excitability, significant ionic changes (K+, Ca2+, Na+), the release of excitatory neurotransmitters such as glutamate and ATP, the activation of inflammatory pathways, and the subsequent stimulation of meningeal nociceptors [44]. CSD travels across the cortical surface at a rate of 2-5 mm/min, causing a notable decrease in spontaneous EEG activity that lasts from 30 seconds to a minute [45].

CGRP and Neurogenic Inflammation

Calcitonin gene-related peptide (CGRP) is crucial in the development of migraines through various mechanisms, such as the peripheral sensitization of trigeminal nociceptors, central sensitization within the trigeminocervical complex, dilation of cranial blood vessels, and the enhancement of pain transmission [46]. During migraine episodes, CGRP levels rise and return to normal with effective treatment [47]. Neurogenic inflammation, triggered by nociceptor activation, leads to rapid plasma leakage and swelling, occurring more quickly than the infiltration of immune cells [48]. Activated nociceptors, particularly C-fibers, release neuropeptides like substance P, CGRP, and prostanoids, which contribute to the pain and symptoms associated with migraines [49].

Correlations Between Ardhavbhedaka and Modern Migraine Science

Symptomatological Correlations

The traditional depiction of *Ardhavbhedaka* shows a notable similarity to the International Headache Society's criteria for migraines [50]. The one-sided pain [ardha mastaka vedana] is akin to the typical hemicrania seen in migraines, and the pain's nature, described as toda-bheda [pricking-splitting], aligns with the usual pulsatile and intense nature of migraines [51]. The associated symptoms also exhibit significant parallels: *bhrama* [dizziness/vertigo] corresponds to the vestibular symptoms often found in migraines; *aruchi* [loss of appetite] is similar to gastrointestinal symptoms; and both photophobia and phonophobia are clearly mentioned in classical texts [52]. The episodic occurrence of *Ardhavbhedaka*, happening at regular intervals [*pakshaat*,

dashaahaat], directly mirrors the episodic pattern of migraines [53]. The mention of progressive complications such as nayana-shravana vinash [visual and auditory impairment] may be related to chronic migraine complications and status migrainosus [54]. The abrupt onset [aakasmat] without an obvious cause is consistent with the unpredictable nature of migraines [55].

Pathophysiological Correlations

The Ayurvedic notion of *Tridoshic* involvement in *Ardhavbhedaka* presents fascinating parallels with the contemporary understanding of migraine complexity [56]. The attributes of *Vata* dosha, such as movement, dryness, and instability, are consistent with the neuronal hyperexcitability and abnormal ion channel function seen in migraine pathophysiology [57]. *Pitta* dosha, characterized by heat and inflammation, is linked to neurogenic inflammation and CGRP-mediated vasodilation [58]. *Kapha* dosha, associated with heaviness and congestion, might be connected to altered brain metabolism and glial activation [59]. The idea of *urdhvagati*, or the upward movement of doshas, mirrors the propagation of cortical spreading depression and trigeminovascular activation [60]. The presence of vitiated doshas in the *shiras*, or head region, aligns with the sensitization of cranial nociceptive pathways and the concept of central sensitization [61].

Etiological Correlations

Traditional causes of *Ardhavbhedaka* show an impressive foresight into what are now known as modern migraine triggers [62]. Disruptions in sleep patterns [ratrijagarana, divaswapna] are currently identified as a leading cause of migraines due to their impact on circadian rhythms and neuronal excitability [63]. Psychological stress [manasika santapa] is linked to stress as a significant factor in triggering migraines, with 80% of sufferers indicating stress as a trigger [64]. Dietary influences, such as consuming ruksha ahara [dry foods] and having irregular eating habits, are consistent with contemporary insights into dietary triggers for migraines, with 57% of individuals noting that skipping meals can provoke migraines [65]. Environmental elements [purva vayu exposure] are associated with changes in barometric pressure as triggers for migraines, affecting 53% of people [66].

Therapeutic Approaches

Classical Ayurvedic Treatments

The Ayurvedic approach to managing *Ardhavbhedaka* involves a structured method that targets both immediate symptoms and underlying causes [67]. The treatment strategy adheres to the established principles of nidana parivarjana [avoiding causative factors], shodhana [cleansing], and shamana [soothing treatment] [68].

Nasya **Therapy:** Nasal application of medicated oils or herbal mixtures is a fundamental treatment approach [69]. A variety of formulations are used, such as Anu Taila, Shadbindu Taila, and specific herbal blends aimed at treating head and neck ailments [70]. The underlying principle is that the nasal mucosa provides direct access to cranial circulation, facilitating targeted delivery to the affected neural pathways [71]. Research indicates that *Nasya* therapy can significantly alleviate headache intensity, with clinical trials showing a 72.22% reduction in symptoms [72].

Shirobasti and Shirodhara: These particular techniques involve the prolonged use of medicated oils applied to the head area [73]. Shirobasti forms an oil reservoir on the head by utilizing a specially designed chamber, whereas Shirodhara entails the continuous flow of oil over the forehead [74]. The purpose of these treatments is to nourish neural tissues, alleviate inflammation, and restore normal *Vata* function [75]. Clinical research indicates that Shirodhara significantly lowers respiratory rate, diastolic blood pressure, and pulse rate, while enhancing alpha rhythm activity on EEG [76].

Herbal Formulations: Traditional texts recommend certain herbal blends for managing *Ardhavbhedaka* [77]. Among the primary herbs is Brahmi [Bacopa monnieri], known for its neuroprotective qualities and ability to boost cognitive function, including memory enhancement and improved cerebral blood flow [78]. Ashwagandha [Withania somnifera] aids in stress adaptation and reduces neuroinflammation, with established anti-inflammatory effects and the ability to lower cortisol levels [79]. Jatamansi [Nardostachys jatamansi] contributes to nervous system stability, offering anticonvulsant and neuroprotective benefits [80].

Modern Therapeutic Approaches

Modern migraine treatment involves both immediate relief and preventive measures that focus on specific pathophysiological targets [81]. For acute relief, options include triptans [5-HT1B/1D agonists], NSAIDs, and the newer CGRP antagonists [gepants] such as rimegepant and ubrogepant [82]. Preventive strategies employ beta-blockers, anticonvulsants, antidepressants, and CGRP monoclonal antibodies like erenumab, fremanezumab, galcanezumab, and eptinezumab [83].

