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Integrative review of *Kakamachi* (*Solanum nigrum* L.) in Mydriasis with Ayurvedic and Ophthalmic Insights

[1]A Karthika, and [2]Khemchandra L. Mahajan

[1,2]Department of Shalakya Tantra, Parul Institute of Ayurved and Research, Vadodara – 391760 (India)

Abstract

Kakamachi (*Solanum nigrum* L.) is a herb mentioned in Ayurveda that has an action on all eye diseases. In ophthalmology, usually for pupil dilation, which is done for dilating the pupil, they use tropicamide and which is used universally as it works well and has a quick action comparatively, but evidences suggest that it also triggers side effects such as burning sensation, narrowing of anterior chamber angles, blurring of vision, difficulty in seeing objects at night, painful irritation, etc. In Ayurvedic classical texts like *Bhavaprakasha Nighantu*, it is quoted that *kakamachi* is *tridoshagna* and *netrahita* and *chakshushya*. Laboratory studies have proved that Solanum nigrum contains active compounds such as solasodine, solasonine and solamargine, which have their parasympathetic action on the central nervous system, which helps in dilation of the pupil. However, proper clinical validation and research have not been conducted to date, and it's still lacking. However, variability in active alkaloid content and lack of standardised extract preparation, including HPLC-based solasodine quantification, limit reproducibility and warrant controlled studies for clinical validation. This review documents classical Ayurvedic references, pharmacological data and available clinical findings on *Kakamchi* compared to the conventional agent Tropicacyl plus. Current evidence provides that *kakamachi* has pupil dilating action as it contains the active compound with fewer risks, so more controlled trials should be done before it can be considered a reliable alternative.

Key words : Kakamachi, *Solanum nigrum*, tropicamide, mydriasis, Ayurveda, integrative ophthalmology.

Pupillary dilation (mydriasis) is a fundamental procedure in ophthalmic practice because it enables clear visualization of the retina, optic nerve and posterior segment of the eye. Pharmacological mydriatics such as tropicamide, phenylephrine, cyclopentolate and atropine are routinely used, with tropicamide being the most commonly preferred agent due

[1]Post Graduate Scholar, [2]Professor

to its rapid onset and short duration of action[10,11,24]. Despite being considered the standard drug for diagnostic dilation, tropicamide is associated with several ocular adverse effects, including photophobia, blurred vision and transient elevation of intraocular pressure, along with systemic effects in susceptible individuals[5,8]. These limitations have prompted the search for safer and better-tolerated alternatives, particularly for populations in whom conventional mydriatics are contraindicated. In Ayurveda, the eyes are regarded as one of the most vital sense organs, and ocular diseases are described extensively in classical texts. Numerous *chakshushya dravyas* have been documented by ancient scholars as herbs beneficial for eye health, among which Kakamachi (*Solanum nigrum*) is frequently mentioned[3,23,26]. Contemporary phytochemical research has identified several bioactive constituents in *Solanum nigrum*, including steroidal alkaloids such as solasodine, solasonine and solamargine, along with flavonoids, polyphenols and glycoproteins[4,9,22,27]. These compounds exhibit anti-inflammatory, antioxidant and neuro-modulatory properties, some of which may influence pupillary function through autonomic nervous system pathways[9,27]. Experimental studies have further demonstrated that extracts of *Solanum nigrum* can modulate smooth muscle activity and neurotransmitter pathways, providing a pharmacological basis for their potential use in ophthalmic conditions[15,22]. With the growing global interest in integrative and complementary medicine, Ayurvedic herbs are gaining attention in ophthalmology. Herbal eye drops have shown promising safety and tolerability profiles; however, well-designed comparative studies are still limited[14,21]. Preliminary clinical and observational reports suggest that Kakamachi-based formulations may induce mild pupil dilation with minimal side effects, although randomized controlled trials are still required[12,14]. Therefore, the exploration of Kakamachi as a potential mydriatic represents a significant convergence of traditional Ayurvedic knowledge and modern pharmacological research. The present review aims to integrate classical Ayurvedic literature, pharmacological evidence and clinical findings related to Kakamachi and pupil dilation, to critically compare its potential with tropicamide and to identify future research directions in integrative ophthalmology.

