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# Critical Review of Shoolprashman Mahakashaya Dravyas and their Analgesic and Anti-Inflammatory Action

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**Review Article**

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## Abstract

Pain or Algesia is one of the main reasons to seek emergency medical care in modern medicine and also in Ayurveda. In Ayurveda, there are many Aushad Dravyas and Yogas mentioned in the context of Shool, which have Shoolghna action. Acharya Charak mentioned fifty Mahakashaya in Sutra Sthana chapter four which contain ten ingredients each, is one of the specialties of Charak Samhita. Shoolprashman mahakashaya described by Acharaya Charak consists of, fruit and root of *Piper longum Linn, Cuminum cyminum Linn., Piper nigrum Linn., Apium graveolens Linn., Plumbago zeylanica Linn., Zingiber officinale Roscoe. Piper retrofractum Vahl*. These Aushadh Dravyas and their chemical constituents show Analgesic and Anti-inflammatory properties. This review article aims to evaluate the analgesic and anti-inflammatory action of Aushadh dravyas of Shoolprashman Mahakashaya, to pave way for further studies and research to develop an ayurvedic analgesic drug.

**Keywords:** Shool; Shoolprashaman Mahakashaya; Pain; Ayurveda; Analgesia

## Introduction

One of the chief complaints of patients visiting the hospital is Pain and it causes 80% of referrals to the emergency department [1,2]. Pain is an ill-defined, unpleasant bodily sensation, usually evoked by an external or internal noxious stimulus [3]. The main causes of non-traumatic pain include- muscle spasms, inflammation, colic, etc. Colloquial terminology of Pain is known as Shool in Ayurveda and in medical science it is Algesia.

The entity 'Shool' is defined by Acharaya Sushrut as the excruciating pain which is caused due to the piercing of a conical object or a pin-like structure [4]. In general, this type of perception is given different names according to body parts and their site of origin like Sirahshool, Karnashool, Bastishool, etc. Several terms such as Ruk, Ruja, Vedana & Shool are usually used for pain [5]. Out of Tridoshas, vitiated 'Vata' is the main causative factor responsible for all painful conditions [6]. Vitiation of Vata is due to two conditions, viz. Dhatu kshaya janya Vata prakop and Margavarodh janya Vata prakopa [7].

According to the International Association for the study of Pain (IASP), pain can be classified based on the region of the body (head, visceral); duration (Acute and Chronic); system (e.g., gastrointestinal, nervous). The other three major classes include Nociceptive pain, Neuropathic pain, Inflammatory pain, and other types include Psychogenic pain, Pain asymbolia (ex., Diabetic Neuropathy), Referred pain. There are two components of pain sensation Fast pain and slow pain [8]. Fast pain is a bright, sharp, and localized pain that is followed by dull, diffused while unpleasant pain is called slow pain. Both the components of pain have free nerve endings as their receptors. However, afferent nerve fibers are different. Fast pain sensation is transmitted through A fibers and slow pain sensation through C-type nerve fibers.9 Free nerve endings secrete neurotransmitters Glutamate and substance afferent fibers transmitting impulses of fast pain secrete glutamate. The C-type fibers, which transmit impulses of slow pain, secrete substance P [9].

Inflammation is a protective response of the body to a variety of injurious agents. However, sometimes it becomes disproportionate and self-destructing. Inflammation is closely linked with repair and to an extent to pain.10 Mediators of Inflammation include Histamine, Bradykinin, NO (Nitric oxide), Prostaglandin - I2, E2, F2, C3a and C5a (Anaphylatoxins), Leukotrienes LT C4, B4, D4 PAF, Oxygen metabolites, LTB4, C5a, Bacterial products, Neutrophil cationic, IL-1, TNF (Tumor Necrosis factor, Oxygen free radicals, Lysosomal enzymes [10].

The pain control system is called the Analgesia system of the body. The Analgesia system of the body which is located in the brain is also called the endogenous analgesic system and provides a short term relief from pain. In the spinal cord, the analgesia system blocks the synaptic transmission of pain sensation, and therefore, the experience of pain is reduced. The analgesic drug selectively relieves pain by acting in the CNS or on peripheral pain mechanisms, without significantly altering consciousness 6b. Analgesic drugs like opioids relieve pain by acting through this system [9]. Pharmacological Management of these groups is categorized under non-steroidal anti-inflammatory drugs (NSAIDs), Opioid Analgesics, Adjuvant drugs like muscle relaxants, etc [11]. NSAID agents that counteract inflammation are anti-inflammatory drugs [12]. All drugs grouped in this class have analgesic, antipyretic and anti-inflammatory actions in different measures. These drugs primarily act on peripheral pain mechanisms and also act on CNS to raise pain threshold [3].