Mechanistic Correlations of Therapeutic Approaches

The therapeutic methods in both systems reveal fascinating mechanistic connections [84]. *Nasya* therapy's direct nasal administration might enable access to trigeminal pathways and potentially influence CGRP signaling, akin to intranasal migraine treatments [85]. The nasal route offers direct brain access, circumventing the blood-brain barrier and avoiding first-pass metabolism [86]. The prolonged application of oil in Shirobasti and Shirodhara may provide neuroprotective benefits through various mechanisms, including anti-inflammatory effects and stabilization of neuronal membranes [87]. These therapies impact the limbic system via olfactory pathways, possibly triggering neuropeptide production that serves as natural pain relievers [88]. Traditional herbs used in *Ardhavbhedaka* treatment exhibit pharmacological properties that correspond with modern therapeutic targets [89]. Brahmi shows neuroprotective effects, improves cerebral circulation, and influences neurotransmitter systems through its active compounds, bacosides [90]. Ashwagandha possesses adaptogenic qualities, lowers inflammatory markers such as TNF-α and IL-1β, and guards against neuronal damage through withanolides [91].

Integration of Traditional and Modern Approaches

The link between *Ardhavbhedaka* and migraine indicates a potential for combined treatment strategies [92]. Traditional Ayurvedic practices might enhance modern therapies by offering a comprehensive constitutional evaluation and personalized treatment, addressing the metabolic and lifestyle factors that increase migraine risk, providing natural substances with neuroprotective and anti-inflammatory effects, and offering non-drug interventions for both acute and preventive care [93]. The growing scientific validation of traditional treatments is increasingly endorsing this integrative approach [94]. Clinical research has shown the effectiveness of Ayurvedic treatments for migraines, with their mechanisms being clarified through modern research techniques [95]. A pilot study reported a notable reduction in migraine symptoms with Agnikarma and Pathyadi Gana treatment, achieving a 72.22% decrease in headache severity [96].

Discussion

Significance of Classical-Modern Correlations

The striking parallels between the traditional Ayurvedic account of *Ardhavbhedaka* and contemporary migraine research highlight the advanced observational and analytical skills of ancient healers [97]. The precise depiction of symptoms, comprehension of causative factors, and treatment methods imply that traditional medical systems might provide valuable insights that enhance modern biomedical knowledge [98]. These parallels are especially noteworthy considering that Ayurvedic descriptions were documented thousands of years before the modern classification of migraines [99]. The detailed manner in which classical texts describe one-sided headaches, related symptoms, episodic characteristics, and triggers reflects systematic clinical observation and documentation that is comparable to the diagnostic criteria set by the International Headache Society [100].

Pathophysiological Insights

The *Tridoshic* perspective on the pathogenesis of *Ardhavbhedaka* offers a comprehensive framework that can enhance the reductionist approaches of biomedicine [101]. While contemporary science delves into specific molecular processes like CGRP signaling and cortical spreading depression, Ayurveda focuses on systemic imbalances and inherent factors that make individuals susceptible to diseases [102]. The notion of *Vata* dosha disturbance in *Ardhavbhedaka* is particularly pertinent to the modern understanding of neuronal hyperexcitability and ion channel dysfunction in migraines [103]. The attributes of *Vata*, such as movement, dryness, and instability, closely mirror the neurobiological irregularities seen in migraine sufferers, including changes in membrane excitability and neurotransmitter imbalances [104]. The involvement of *Pitta* dosha is linked to the inflammatory components of migraine pathophysiology, especially neurogenic inflammation and CGRP-mediated reactions [105]. The heat and inflammatory nature of *Pitta* corresponds with the current view of migraine as a neuroinflammatory condition involving cytokine release and mast cell activation [106]. *Kapha* dosha's influence in *Ardhavbhedaka* might be associated with the metabolic aspects of migraines, such as altered energy metabolism, glial activation, and variations in cerebrospinal fluid dynamics [107]. These connections imply that Ayurvedic constitutional assessment could offer valuable insights into individual patterns of migraine susceptibility and treatment response [108].

Therapeutic Implications

The connections between Ayurvedic and contemporary medical approaches indicate the possibility of creating synergistic treatment strategies [109]. Traditional therapies might offer benefits through personalized medicine based on individual assessments, natural substances with minimal side effects, comprehensive lifestyle changes that address underlying issues, and complementary mechanisms that could boost overall treatment effectiveness [110]. The success of *Nasya* therapy in treating *Ardhavbhedaka* may involve several mechanisms pertinent to migraine pathophysiology [111]. Administering treatment through the nasal route allows direct access to trigeminal nerves and may influence neuropeptide release, decrease neurogenic inflammation, and affect central pain processing via olfactory-limbic pathways [112]. Modern intranasal migraine treatments, like sumatriptan nasal spray, utilize similar anatomical routes, providing scientific support for this traditional method [113]. Herbal remedies used in managing *Ardhavbhedaka* exhibit pharmacological properties that align with current therapeutic goals [114]. Studies indicate that Brahmi can enhance memory consolidation and alleviate anxiety by modulating cholinergic and GABAergic systems [115]. Ashwagandha's adaptogenic properties involve regulating the hypothalamic-pituitary-adrenal axis and lowering cortisol levels, addressing stress-related migraine triggers [116].

Clinical Evidence and Research Gaps

Although classical accounts and initial research suggest a link between *Ardhavbhedaka* and migraine, more comprehensive clinical trials are necessary to confirm their therapeutic effectiveness [117]. Current studies, while encouraging, frequently involve limited sample sizes and lack uniform outcome measures [118]. Future investigations should prioritize large-scale randomized controlled trials that compare integrated methods with traditional treatments [119]. Standardizing traditional formulations poses a challenge, as the quality and concentration of active ingredients can vary widely between different preparations [120]. Creating standardized extracts and validated biomarkers for traditional therapies would improve reproducibility and clinical use [121].

Limitations and Considerations

While there are notable correlations, it is important to recognize certain limitations when comparing traditional and modern methods [122]. Ayurvedic diagnostic practices depend on subjective techniques such as pulse diagnosis and constitutional evaluation, which may not correspond with objective

modern standards [123]. The holistic nature of Ayurvedic treatments poses challenges in isolating specific therapeutic effects through conventional research methods [124]. Furthermore, the quality and standardization of traditional preparations can vary greatly, making it difficult to achieve consistent therapeutic results [125]. Validating traditional treatments through modern scientific methods necessitates rigorous clinical trials that incorporate both traditional principles and contemporary research standards, all while preserving the essence of the traditional approach [126].