Data Sources :

Classical Ayurvedic scriptures and modern biomedical databases were used to ensure comprehensive coverage of the topic. Classical sources included the *Charaka Samhita*, *Sushruta Samhita*, and later Nighantus such as the *Bhavaprakasha Nighantu*, with particular emphasis on references describing *chakshushya dravyas* and the ophthalmic relevance of Kakamachi[3,20,23]. Relevant verses were carefully transliterated, interpreted into contextual English and cross-verified with authoritative commentaries to ensure accuracy and relevance. Ayurvedic literature was systematically reviewed with special focus on references related to *netra roga* and pharmacological attributes of Kakamachi. For modern evidence, peer-reviewed biomedical literature was retrieved from PubMed, Scopus, Web of Science and ScienceDirect using keywords such as *Solanum nigrum*, Kakamachi, pupil dilation, mydriasis, Ayurvedic ophthalmology, ocular pharmacology and herbal eye drops. Boolean operators and MeSH terms were

applied to refine the search strategy. Recent studies evaluating the neuroprotective, anti-inflammatory and pharmacological effects of *Solanum nigrum* and herbal ophthalmic formulations were particularly emphasized[9,21].

Search Strategy :

The literature search was designed to be systematic and comprehensive. Initially, classical Ayurvedic concepts related to ocular health and pupillary modulation were identified from authoritative texts. This was followed by retrieval of modern experimental and clinical studies investigating the pharmacological effects of *Solanum nigrum* and agents influencing pupillary dilation[9,21]. References of the selected articles were manually screened to identify additional relevant publications that may not have been captured during the initial database search. Grey literature, including doctoral theses and institutional reports from Ayurvedic universities and research institutes in India, was also consulted to broaden the scope and include relevant unpublished data where available.

Inclusion Criteria :

The inclusion criteria were limited to studies describing pharmacological activities relevant to ocular health, including anti-inflammatory, neuro-modulatory and smooth muscle-modulating properties. Experimental and clinical studies evaluating *Solanum nigrum* for ocular use, as well as studies assessing herbal ophthalmic preparations and their effects on pupillary response, were included. Additionally, articles describing pupillary responses to conventional mydriatic agents were considered for comparative analysis[9,21].

Exclusion criteria :

Studies were excluded if they were limited to conference abstracts without full-text availability, anecdotal reports lacking empirical evidence, or publications that had not undergone peer review. These criteria ensured that the evidence included in the review remained scientifically reliable and robust[9,21].

Ethical considerations :

All procedures undertaken in this literature review adhered to established standards of academic integrity. Proper referencing of classical Ayurvedic texts and modern scientific literature was maintained to ensure transparency and authenticity. This approach supported the integration of traditional knowledge with contemporary scientific evidence[18].

Review of Literature :

Ayurvedic perspective :

Ayurveda places strong emphasis on ocular health and describes vision (*chakshu-rendriya*) as one of the most important senses for maintaining quality of life. Classical treatises provide detailed descriptions of *netra roga* and their management. Within this framework, several herbs are categorized as *chakshushya dravyas*, indicating their specific benefits for eye health. Among these, Kakamachi (*Solanum nigrum*) occupies a prominent place. The *Charaka Samhita*

describes *chakshushya dravyas* as possessing cooling, nourishing and dosha-balancing properties that support ocular function[23]. Similarly, the *Sushruta Samhita* provides detailed descriptions of ophthalmic diseases and formulations aimed at preserving visual acuity and managing disorders associated with aggravated pitta[20].

The *Bhavaprakasha Nighantu* clearly describes Kakamachi as *tridoshaghna*, *chakshushya* and *rasayana*, indicating its ability to pacify all three doshas, promote ocular health and provide rejuvenative effects[3]. Other Nighantus such as the *Kaiyadeva Nighantu* also describe similar properties supporting its role in maintaining eye health[26]. Pharmacodynamically, Kakamachi is described as having *tikta rasa* (bitter taste), *laghu guna* (lightness), *sheeta virya* (cool potency) and *madhura vipaka* (sweet post-digestive effect). These attributes suggest its usefulness in pacifying pitta and rakta disorders, which are commonly implicated in ocular pathologies.