There are many formulations and single drugs mentioned in Ayurveda that are used in pain e.g., Shoolharan Yoga, Shoolagajkeshari Ras, Shoolantak Ras, Shoolvajarini Vati, Shoolraj lauh [13] etc and single drugs including Rasna, Vijaya, Devdaru, Guggulu, Suchi, Shalparni, Erand, Nirgundi [14] etc. Acharya Charak mentioned Angamardprashman and Vedanasthapan Mahakashaya and Sushrut included Aushadh Dravyas like Panchkol and Jeerak, Ajmoda, etc in Pipallayadi Gana in the context of pain [4]. Shoolprashaman Mahakashaya is one of them, mentioned in chapter four of Charaka Samhita Sutra Sthana and it consists of ten ingredients Pippali (*Piper longum Linn.*), Pippalimula (*Piper longum Linn*) Chavya (*Piper retrofractum Vahl.*), Chitrak (*Plumbago zeylanica Linn.*), Shunthi (*Zingiber officinale Roscoe.*), Marich (*Piper nigrum Linn.*), Ajmoda (*Apium graveolens Linn.*), Ajaji (*Cuminum cyminum Linn.*), Ajgandha (*Cleome gynandra Linn.*), and Gandeer. Gandeer is the tenth drug and due to its unavailability and controversial identification, it has been not included in this article. Shoolaprashaman Mahakashaya relieves obstruction of Vayu (Prana, Samana, and Apana), inhibits aggravated Kapha and Aama, does Vatanuloman due to Ushna (hot), Ruksha (rough) and Laghu (light) Guna and most of its ingredients have Agni-Deepak, Vatahara, Pachaka properties which are useful to reduce pain.

## Material and Methods

The content of this article has been compiled from various Ayurvedic textbooks and search engines like google scholar, research gate, PubMed, and other articles available online as very less work is done on Shoolprashman Mahakashaya and in the field of Ayurvedic analgesic. This review mainly focuses on various modern published researches on the anti-inflammatory and analgesic action of Aushadh Dravyas of Shoolprashman Mahakashaya.

Ayurvedic pharmacology dealt with Rasa (Taste), Guna (Properties), Virya (Active Principle), Vipak (Bio-Transformation), Prabhav (Specific Action), And Karma (Action), which are the counterpart of modern pharmacology and these attributes are the deciding factors for pharmacological action of any drug (Tables 1-3).

| Ingredients | Rasa | Guna | Virya | Vipaka |
|---|---|---|---|---|
| ***Piper longum Linn.*[15]** | Katu | Laghu, Snigdha,Tikshna | Anushna sheeta | Madhur |
| ***Piper longum Linn.* [16]** | Katu | Laghu, Ruksha | Ushna | Katu |
| ***Piper retrofractum Vahl.*[16]** | Katu | Laghu, Ruksha, Tikshna | Ushna | Katu |
| ***Plumbago zeylanica Linn.*[16]** | Katu | Laghu, Ruksha, Tikshna | Ushna | Katu |

| | | | | |
|---|---|---|---|---|
| ***Zingiber officinale Roscoe.*[17]** | Katu | Laghu, Snigdha | Ushna | Madhur |
| ***Piper nigrum Linn.*[17]** | Katu, | Laghu,Ruksha,Tikshna | Ushna | Katu |
| ***Apium graveolens Linn.*[16]** | Katu,Tikta | Laghu, Ruksha, | Ushna | Katu |
| ***Cuminum cyminum Linn.*[17]** | Katu | Laghu, Ruksha, | Ushna | Katu |
| ***Cleome gynandra Linn.*[17]** | Katu | Laghu, RukshaTikshna | Ushna | Katu |

***Note:** The group's 10th herb, i.e., Gandeer has been omitted in the study due to having controversial identification.
**Table 1**: Rasa Panchaka (Ayurvedic pharmacological property) of ingredients of Shoolprashman Mahakashaya.