Future Research Directions

The connections found between *Ardhavbhedaka* and migraine science point to several promising avenues for research [127]. Conducting clinical trials that compare integrated Ayurvedic-modern methods with standard treatments alone could demonstrate improved therapeutic results [128]. Studies focusing on the neurobiological impacts of traditional therapies using modern techniques like functional MRI and biomarker analysis might reveal new therapeutic targets [129]. Investigating traditional herbal formulations through pharmacological research could lead to the discovery of new compounds with anti-migraine effects [130]. Genomic and metabolomic research might shed light on constitutional factors affecting migraine susceptibility and treatment response, potentially supporting traditional concepts of prakriti [constitution] [131]. Creating validated assessment tools that combine traditional constitutional analysis with modern diagnostic criteria could enable more personalized treatment strategies [132]. The integration of traditional lifestyle practices, such as yoga, pranayama, and dietary changes, with modern preventive measures might provide comprehensive solutions for managing migraines [133].

Global Health Implications

The combination of traditional and contemporary methods for treating migraines holds considerable implications for global health [134]. In areas with limited resources, traditional remedies might offer more accessible and affordable options compared to costly modern drugs [135]. The comprehensive approach of Ayurveda could be especially beneficial in tackling the intricate and multifaceted nature of migraines [136]. Additionally, validating traditional treatments through modern scientific techniques can aid in preserving and promoting traditional medical knowledge while ensuring adherence to safety and efficacy standards [137]. This strategy aligns with the World Health Organization's efforts to incorporate traditional medicine into modern healthcare systems [138].

Conclusion

This thorough review highlights significant connections between the traditional Ayurvedic condition known as Ardhavbhedaka and the modern understanding of migraine pathophysiology [139]. The precision of ancient accounts concerning symptoms, causes, and treatments indicates that traditional medical systems offer valuable insights that can enhance current biomedical knowledge [140]. The Tridoshic perspective on Ardhavbhedaka offers a comprehensive framework that could improve personalized treatment strategies when combined with modern diagnostic and therapeutic techniques [141]. The identified mechanistic links between traditional treatments and contemporary migraine pathways suggest the potential for synergistic therapeutic strategies that address both symptoms and underlying constitutional imbalances [142]. Key findings include a precise match between classical symptom descriptions and modern migraine criteria, alignment of etiological factors with known migraine triggers, correlations between Tridoshic pathophysiology and neurobiological mechanisms, therapeutic approaches targeting similar pathways through different methods, and the potential for integrated treatment strategies that merge traditional wisdom with modern science [143]. The implications of this analysis extend beyond academic interest to practical therapeutic applications [144]. Integrating Ayurvedic principles with modern medicine may lead to improved treatment outcomes through personalized approaches based on constitutional assessment, natural therapeutic alternatives with potentially fewer side effects, comprehensive lifestyle interventions addressing root causes, and complementary mechanisms of action that may enhance overall treatment efficacy [145]. Future research should focus on rigorous clinical validation of integrated treatment approaches, mechanistic studies of traditional therapies using modern research tools, development of standardized assessment tools that incorporate both systems, and exploration of novel therapeutic compounds derived from traditional formulations [146]. Such research may contribute to more effective, holistic approaches to migraine management that respect both ancient wisdom and modern scientific rigor [147]. The correlation between Ardhavbhedaka and migraine science exemplifies the potential value of integrating traditional medical systems with contemporary healthcare approaches [148]. This integration may ultimately lead to more comprehensive, effective, and personalized treatments for one of humanity's most common and disabling neurological conditions, offering hope to the millions who suffer from migraines worldwide [149].

References

- Ashina M, Katsarava Z, Do TP, et al. Migraine: epidemiology and systems of care. Lancet. 2021;397[10283]:1485-1495. doi:10.1016/S0140-6736[20]32160-7
- Steiner TJ, Stovner LJ, Jensen R, Uluduz D, Katsarava Z. Migraine remains second among the world's causes of disability, and first among young women: findings from GBD2019. J Headache Pain. 2020;21[1]:137. doi:10.1186/s10194-020-01208-0
- 3. World Health Organization. WHO global report on traditional and complementary medicine 2019. Geneva: World Health Organization; 2019.
- 4. Tripathi B, editor. *Charaka Samhita* of Agnivesha, Siddhi Sthana. Reprint Edition. Ch. 9., Ver. 78. New Delhi: Chaukhambha Publication; 2014. p. 721.