Modern Pharmacological Insights :

Phytochemical investigations of *Solanum nigrum* have revealed a diverse range of active constituents, including steroidal glycoalkaloids such as solasodine, solasonine and solamargine, along with flavonoids, tannins and phenolic acids[4,9,22,27]. These compounds demonstrate antioxidant, anti-inflammatory, cytoprotective and neuro-modulatory activities that may contribute to ocular tissue protection[9, 22,27]. The antioxidant properties of *Solanum nigrum* may help protect ocular tissues from oxidative stress, a key factor in many eye disorders, while neuro-modulatory effects may influence pupillary dynamics[9,27]. Experimental studies have shown that extracts of *Solanum nigrum* can regulate smooth muscle activity, which is relevant to the sphincter and dilator muscles of the iris[15]. Additionally, solasodine derivatives have been investigated for their influence on cholinergic and adrenergic neurotransmitter pathways that regulate pupillary function[27]. These findings provide a plausible pharmacological explanation for the mild mydriatic potential of Kakamachi.

Clinical and Experimental Studies :

Clinical studies evaluating Ayurvedic ophthalmic formulations remain limited but are gradually increasing. Herbal eye drops containing *chakshushya* herbs such as Kakamachi have shown promising results in the management of ocular inflammation and discomfort without major adverse effects[14]. Direct comparative studies between tropicamide and herbal preparations are scarce; however, preliminary reports suggest that while tropicamide produces rapid mydriasis, herbal formulations may provide slower but more sustained dilation with improved tolerability[12]. Pupillometry has emerged as an objective technique for measuring pupillary responses and is increasingly used in clinical pharmacology to assess drug effects on the iris[2,17]. Incorporation of such objective methods in future studies of Kakamachi-based formulations may provide more reliable efficacy data. The safety of herbal extracts is particularly relevant for vulnerable populations such as pediatric, geriatric and glaucoma-prone patients, in whom synthetic mydriatics may pose additional risks[5,8].

Comparative Analysis of Kakamachi (*Solanum Nigrum* L.) *and Tropicamide for Mydriasis:*

A mechanistic comparison begins with the understanding that tropicamide is a short-acting antimuscarinic drug that inhibits parasympathetic innervation of the iris sphincter, producing rapid pupil dilation within 15–30 minutes and a relatively short duration of action[8,24]. This predictable pharmacodynamic profile explains its widespread use in diagnostic fundus examination[10,11]. In contrast, Kakamachi does not act through a single receptor target. Its phytochemical composition, particularly steroidal glycoalkaloids and polyphenols, suggests a multimodal mechanism involving antioxidant, anti-inflammatory and neuro-modulatory effects influencing ocular smooth muscle tone and autonomic control[4,9,22,27].

From an Ayurvedic perspective, Kakamachi is described as *chakshushya*, *tridoshaghna* and *rasayana*, indicating a broader role in maintaining ocular homeostasis rather than producing intense pharmacological dilation[3]. Clinically, this corresponds to observations that herbal preparations may produce milder but more sustained pupillary changes with improved tolerability, though with slower onset and lower peak dilation compared with tropicamide[12,14]. When efficacy is defined by the speed and magnitude of dilation required for posterior segment examination, tropicamide remains superior because it can reliably achieve adequate dilation in most adults, sometimes supplemented with phenylephrine in resistant cases[10,11]. However, the adverse-effect profile of tropicamide, including photophobia, transient blurred vision, increased intraocular pressure and the risk of precipitating angle-closure glaucoma in predisposed individuals, limits its use in patients with narrow angles, extreme age groups and cardiovascular comorbidities[5,8]. In contrast, Ayurvedic ophthalmic preparations generally demonstrate good local tolerability and low incidence of systemic reactions, although high-quality comparative trials remain limited[12,14]. Pharmacokinetic differences further distinguish these approaches. Tropicamide shows rapid corneal penetration and short intraocular residence time, enabling quick recovery after examination[8,24]. In contrast, variability in alkaloid concentration and extraction methods of *Solanum nigrum* may influence ocular retention and bioavailability, highlighting the importance of phytochemical standardisation and HPLC-based quantification before valid comparisons can be made[27]. Future studies should incorporate digital pupillometry to measure time to dilation, maximum pupil diameter and recovery slope to provide objective endpoints for comparison[2,17]. Safety profiles also differ significantly. Tropicamide may induce acute angle-closure glaucoma, transient intraocular pressure spikes and systemic anticholinergic effects, necessitating careful patient screening and counselling[5,8]. Herbal formulations require strict sterility, standardised dosing and prospective monitoring of adverse effects to ensure safety and reproducibility[14]. Until controlled trials directly compare Kakamachi and tropicamide using standardised outcomes, Kakamachi should be considered a complementary or alternative option in patients who cannot tolerate conventional mydriatics rather than a direct replacement[10,11,12,14]. From a broader perspective, tropicamide is designed to produce a rapid and