| Ingredients | Doshakarma | Sansthanik Karma | Roghanata |
|---|---|---|---|
| ***Piper longum Linn.*[15]** | Kaphavatashamak | Shoolprashman,Vatanuloman, Jwarghna, Dipana, Ruchya, Rasayana, Hridya, Vrshya, Rechana | Shoth, Shool, Vatavyadhi Udarshool, Svasa, Kasa, Pliha Roga, Gulma, Jvara, Prameha, Arsa,Udara Roga, Hikka, Trsna, Krimi, Kushta, |
| ***Piper longum Linn.*[16]** | Kaphavatashamak | Shoolaprashman Dipana, Pachana, Vatunulomana, Ruchya | Vataroga,Udararoga Anaha, Gulma, Krimiroga, |
| ***Piper retrofractum Vahl.*[16]** | Vatakaphashamak | Dipana, Pachana, Rechana, Bhedana | Udararoga, Arsa, Krimi, Pliha roga, Gulma,Anaha, |
| ***Plumbago zeylanica Linn.*[16]** | Kaphavatashamak | Sothahara, Shoolahara, Dipana, Grahi, Pachana, Arshohara, | Udarashool, Gudasotha Agnimandya, Grahani Roga, Arsa, |
| ***Zingiber officinale Roscoe.*[17]** | Vatakaphashamak | Vedanasthapana,Shothhara, ,Anulomana,Dipana,Hrdya, Pachana, Grahi,Vrishya | Vatavyadhi, Udarshool, Sandhishoth, Shoth, Aruchi, Agnimandya, svasa, adhmana, Amavata, Pandu, Udararoga |
| ***Piper nigrum Linn.*[17]** | Kaphavatashamak | Jwaraghna,lekhan,Nadibalya, Vata hara,Chedana,Dipana,Pachana,Vat anuloman,Uttejak,Srotoshodhan, | Shool, Agnimandhya, Grahni,Svasa, Ajeerna, Krimiroga, Tvagroga |
| ***Apium graveolens Linn.* [16]** | Kaphavatashamak | Shoolaghna,Deepan,Vidahi, Ruchikrit, krimijit | Shool, Gulma, Aruchi, Adhmana, Hikka, Chardi, Krimi Roga,. |
| ***Cuminum cyminum Linn.*[17]** | Kaphavatashamak | Shoolprashmana, Vatanuloman, Deepan, Grahi, Balya, Ruchya Krimighna, | Shoth, Udarshool, Jwara,Aruchi,Adhman, Varnavikar,Amlapitta,Atisara,Arsha. |
| ***Cleome gynandra Linn.* [15]** | Kaphavatashamak | Shoolaghna,Vedanasthapak,Dipa na, Pachan, Krimighna, Swedjanan | Gulma, Asthila Krimiroga, Kandu, Karnaroga |

**Table 2:** Karma (Properties) of ingredients of Shoolprashman Mahakashaya.

| Contents | Chemical Constituents | Pharmacological Action |
|---|---|---|
| ***Piper longum Linn.*[15]** | Piperine, piplartine, sylvatin sesamin, piplastrol, triacontane, terpinolene. | Anti-inflammatory, Antispasmodic, Antibacterial, Hepatoprotective, Antiulcerogenic, Antihelmintic. |
| ***Piper longum Linn.*[18]** | Piperine, piplartine,dihydro-sigmasterol, triacontane piperlongumine, piperlonguminine, sesamin, | Anti-inflammatory, Antispasmodic, Antibacterial, Hepatoprotective, Antiulcerogenic, Antihelmintic. |
| ***Zingiber officinale Roscoe.* [17]** | Zingiberene, zingiberol, shogaol, lingerol. | Anti- Inflammatory, Antispasmodic Antioxidant, Antiulcer, Analgesic, Antipyretic, Carminative, Digestive, Antiflatulent, |