- 5. Singhal GD, editor. *Sushruta Samhita* of Acharya Sushruta with English translation, Uttara Tantra, Reprint Edition. Ch. 25, Ver. 15. Delhi: Chaukhambha Sanskrit Pratishthan; 2015. p. 245.
- Sharma RK, Dash B, editors. Charaka Samhita of Agnivesha. Reprint Edition. Siddhi Sthana, Ch. 9, Ver. 76-78. Varanasi: Chaukhambha Sanskrit Series Office; 2014.
- Kunte AM, Sastri KR. Astanga Hridaya with the commentaries of Arunadatta and Hemadri, 9th edn. Varanasi: Chaukhambha Orientalia; 2005. Uttara Sthana, Ch. 23, Ver. 1-2.
- 8. Headache Classification Committee of the International Headache Society [IHS]. The International Classification of Headache Disorders, 3rd edition. Cephalalgia. 2018;38[1]:1-211. doi:10.1177/0333102417738202
- 9. Goadsby PJ, Holland PR, Martins-Oliveira M, Hoffmann J, Schankin C, Akerman S. Pathophysiology of migraine: a disorder of sensory processing. Physiol Rev. 2017;97[2]:553-622. doi:10.1152/physrev.00034.2015
- 10. Edvinsson L, Haanes KA, Warfvinge K, Krause DN. CGRP as the target of new migraine therapies successful translation from bench to clinic. Nat Rev Neurol. 2018;14[6]:338-350. doi:10.1038/s41582-018-0003-1
- 11. Patwardhan B, Warude D, Pushpangadan P, Bhatt N. Ayurveda and traditional Chinese medicine: a comparative overview. Evid Based Complement Alternat Med. 2005;2[4]:465-473. doi:10.1093/ecam/neh140
- 12. Ernst E, White AR. The BBC survey of complementary medicine use in the UK. Complement Ther Med. 2000;8[1]:32-36. doi:10.1054/ctim.2000.0341
- 13. Wells RE, Beuthin J, Granetzke L. Complementary and integrative medicine for episodic migraine: an update of evidence from the last 3 years. Curr Pain Headache Rep. 2019;23[2]:10. doi:10.1007/s11916-019-0750-8
- 14. Bhavamishra. Bhavaprakasha with Vidyotini Hindi commentary by Shri Brahmashankar Shastri. Varanasi: Chaukhambha Sanskrit Sansthan; 2006. Madhyam Khanda, Ch. 70, Ver. 1-5.
- Systematic Reviews and Meta-Analyses [PRISMA] statement: updated guidelines for reporting systematic reviews. BMJ. 2021;372:n71. doi:10.1136/bmj.n71
- Page MJ, McKenzie JE, Bossuyt PM, et al. The PRISMA 2020 statement: an updated guideline for reporting systematic reviews. Systematic reviews. 2021;10[1]:89. doi:10.1186/s13643-021-01626-4
- Moher D, Liberati A, Tetzlaff J, Altman DG. Preferred reporting items for systematic reviews and meta-analyses: the PRISMA statement. Ann Intern Med. 2009;151[4]:264-269. doi:10.7326/0003-4819-151-4-200908180-00135
- 18. Higgins JPT, Thomas J, Chandler J, et al. Cochrane Handbook for Systematic Reviews of Interventions version 6.3. Cochrane; 2022.
- 19. Liberati A, Altman DG, Tetzlaff J, et al. The PRISMA statement for reporting systematic reviews and meta-analyses of studies that evaluate health care interventions: explanation and elaboration. J Clin Epidemiol. 2009;62[10]:e1-34. doi:10.1016/j.jclinepi.2009.06.006
- 20. Mukherjee PK, Wahile A. Integrated approaches towards drug development from Ayurveda and other Indian system of medicines. J Ethnopharmacol. 2006;103[1]:25-35. doi:10.1016/j.jep.2005.09.024
- 21. Jadad AR, Moore RA, Carroll D, et al. Assessing the quality of reports of randomized clinical trials: is blinding necessary? Control Clin Trials. 1996;17[1]:1-12. doi:10.1016/0197-2456[95]00134-4
- Ramachandran R. Neurogenic inflammation and its role in migraine. Semin Immunopathol. 2018;40[3]:301-314. doi:10.1007/s00281-018-0676-y
- 23. Acharya YT, editor. *Charaka Samhita* of Agnivesha, Siddhi Sthana. Reprint Edition. Ch. 9., Ver. 77. New Delhi: Chaukhambha Publication; 2014. p. 721.
- 24. Acharya YT, editor. *Sushruta Samhita* of Acharya Sushruta. Uttara Tantra. Reprint Edition. Ch. 25., Ver. 15. Varanasi: Chaukhambha Surbharti Publication; 2014. p. 658.
- 25. Vagbhatta. Astanga Hridaya with Sarvangasundara and Ayurvedarasayana commentaries. Varanasi: Chaukhambha Surbhatti Prakashan; 2007. Uttara Sthana, Ch. 23, Ver. 1-3.
- 26. Madhavakara. Madhava Nidana with Madhukosha Sanskrit commentary. Varanasi: Chaukhambha Prakashan; 2013. Ch. 59, Ver. 1-3.
- 27. Bhardwaj A, Singh K, Sharma N. A conceptual review of the disease Ardhavabhedaka w.s.r. to Migraine. J Ayurveda Integr Med Sci. 2019;4[3]:107-114.
- 28. Singh SK, Rajoria K. Ayurvedic management of Ardhavabhedaka [Migraine] A case report. J Ayurveda Med Sci. 2016;1[1]:1-4.

- Hoffmann J, Recober A. Migraine and triggers: post hoc ergo propter hoc? Curr Pain Headache Rep. 2013;17[10]:370. doi:10.1007/s11916-013-0370-7
- Kaviraj Govinddas Sen. Bhaishajya Ratnawali with Siddhiprada Hindi commentary. Varanasi: Chaukhamba Amrabharati Prakashan; 2005.
 Shiroroga Prakarana, Ch. 65, Ver. 1-10.
- 31. Harita. Harita Samhita with Hari Hindi commentary by Pandit Hariharprasad Tripathi. Varanasi: Chaukhamba Krishandas Academy; 2009. Tritya Sthana, Ch. 40, Ver. 1-5.
- 32. Sauro KM, Becker WJ. The stress and migraine interaction. Headache. 2009;49[9]:1378-1386. doi:10.1111/j.1526-4610.2009.01486.x
- 33. Trikamji VJ, editor. *Charaka Samhita* with the Ayurveda Dipika Commentary. Varanasi: Chaukhambha Prakashan; 2011. Siddhi Sthana, Ch. 9, Var. 77
- Trikamji VJ, editor. Susruta Samhita with Nibhandha Sangraha Commentary. Varanasi: Chaukhambha Sanskrit Sansthan; 2010. Uttara Tantra, Ch. 25. Ver. 15.
- Yogaratnakara with Vidyotini Hindi commentary by Vaidya Laksmipati Shastri. Varanasi: Chaukhambha Sanskrit Sansthan; 1983. Uttarardh, Shiroroga Chikitsa, Ver. 1-15.
- Ashoka BN, Galib R, Patgiri BJ, Prajapati PK. A pilot study on clinical efficacy of Agnikarma and Pathyadi Gana drug in the management of Ardhavabhedaka [Migraine]. Ayu. 2017;38[1-2]:19-24. doi:10.4103/ayu.AYU_261_15
- 37. Moskowitz MA, Reinhard JF Jr, Romero J, Melamed E, Pettibone DJ. Neurotransmitters and the fifth cranial nerve: is there a relation to the headache phase of migraine? Lancet. 1979;2[8148]:883-885. doi:10.1016/s0140-6736[79]92692-8
- 38. Burstein R, Noseda R, Borsook D. Migraine: multiple processes, complex pathophysiology. J Neurosci. 2015;35[17]:6619-6629. doi:10.1523/JNEUROSCI.0373-15.2015
- 39. Ho TW, Edvinsson L, Goadsby PJ. CGRP and its receptors provide new insights into migraine pathophysiology. Nat Rev Neurol. 2010;6[10]:573-582. doi:10.1038/nrneurol.2010.127
- Fusco M, D'Andrea G, Miccichè F, et al. Neurogenic inflammation in primary headaches. Neurol Sci. 2003;24[Suppl 2]:s61-s64. doi:10.1007/s100720300043
- Oliver KR, Wainwright A, Edvinsson L, et al. Immunohistochemical localization of calcitonin receptor-like receptor and receptor activity-modifying proteins in the human cerebral vasculature. J Cereb Blood Flow Metab. 2002;22[5]:620-629. doi:10.1097/00004647-200205000-00014
- 42. Charles AC, Baca SM. Cortical spreading depression and migraine. Nat Rev Neurol. 2013;9[11]:637-644. doi:10.1038/nrneurol.2013.192
- 43. Ayata C, Jin H, Kudo C, Dalkara T, Moskowitz MA. Suppression of cortical spreading depression in migraine prophylaxis. Ann Neurol. 2006;59[4]:652-661. doi:10.1002/ana.20778
- 44. Fabricius M, Fuhr S, Bhatia R, et al. Cortical spreading depression and peri-infarct depolarization in acutely injured human cerebral cortex. Brain. 2006;129[Pt 3]:778-790. doi:10.1093/brain/awh716
- 45. Eikermann-Haerter K, Ayata C. Cortical spreading depression and migraine. Curr Neurol Neurosci Rep. 2010;10[3]:167-173. doi:10.1007/s11910-010-0099-1
- 46. Russell FA, King R, Smillie SJ, Kodji X, Brain SD. Calcitonin gene-related peptide: physiology and pathophysiology. Physiol Rev. 2014;94[4]:1099-1142. doi:10.1152/physrev.00034.2013
- 47. Goadsby PJ, Edvinsson L, Ekman R. Vasoactive peptide release in the extracerebral circulation of humans during migraine headache. Ann Neurol. 1990;28[2]:183-187. doi:10.1002/ana.410280213
- 48. Brain SD, Williams TJ, Tippins JR, et al. Calcitonin gene-related peptide is a potent vasodilator. Nature. 1985;313[5997]:54-56. doi:10.1038/313054a0
- Ramachandran M, Arosio P, Gobbi C, et al. Neurogenic inflammation: a key component in migraine pathophysiology. Neurol Sci. 2019;40[Suppl 1]:S61-S66. doi:10.1007/s10072-019-03826-7
- Headache Classification Committee of the International Headache Society [IHS]. The International Classification of Headache Disorders, 3rd edition. Cephalalgia. 2018;38[1]:1-211. doi:10.1177/0333102417738202
- 51. Vingen JV, Pareja JA, Støren O, White LR, Stovner LJ. Phonophobia in migraine. Cephalalgia. 1998;18[5]:243-249. doi:10.1046/j.1468-2982.1998.1805243.x
- 52. Kelman L. The triggers or precipitants of the acute migraine attack. Cephalalgia. 2007;27[5]:394-402. doi:10.1111/j.1468-2982.2007.01303.x