predictable pharmacological effect, whereas Kakamachi, traditionally described as *chakshushya* and *rasayana*, has been associated with ocular comfort and homeostasis. Its mydriatic effect is likely mild and context-dependent, potentially accompanied by protective effects on ocular tissues through antioxidant and anti-inflammatory mechanisms[3,9,22,27]. Future integrative research should evaluate both objective dilation outcomes and patient-centred measures such as photophobia recovery and visual comfort using standardised herbal preparations and validated pharmacological comparators[12,14,15,16].

Modern Clinical use of Tropicamide and Allied agents, and emerging Clinical Signals for Kakamachi :

In modern ophthalmic practice, tropicamide and related pharmacological agents remain the preferred drugs for diagnostic mydriasis due to their well-established pharmacokinetics, ease of administration and ability to provide reproducible objective endpoints such as pupil diameter, onset time and duration of action[8,10,11,24]. Tropicamide ophthalmic solution (0.5% or 1%) acts competitively on muscarinic receptors of the sphincter pupillae, producing predictable muscle relaxation within 15–40 minutes. Phenylephrine is frequently combined with tropicamide to enhance dilation through alpha-adrenergic stimulation of the dilator pupillae[8,24]. These pharmacological characteristics are widely supported by clinical evidence and form part of routine screening and preoperative ophthalmic care. However, known adverse effects include transient photophobia, blurred vision and the possibility of precipitating angle-closure glaucoma in anatomically predisposed individuals without adequate screening[5,7]. Consequently, clinical practice guidelines emphasize pre-dilation angle assessment, patient counselling regarding risks, punctal occlusion and use of minimal effective dosing to reduce systemic absorption and adverse effects[1,8]. Other mydriatic agents such as cyclopentolate, atropine and phenylephrine are selected according to clinical requirements, particularly when stronger or longer-acting cycloplegia is needed. The balance between rapid onset, adequate dilation and patient comfort has established tropicamide as the first-line agent for routine clinical dilation[10,11]. From a research perspective, pupillometry and slit-lamp-based standardized measurements provide objective endpoints that allow robust comparison between mydriatic agents and should be incorporated into trials evaluating herbal ophthalmic preparations[2,17]. In contrast, emerging experimental and preliminary clinical evidence suggests that Kakamachi (*Solanum nigrum*) may exhibit a different pharmacological profile. Rather than producing immediate antimuscarinic blockade, standardised extracts appear to act through neuro-modulatory, anti-inflammatory and smooth muscle-modulating mechanisms that influence pupillary behaviour more gradually[9,22,27]. Phytochemical studies identify steroidal alkaloids and polyphenolic compounds that may contribute to autonomic modulation and ocular tissue protection, providing a theoretical basis for mild-to-moderate mydriasis with improved

tolerability[9,27]. Small pilot studies and ethnopharmacological reports have described acceptable ocular surface tolerability and occasional measurable changes in pupillary diameter; however, variability in preparation methods, concentrations and outcome measures limits direct comparison with commercially available mydriatic eye drops[12,14].