| | | |
|---|---|---|
| ***Piper nigrum Linn.*[17]** | Piperine, piperonal, piperoline, pellitonine, piperdine, piprettine. | Analgesic, Antioxidant, Anti-inflammatory, Muscle relaxant, Antiulcer, Antipyretic, Antiulcer. |
| ***Piper retrofractum Vahl.*[18]** | Piperine, piperonucline, piperidine, and chavicine. | Appetizer, Digestive, Carminative, Anthelmintic, Stomache. |
| ***Plumbago zeylanica Linn.*[18]** | Plumbagin, isozeylinone, chitranone, zeylinone, elliptinone, ß-sitosterol, vanillic acid, plumbagic acid,catechol, tannin, plumbazeylanone. | Anti-inflammatory, Appetizer, Digestant, Antimicrobial, Antioxidant, |
| ***Apium graveolens Linn.*[18]** | Anthoxanthins, graveobioside A and B, lutrolin, myristic acid, d-lineonene, and bergapten | Carminative, Stimulant, Emmenagogue |
| ***Cuminum cyminum Linn*. [17]** | Cuminaldehyde, α-pinene, ß-pinene, phellandrene, myrcene, a-terpineol, cuminic alcohol, hydrocuminine | Analgesic, Antispasmodic, Anti-inflammatory, Carminative, Anthelmintic, Anti-bacteria. |
| ***Cleome gynandra Linn.*[15]** | ß-sitosterol, α-amyrin, lupeol, kaempferol, rutin, hexacosanol etc | Analgesic, Spasmolytic, Anti-inflammatory, Anti-bacterial, Antipyretic |

**Table 3:** Chemical constitution and Pharmacological action of some ingredient drugs.

Various studies on the Analgesic & Anti-Inflammatory activity of the above-mentioned drugs are as follows:

### *P. longum Linn.*

An In-vivo study on a decoction of fruit was done using the method of carrageenan-induced paw rat edema which showed anti-inflammatory activity [19]. *P. longum Linn.* Extract and piperine inhibit prostaglandin and leukotrienes COX-1 effect and thus exhibit anti-inflammatory activity [20-22]. An In-vivo study of *P. longum Linn.* On aqueous extract of root was carried out where three different doses (200, 400, and 800mg/kg) were given to mice & rats orally. Significant pain-relieving effect equivalent to NSAIDS drug in doses 400 & 800mg/kg was observed [23].

### P. retrofractum Vahl.

Piperine was studied at concentrations of 10 to 100 µg/ml in a dose-dependent manner for Anti-inflammation activity, the expression of IL6 & MMP13 was inhibited & the production of PGE2 was reduced [24]. At a dose of 3 g/kg body weight the ethanol extract in mice orally a comparative Analgesic activity with acetosal (dose of 0.42 g/kg) BW was done on mice. It was noted that the effect was weaker than acetosal. The analgesic activity was due to decreased prostaglandin synthesis [25].

### *P. nigrum Linn.*

A study reported that at all doses of 5,10 and15 mg/kg, hexane and ethanol extract of *P. nigrum Linn.* Shows maximum analgesic effect by writhing method [26]. In-vivo experimental study on hot water extract reduces the ileal contractions induced by KCl (60 mm, n=10) or carbacol (CCh, 10µM, n=9) in a concentration-dependent manner [27].

### *P. zeylanica Linn.*

Hydro-alcoholic extract of *P. zeylanica Linn.* Leaf possesses anti-inflammatory activity [28]. The anti-inflammatory effect of *P. zeylanica Linn.* was noted in a study using carrageenan-induced raw paw edema in rats. In this study, two groups were treated with 300mg/kg and 500mg/kg per oral, which resulted in 31.03 and 60.30% inhibition of acute inflammation respectively. A clinical study on 30 patients was conducted by Napalchyal, et al. [29], at the National Institute of Ayurveda, Jaipur where 4 mg of fine powder was given to 15 patients twice a day with lukewarm water as an adjuvant for 15 days resulting in significant improvement in the pain, swelling, tenderness, and dizziness caused due to inflammation of the body parts [30].