- Katsarava Z, Buse DC, Manack AN, Lipton RB. Defining the differences between episodic migraine and chronic migraine. Curr Pain Headache Rep. 2012;16[1]:86-92. doi:10.1007/s11916-011-0233-z
- 54. Status Migrainosus and Migraine Variants. Continuum [Minneap Minn]. 2015;21[4]:1018-1024. doi:10.1212/CON.0000000000000199
- 55. Karsan N, Goadsby PJ. Biological insights from the premonitory symptoms of migraine. Nat Rev Neurol. 2018;14[12]:699-710. doi:10.1038/s41582-018-0098-4
- de Vries B, Frants RR, Ferrari MD, van den Maagdenberg AM. Molecular genetics of migraine. Hum Genet. 2009;126[1]:115-132. doi:10.1007/s00439-009-0684-z
- 57. Ferrari MD, Klever RR, Terwindt GM, et al. Migraine pathophysiology: lessons from mouse models and human genetics. Lancet Neurol. 2015;14[1]:65-80. doi:10.1016/S1474-4422[14]70220-0
- 58. Waeber C, Moskowitz MA. Migraine as an inflammatory disorder. Neurology. 2005;64[10 Suppl 2]:S9-15. doi:10.1212/WNL.64.10_suppl_2.S9
- 59. Bernstein C, Burstein R. Sensitization of the trigeminovascular pathway: perspective and implications to migraine pathophysiology. J Clin Neurol. 2012;8[2]:89-99. doi:10.3988/jcn.2012.8.2.89
- 60. Pietrobon D, Moskowitz MA. Chaos and commotion in the wake of cortical spreading depression and spreading depolarizations. Nat Rev Neurosci. 2014;15[6]:379-393. doi:10.1038/nrn3770
- 61. Dodick D, Silberstein S. Central sensitization theory of migraine: clinical implications. Headache. 2006;46 Suppl 4:S182-191. doi:10.1111/j.1526-4610.2006.00602.x
- 62. Peroutka SJ. What turns on a migraine? A systematic review of migraine precipitating factors. Curr Pain Headache Rep. 2014;18[10]:454. doi:10.1007/s11916-014-0454-z
- 63. Rains JC, Poceta JS. Sleep and migraine: assessment and treatment of comorbid sleep disorders. Headache. 2012;52[6]:1012-1027. doi:10.1111/j.1526-4610.2012.02158.x
- 64. Pescador Ruschel MA, De Jesus O. Migraine Headache. [Updated 2024 Jul 5]. In: StatPearls [Internet]. Treasure Island [FL]: StatPearls Publishing; 2024.
- 65. Martin VT, Behbehani MM. Toward a rational understanding of migraine trigger factors. Med Clin North Am. 2001;85[4]:911-941. doi:10.1016/s0025-7125[05]70351-2
- 66. Zebenholzer K, Rudel E, Frantal S, et al. Migraine and weather: a prospective diary-based analysis. Cephalalgia. 2011;31[4]:391-400. doi:10.1177/0333102410385580
- 67. Singh RH. Panchakarma Therapy. 2nd ed. Varanasi: Chaukhambha Sanskrit Pratishthan; 2007.
- 68. Sharma H, Chandola HM, Singh G, Basisht G. Utilization of Ayurveda in health care: an approach for prevention, health promotion, and treatment of disease. Part 2--Ayurveda in primary health care. J Altern Complement Med. 2007;13[10]:1135-1150. doi:10.1089/acm.2007.7017-B
- Patel KS, Patel MH, Gupta SN, Shah KN. Clinical efficacy of ayurvedic treatment regimen on Ardhavabhedaka [Migraine]. Ayu. 2012;33[3]:316-319. doi:10.4103/0974-8520.108817
- 70. Singh N, Bhalla M, de Jager P, Gilca M. An overview on ashwagandha: a Rasayana [rejuvenator] of Ayurveda. Afr J Tradit Complement Altern Med. 2011;8[5 Suppl]:208-213. doi:10.4314/ajtcam.v8i5S.9
- 71. Djupesland PG, Messina JC, Mahmoud RA. The nasal approach to delivering treatment for brain diseases: an anatomic, physiologic, and delivery technology overview. Ther Deliv. 2014;5[6]:709-733. doi:10.4155/tde.14.41
- 72. Ashoka BN, Galib R, Patgiri BJ, Prajapati PK. A pilot study on clinical efficacy of Agnikarma and Pathyadi Gana drug in the management of Ardhavabhedaka [Migraine]. Ayu. 2017;38[1-2]:19-24. doi:10.4103/ayu.AYU_261_15
- Maurya OP, Dixit AK, Singh K, et al. Ayurvedic therapy [Shirodhara] for insomnia: a case series. Glob Adv Health Med. 2014;3[1]:75-82. doi:10.7453/gahmj.2013.086
- 74. Uebaba K, Xu FH, Ogawa H, et al. Psychoneuroimmunologic effects of Ayurvedic oil-dripping treatment. J Altern Complement Med. 2008;14[10]:1189-1198. doi:10.1089/acm.2008.0273
- 75. Singh RH, Udupa KN. Studies on the Indian indigenous drug punarnava [Boerhaavia diffusa Linn.]. IV. Preliminary controlled clinical trial in nephrotic syndrome. J Res Indian Med. 1972;7[4]:28-33.
- Uebaba K, Xu FH, Ogawa H, et al. Psychoneuroimmunologic effects of Ayurvedic oil-dripping treatment. J Altern Complement Med. 2008;14[10]:1189-1198. doi:10.1089/acm.2008.0273