Critical Discussion and Integrative Implications :

The current evidence base supporting Kakamachi (*Solanum nigrum*) as an ophthalmic agent includes three complementary domains: classical Ayurvedic literature describing the plant as *chakshushya* and *rasayana*, phytochemical and preclinical studies demonstrating steroidal alkaloids with anti-inflammatory and antioxidant properties, and a small but growing body of clinical and ethnopharmacological reports indicating good tolerability with occasional objective pupillary effects. Although these findings provide a promising translational pathway, they do not yet meet the level of robust and reproducible evidence required by clinical guidelines and regulatory bodies before a herbal preparation can be recommended as a routine diagnostic mydriatic[12,14]. Classical texts provide valuable historical and conceptual support, but modern standards demand pharmaceutical standardisation, sterility testing, toxicological evaluation and controlled clinical trials to establish safety and efficacy in contemporary practice. Methodologically, several gaps remain evident. First, the heterogeneity of phytochemical composition in *Solanum nigrum* preparations represents a major challenge. Variability in levels of steroidal alkaloids such as solasodine, solasonine and solamargine due to differences in plant source, harvesting conditions and extraction methods directly influences both efficacy and safety. Without uniform standardisation using validated techniques such as HPLC or LC-MS quantification, it is difficult to define therapeutic dosing or compare outcomes across studies[27]. Future investigations should employ standardised extracts with detailed reporting of pharmaceutical parameters such as concentration, pH, osmolarity, sterility and stability to enable reproducibility and meaningful comparison with conventional mydriatics.

Second, most clinical studies to date are observational or uncontrolled, lacking blinded randomised designs and objective endpoints such as pupillometry, intraocular pressure monitoring and anterior chamber angle assessment that would permit direct comparison with tropicamide. Third, pharmaceutical quality parameters such as sterility, preservative safety and particulate limits are rarely reported despite their importance in determining ocular safety. Future translational research must therefore focus on standardisation, rigorous clinical trial design and pharmaceutical quality assurance if Kakamachi is to progress beyond an ethnobotanical candidate[27].

Despite these limitations, pragmatic clinical applications may be considered. In patients with contraindications to antimuscarinic mydriatics, such as those with narrow anterior chamber angles, cardiovascular comorbidities or anticholinergic sensitivity, a standardised Kakamachi preparation may serve as a lower-dose alternative for limited diagnostic use when

appropriate screening and sterility testing have been completed. However, clinicians must recognise that the magnitude and onset of dilation are likely to be less and slower than with tropicamide[8,24]. Translation into clinical practice must also follow ethical and regulatory frameworks. Future trials should be prospectively registered in the Clinical Trials Registry of India and conducted according to AYUSH Good Clinical Practice guidelines and CONSORT recommendations for herbal interventions to ensure transparency and reproducibility[6,18,19]. Publication of authenticated plant specimens, detailed extraction procedures and batch-release testing, including sterility, endotoxin levels, pH, osmolarity and HPLC fingerprinting, is essential for regulatory acceptance and scientific credibility. A phased clinical research pathway is recommended, beginning with in vitro cytotoxicity and ocular irritation testing, followed by in vivo tolerability and dose-finding studies, and subsequently small randomised pilot trials evaluating pupillometry endpoints, intraocular pressure changes and ocular surface safety. If safety and efficacy signals are favourable, larger randomised noninferiority trials using standardised extracts and objective measurements can be undertaken. Comprehensive reporting of phytochemical characterisation and pharmaceutical manufacturing details will be essential for reproducibility. Beyond efficacy and safety, integrative implications are noteworthy. Standardised Kakamachi-based ophthalmic preparations may expand access to community eye care in low-resource settings where refrigeration and cold-chain distribution of synthetic drugs are challenging. A preparation producing milder but more sustained dilation may be suitable for screening programs and for patients who require rapid return to near work after examination. However, the slower onset and smaller magnitude of dilation suggest that Kakamachi is unlikely to replace tropicamide for surgical or high-intensity diagnostic applications. Instead, its role may lie in specific evidence-based niches where cultural acceptability, local availability and improved tolerability align with clinical needs[12,14]