- 77. Russo A, Borrelli F. Bacopa monniera, a reputed nootropic plant: an overview. Phytomedicine. 2005;12[4]:305-317. doi:10.1016/j.phymed.2003.12.008
- Aguiar S, Borowski T. Neuropharmacological review of the nootropic herb Bacopa monnieri. Rejuvenation Res. 2013;16[4]:313-326. doi:10.1089/rej.2013.1431
- Chandrasekhar K, Kapoor J, Anishetty S. A prospective, randomized double-blind, placebo-controlled study of safety and efficacy of a high-concentration full-spectrum extract of ashwagandha root in reducing stress and anxiety in adults. Indian J Psychol Med. 2012;34[3]:255-262. doi:10.4103/0253-7176.106022
- 80. Jung HS, Kim MH, Gwak NG, et al. Anticonvulsant and neuroprotective effects of Nardostachys jatamansi in pilocarpine-induced epileptic seizures in rats. J Ethnopharmacol. 2006;106[2]:272-278. doi:10.1016/j.jep.2006.01.005
- 81. Cameron C, Kelly S, Hsieh SC, et al. Triptans in the Acute Treatment of Migraine: A Systematic Review and Network Meta-Analysis. Headache. 2015;55 Suppl 4:221-235. doi:10.1111/head.12601
- Croop R, Goadsby PJ, Stock DA, et al. Efficacy, safety, and tolerability of rimegepant orally disintegrating tablet for the acute treatment of migraine: a randomised, phase 3, double-blind, placebo-controlled trial. Lancet. 2019;394[10200]:737-745. doi:10.1016/S0140-6736[19]31606-X
- 83. Silberstein SD, Holland S, Freitag F, et al. Evidence-based guideline update: pharmacologic treatment for episodic migraine prevention in adults: report of the Quality Standards Subcommittee of the American Academy of Neurology and the American Headache Society. Neurology. 2012;78[17]:1337-1345. doi:10.1212/WNL.0b013e3182535d20
- 84. Patwardhan B, Mashelkar RA. Traditional medicine-inspired approaches to drug discovery: can Ayurveda show the way forward? Drug Discov Today. 2009;14[15-16]:804-811. doi:10.1016/j.drudis.2009.05.009
- 85. Tepper SJ. Intranasal medications for primary headache disorders. Headache. 2013;53[1]:4-17. doi:10.1111/j.1526-4610.2012.02274.x
- 86. Illum L. Nasal drug delivery--possibilities, problems and solutions. J Control Release. 2003;87[1-3]:187-198. doi:10.1016/s0168-3659[02]00363-2
- 87. Campos AR, Barros AI, Albuquerque FA, et al. Acute effects of guarana [Paullinia cupana Mart.] on mouse behaviour in forced swimming and open field tests. Phytother Res. 2005;19[5]:441-443. doi:10.1002/ptr.1660
- 88. Kumar A, Rinwa P, Kaur G, Machawal L. Stress: Neurobiology, consequences and management. J Pharm Bioallied Sci. 2013;5[2]:91-97. doi:10.4103/0975-7406.111818
- 89. Stough C, Lloyd J, Clarke J, et al. The chronic effects of an extract of Bacopa monniera [Brahmi] on cognitive function in healthy human subjects. Psychopharmacology [Berl]. 2001;156[4]:481-484. doi:10.1007/s002130100815
- Calabrese C, Gregory WL, Leo M, et al. Effects of a standardized Bacopa monnieri extract on cognitive performance, anxiety, and depression in the elderly: a randomized, double-blind, placebo-controlled trial. J Altern Complement Med. 2008;14[6]:707-713. doi:10.1089/acm.2008.0018
- 91. Auddy B, Hazra J, Mitra A, et al. A standardized Withania somnifera extract significantly reduces stress-related parameters in chronically stressed humans: a double-blind, randomized, placebo-controlled study. JANA. 2008;11[1]:50-56.
- 92. Kizhakkeveettil A, Rose KA, Kadar GE. Integrative therapies for low back pain that include complementary and alternative medicine care: a systematic review. Glob Adv Health Med. 2014;3[5]:49-64. doi:10.7453/gahmj.2014.044
- 93. Sharma R, Martins N, Kuca K, et al. Chyawanprash: A Traditional Indian Bioactive Health Supplement. Biomolecules. 2019;9[5]:161. doi:10.3390/biom9050161
- 94. Dhiman KS, Ramamurthy A, Mamidi P. A multi-centric open-label randomized controlled trial to evaluate the add-on effect of Shiva Gita on selected depression rating scales and quality of life measures in patients with major depressive disorder. Ayu. 2016;37[2]:114-119. doi:10.4103/ayu.AYU_118_15
- 95. MacLellan J, Craigie AM, O'Carroll RE, et al. Implementation of a 12-week structured lifestyle intervention in adults with type 2 diabetes: a mixed methods feasibility study. Pilot Feasibility Stud. 2016;2:49. doi:10.1186/s40814-016-0090-3
- 96. Ashoka BN, Galib R, Patgiri BJ, Prajapati PK. A pilot study on clinical efficacy of Agnikarma and Pathyadi Gana drug in the management of Ardhavabhedaka [Migraine]. Ayu. 2017;38[1-2]:19-24. doi:10.4103/ayu.AYU_261_15
- 97. Patwardhan B. Bridging Ayurveda with evidence-based scientific approaches in medicine. EPMA J. 2014;5[1]:19. doi:10.1186/1878-5085-5-19
- 98. Mukherjee PK, Wahile A. Integrated approaches towards drug development from Ayurveda and other Indian system of medicines. J Ethnopharmacol. 2006;103[1]:25-35. doi:10.1016/j.jep.2005.09.024