The integration of Ayurvedic pharmacology with contemporary ophthalmic practice presents both opportunities and challenges. Pupillary dilation, a routine diagnostic and therapeutic procedure, is currently achieved primarily through synthetic antimuscarinic and sympathomimetic agents such as tropicamide and phenylephrine, whose pharmacological effects are standardized and reproducible[8,10,11,24]. Despite their effectiveness, these medications are associated with limitations including transient blurred vision, photophobia, risk of precipitating acute angle-closure glaucoma in predisposed eyes and systemic adverse effects resulting from nasolacrimal absorption[5,8]. These concerns highlight the need to explore milder, safer and culturally acceptable alternatives, particularly for patients who cannot tolerate conventional mydriatics. Ayurvedic literature offers valuable leads in this regard. Plants categorized as *chakshushya dravyas*, particularly Kakamachi (*Solanum nigrum*), hold a prominent position in classical texts for their ocular benefits and potential to improve visual function[3,23,26]. Modern phytochemical research supports these traditional claims by identifying steroidal

alkaloids and flavonoids with antioxidant, anti-inflammatory and neuro-modulatory properties that may influence autonomic control of the pupil[9,22,27]. Preliminary clinical and ethnopharmacological observations reporting pupillary effects further support the potential ophthalmic relevance of Kakamachi[12,14]. However, translating traditional and preclinical evidence into clinical practice requires rigorous methodology. One major limitation of existing studies is heterogeneity in preparation techniques, concentration and quality control. Without phytochemical standardisation using marker compounds such as solasodine quantified through validated analytical methods, reproducibility across studies remains difficult[27]. Most available clinical reports are small, observational or uncontrolled and lack objective endpoints such as pupillometry, anterior chamber angle assessment and intraocular pressure monitoring, which are essential for safety evaluation in mydriatic trials[2,17]. Additionally, pharmaceutical parameters such as sterility, pH, osmolarity and preservative safety have rarely been reported despite their importance in ophthalmic formulations. Regulatory and ethical considerations are equally critical. Translation of Kakamachi into clinical ophthalmic practice must adhere to established frameworks such as AYUSH Good Clinical Practice guidelines and CONSORT recommendations for herbal interventions[18,19]. Prospective trial registration, authenticated plant specimen documentation and transparent reporting are essential for scientific credibility and reproducibility[6]. If these challenges are systematically addressed, Kakamachi may serve as an adjunct or alternative in selected clinical contexts. For example, in community eye care settings where cold-chain storage of synthetic drugs is challenging or in patients sensitive to antimuscarinic agents, a standardized herbal mydriatic with moderate efficacy and good tolerability may be useful. However, the slower onset and reduced peak dilation compared with tropicamide suggest that it is unlikely to replace synthetic mydriatics in surgical or high-demand diagnostic situations[10,11]. The realistic goal is integration rather than replacement, guided by evidence-based research.

This review highlights the evolving dialogue between traditional Ayurvedic knowledge and modern ophthalmic science in the field of pharmacological mydriasis. Tropicamide and related synthetic agents remain the gold standard due to their reliability and predictable effects, but their limitations justify exploration of complementary alternatives[8,10,11,24]. Kakamachi (*Solanum nigrum*), described in Ayurveda as a *chakshushya rasayana*, demonstrates phytochemical plausibility and preliminary clinical indications as a potential natural mydriatic[3,9,22,27].

However, current evidence remains insufficient for routine clinical adoption. Key limitations include a lack of phytochemical standardisation, limited controlled clinical data and inadequate pharmaceutical quality reporting. Addressing these gaps will require a staged translational approach involving robust phytochemical profiling, standardised manufacturing with sterility and stability testing,

controlled pilot trials using objective pupillometry endpoints and larger randomised non-inferiority studies[27]. Ethical compliance, trial registration and adherence to reporting standards will be essential throughout this process[18,19]. If these rigorous steps are implemented, Kakamachi may emerge as a scientifically validated adjunctive mydriatic, particularly valuable in integrative and community eye care settings where cultural acceptability and accessibility align with clinical needs. This journey from classical textual knowledge to evidence-based ophthalmic therapy reflects the broader potential of integrative medicine to complement modern pharmacology and expand global therapeutic options.

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