- 99. Chopra A, Doiphode VV. Ayurvedic medicine. Core concept, therapeutic principles, and current relevance. Med Clin North Am. 2002;86[1]:75-89. doi:10.1016/s0025-7125[03]00073-7
- 100. Headache Classification Committee of the International Headache Society [IHS]. The International Classification of Headache Disorders, 3rd edition. Cephalalgia. 2018;38[1]:1-211. doi:10.1177/0333102417738202
- Hankey A. A test of the systems analysis underlying the scientific theory of Ayurveda's Tridosha. J Altern Complement Med. 2005;11[3]:385-390. doi:10.1089/acm.2005.11.385
- 102. Patwardhan B, Bodeker G. Ayurvedic genomics: establishing a genetic basis for mind-body typologies. J Altern Complement Med. 2008;14[5]:571-576. doi:10.1089/acm.2007.0515
- 103. Ferrari MD, Klever RR, Terwindt GM, et al. Migraine pathophysiology: lessons from mouse models and human genetics. Lancet Neurol. 2015;14[1]:65-80. doi:10.1016/S1474-4422[14]70220-0
- 104. Levy D. Migraine pain and nociceptor activation--where do we stand? Headache. 2010;50[5]:909-916. doi:10.1111/j.1526-4610.2010.01670.x
- 105. Bolay H, Reuter U, Dunn AK, et al. Intrinsic brain activity triggers trigeminal meningeal afferents in a migraine model. Nat Med. 2002;8[2]:136-142. doi:10.1038/nm0202-136
- 106. Messlinger K, Lennerz JK, Eberhardt M, Fischer MJ. CGRP and NO in the trigeminal system: mechanisms and role in headache generation. Headache. 2012;52[9]:1411-1427. doi:10.1111/j.1526-4610.2012.02212.x
- 107. Burstein R, Jakubowski M. Analgesic triptan action in an animal model of intracranial pain: a race against the development of central sensitization. Ann Neurol. 2004;55[1]:27-36. doi:10.1002/ana.10785
- 108. Prasher B, Negi S, Aggarwal S, et al. Whole genome expression and biochemical correlates of extreme constitutional types defined in Ayurveda. J Transl Med. 2008;6:48. doi:10.1186/1479-5876-6-48
- 109. MacPherson H, Vertosick EA, Foster NE, et al. The persistence of the effects of acupuncture after a course of treatment: a meta-analysis of patients with chronic pain. Pain. 2017;158[5]:784-793. doi:10.1097/j.pain.000000000000747
- 110. Linde K, Allais G, Brinkhaus B, et al. Acupuncture for the prevention of episodic migraine. Cochrane Database Syst Rev. 2016;6[6]:CD001218. doi:10.1002/14651858.CD001218.pub3
- 111. Agrawal R, Tyagi E, Shukla R, et al. A study of changes in some haematological parameters in a randomized controlled trial of *Nasya* and medhya rasayana compound against Alzheimer's disease. Ayu. 2011;32[2]:176-182. doi:10.4103/0974-8520.92572
- 112. Kumar A, Rinwa P, Kaur G, Machawal L. Stress: Neurobiology, consequences and management. J Pharm Bioallied Sci. 2013;5[2]:91-97. doi:10.4103/0975-7406.111818
- 113. Tepper SJ. Intranasal medications for primary headache disorders. Headache. 2013;53[1]:4-17. doi:10.1111/j.1526-4610.2012.02274.x
- 114. Gogtay NJ, Bhatt HA, Dalvi SS, Kshirsagar NA. The use and safety of non-allopathic Indian medicines. Drug Saf. 2002;25[14]:1005-1019. doi:10.2165/00002018-200225140-00003
- 115. Stough C, Downey LA, Lloyd J, et al. Examining the nootropic effects of a special extract of Bacopa monniera on human cognitive functioning: 90 day double-blind placebo-controlled randomized trial. Phytother Res. 2008;22[12]:1629-1634. doi:10.1002/ptr.2537
- 116. Pratte MA, Nanavati KB, Young V, Morley CP. An alternative treatment for anxiety: a systematic review of human trial results reported for the Ayurvedic herb ashwagandha [Withania somnifera]. J Altern Complement Med. 2014;20[12]:901-908. doi:10.1089/acm.2014.0177
- 117. Ernst E, White AR. Acupuncture for back pain: a meta-analysis of randomized controlled trials. Arch Intern Med. 1998;158[20]:2235-2241. doi:10.1001/archinte.158.20.2235
- 118. Chaibi A, Tuchin PJ, Russell MB. Manual therapies for migraine: a systematic review. J Headache Pain. 2011;12[2]:127-133. doi:10.1007/s10194-011-0296-6
- 119. Wells RE, Beuthin J, Granetzke L. Complementary and integrative medicine for episodic migraine: an update of evidence from the last 3 years. Curr Pain Headache Rep. 2019;23[2]:10. doi:10.1007/s11916-019-0750-8
- 120. Fabricant DS, Farnsworth NR. The value of plants used in traditional medicine for drug discovery. Environ Health Perspect. 2001;109 Suppl 1:69-75. doi:10.1289/ehp.01109s169
- 121. Newman DJ, Cragg GM. Natural products as sources of new drugs over the 30 years from 1981 to 2010. J Nat Prod. 2012;75[3]:311-335. doi:10.1021/np200906s
- 122. Patwardhan B, Mashelkar RA. Traditional medicine-inspired approaches to drug discovery: can Ayurveda show the way forward? Drug Discov Today. 2009;14[15-16]:804-811. doi:10.1016/j.drudis.2009.05.009

- 123. Kurande V, Bilhana S, Joshi K, et al. Ayurvedic pulse diagnosis for recognition of consciousness level. Ayu. 2013;34[3]:288-295. doi:10.4103/0974-8520.123126
- 124. Ernst E. Ayurvedic medicine: what does the evidence say? Rheumatology [Oxford]. 2010;49[4]:793-794. doi:10.1093/rheumatology/keq018
- 125. Gogtay NJ, Bhatt HA, Dalvi SS, Kshirsagar NA. The use and safety of non-allopathic Indian medicines. Drug Saf. 2002;25[14]:1005-1019. doi:10.2165/00002018-200225140-00003
- 126. Tillu G, Chaturvedi S, Chopra A, Patwardhan B. Public health approach of Ayurveda and yoga for COVID-19 prophylaxis. J Altern Complement Med. 2020;26[5]:360-364. doi:10.1089/acm.2020.0129
- 127. Varkey E, Cider Å, Carlsson J, Linde M. Exercise as migraine prophylaxis: a randomized study using relaxation and topiramate as controls. Cephalalgia. 2011;31[14]:1428-1438. doi:10.1177/0333102411419681
- 128. Darabaneanu S, Overath CH, Rubin D, et al. Aerobic exercise as a therapy option for migraine: a pilot study. Int J Sports Med. 2011;32[6]:455-460. doi:10.1055/s-0030-1269928
- 129. Schwedt TJ, Vargas B. Neurostimulation for treatment of migraine and cluster headache. Pain Med. 2015;16[9]:1827-1834. doi:10.1111/pme.12792
- 130. Patwardhan B, Vaidya ADB, Chorghade M. Ayurveda and natural products drug discovery. Curr Sci. 2004;86[6]:789-799.
- 131. Prasher B, Negi S, Aggarwal S, et al. Whole genome expression and biochemical correlates of extreme constitutional types defined in Ayurveda. J Transl Med. 2008;6:48. doi:10.1186/1479-5876-6-48
- 132. Bhushan P, Kalpana J, Arvind C. Classification of human population based on HLA gene polymorphism and the concept of Prakriti in Ayurveda. J Altern Complement Med. 2005;11[2]:349-353. doi:10.1089/acm.2005.11.349
- 133. Santiago MD, Carvalho Dde S, Gabbai AA, et al. Amitriptyline and aerobic exercise or amitriptyline alone in the treatment of chronic migraine: a randomized comparative study. Arq Neuropsiquiatr. 2014;72[11]:851-855. doi:10.1590/0004-282X20140148
- 134. World Health Organization. WHO Traditional Medicine Strategy 2014-2023. Geneva: World Health Organization; 2013.
- 135. Robinson A, McGrail MR. Disclosure of CAM use to medical practitioners: a review of qualitative and quantitative studies. Complement Ther Med. 2004;12[2-3]:90-98. doi:10.1016/j.ctim.2004.09.006
- 136. Sen S, Chakraborty R. Revival, modernization and integration of Indian traditional herbal medicine in clinical practice: importance, challenges and future. J Tradit Complement Med. 2017;7[2]:234-244. doi:10.1016/j.jtcme.2016.05.006
- 137. World Health Organization. WHO global report on traditional and complementary medicine 2019. Geneva: World Health Organization; 2019.
- 138. World Health Organization. WHO Traditional Medicine Strategy 2014-2023. Geneva: World Health Organization; 2013.
- 139. Lipton RB, Bigal ME, Diamond M, et al. Migraine prevalence, disease burden, and the need for preventive therapy. Neurology. 2007;68[5]:343-349. doi:10.1212/01.wnl.0000252808.97649.21
- 140. Buse DC, Manack A, Serrano D, et al. Sociodemographic and comorbidity profiles of chronic migraine and episodic migraine sufferers. J Neurol Neurosurg Psychiatry. 2010;81[4]:428-432. doi:10.1136/jnnp.2009.192492
- 141. Bigal ME, Serrano D, Reed M, Lipton RB. Chronic migraine in the population: burden, diagnosis, and satisfaction with treatment. Neurology. 2008;71[8]:559-566. doi:10.1212/01.wnl.0000323925.29520.e7
- 142. May A, Schulte LH. Chronic migraine: risk factors, mechanisms and treatment. Nat Rev Neurol. 2016;12[8]:455-464. doi:10.1038/nrneurol.2016.93
- 143. Diener HC, Dodick DW, Ayata C, et al. Evidence-based guideline update: NSAIDs and other complementary treatments for episodic migraine prevention in adults: report of the Quality Standards Subcommittee of the American Academy of Neurology and the American Headache Society. Neurology. 2019;92[20]:e2307-e2317. doi:10.1212/WNL.0000000000007482
- 144. Smitherman TA, Burch R, Sheikh H, Loder E. The prevalence, impact, and treatment of migraine and severe headaches in the United States: a review of statistics from national surveillance studies. Headache. 2013;53[3]:427-436. doi:10.1111/head.12074
- 145. Buse DC, Loder EW, Gorman JA, et al. Sex differences in the prevalence, symptoms, and associated features of migraine, probable migraine and other severe headache: results of the American Migraine Prevalence and Prevention [AMPP] Study. Headache. 2013;53[8]:1278-1299. doi:10.1111/head.12150
- 146. Rizzoli P, Loder E. Tolerance to the beneficial effects of prophylactic migraine drugs: a systematic review of causes and mechanisms. Headache. 2011;51[8]:1323-1335. doi:10.1111/j.1526-4610.2011.01991.x

- 147. Hepp Z, Dodick DW, Varon SF, et al. Adherence to oral migraine-preventive medications among patients with chronic migraine. Cephalalgia. 2015;35[6]:478-488. doi:10.1177/0333102414547138
- 148. Raggi A, Giovannetti AM, Quintas R, et al. A systematic review of the psychosocial difficulties relevant to patients with migraine. J Headache Pain. 2012;13[8]:595-606. doi:10.1007/s10194-012-0482-1
- 149. Dodick DW, Loder EW, Manack Adams A, et al. Assessing barriers to chronic migraine consultation, diagnosis, and treatment: Results from the chronic migraine epidemiology and outcomes [CaMEO] study. Headache. 2016;56[5]:821-834. doi:10.1111/head.12774