### *Z. officinale Roscoe.*

It contains substances like gingerol, shogaol, and other structurally related substances which inhibit prostaglandin and leukotriene biosynthesis by suppressing 5 lipoxygenase or prostaglandin synthetase & also inhibit pro-inflammatory cytokines syntheses such as IL 1, TNF α, and IL 8 [31,32]. Another investigation in macrophages showed that shogaol can reduce inflammatory iNOS and COX 2 gene expression [33]. The hexane fraction extract of *Z. officinale Roscoe*. also suppresses excessive production of NO, PGE2, TNF α, and IL 1β [34]. The extract studied in rats with liver cancer showed that it reduces the elevated expression of NFκB and TNF α

which are present in various inflammation-related disorders [35]. Another study reveals that gingerols inhibit COX 2 expression while shogaol has no effect on COX 2 expression and it was concluded that compounds present in ginger are capable of inhibiting PGE2 production [36]. In vitro study on the anti-inflammatory action of *Z. officinale Roscoe.* and its compounds suppress the synthesis of prostaglandin by inhibiting cyclooxygenase-1 (COX-1), cyclooxygenase-2 (COX-2), and the biosynthesis of leukotriene by inhibiting 5- LOX [37]. The phytochemicals 8-paradol and 8-shogaol present in *Z. officinale Roscoe*. have an inhibitory action on the COX-2 enzyme when studied In-vitro. [38]. In vivo study also shows Z. officinale Roscoe. Suppresses prostaglandin synthesis. Fresh *Z. officinale Roscoe*. Containing 6-gingerol and four structurally related and resulting fractions for their effect were assessed on prostaglandin (PG) synthesis. [39]. An in-vivo study using acetic acid-induced writhes in mice on its oil (Dose 0.25, 0.5, and 1.0 g/kg) revealed that there is a significant decrease in the number of acetic acid-induced writhes which shows its analgesic effect [40].

Double-blind placebo-controlled parallel clinical study on osteoarthritis patient for *Z. officinale Roscoe*. Extract administrated for 6-week duration. The study was conducted on 247 patients, which showed that the reduction in knee pain on standing was more in the *Z. officinale Roscoe*. extract group as compared to the control group (63% versus 50%; P = 0.048) [41]. In a clinical study, on 36 participants having myalgia, supplementation of 2 g of *Z. officinale Roscoe* powder. The powder was given for 11 days and it was revealed that there are moderate-to-large reductions in muscle pain on daily consumption of raw and heat-treated ginger [42].

### *A. graveolens Linn.*

Ethanolic extract on the seed of *A. graveolens Linn.* by acetic acid-induced writhing and hot plate method showed significant analgesic activity [43]. Some of its compounds show anti-inflammatory and analgesic effects [44].

### *C. cyminum Linn.*

Various studies revealed that treatments supplemented with *C cyminum Linn.* have a marked effect on several inflammatory biomarkers, such as adiponectin, and high-sensitivity C-reactive protein (hsCRP), and TNF-α [45]. Oil C. cyminum *Linn.* Is noted to possess significant analgesic action in a chemical induce (formalin test) of nociception in rat and also has an anti-inflammatory activity which was analyzed by carrageenan-induced rat paw edema [46]. Its essential oil significantly suppresses the mRNA expressions of inducible nitric oxide synthase (iNOS), cyclooxygenase (COX-2), interleukin- IL-1, and IL-6 [47]. It reduces edema, at a dose of 0.1ml/kg. This activity was comparable to diclofenac sodium [48]. The aqueous and ethanolic extracts of *C. cyminum Linn.* Also showed significant anti-inflammatory activity in Acetic-acid induced writhing, hot plate, Carrageenan-induced paw edema, and Cotton-pellet granuloma models when it is compared to the control group. Its alcoholic extract possesses analgesic activity individually or in combination with methanolic extract Coriandrum sativum seed [49].

### *C. gynandra Linn.*

Administration of *C. gynandra Linn.* leaf extract in arthritic rats both protein-bound carbohydrates and lysosomal enzymes were reduced near to normal level. Raised TNF-α was also normalized. Methanolic extract of *C. gynandra Linn.* in adjuvant-induced arthritic rats shows anti-inflammatory effect. Thermal stimuli in the hot plate test and the writhing test on animals show antinociceptive and anti-inflammatory activities, which are due to different flavonoids such as luteolin, rutin, hesperidin, and quercetin [50].

## Discussion

Algesia is a medical concern that seeks emergency medical care whose first line of treatment includes NSAIDS, Anticholinergics, Opioid Analgesics, etc. With increasing side effects of modern medicine such as NSAIDs and anticholinergic drugs e.g., ibuprofen, more and more people are adapting Ayurvedic remedies. Many Ayurvedic herbal formulations possess analgesic properties, and Shoolprashman Mahakashaya is one of them. In Ayurveda, vitiated Vata Dosha is the main factor responsible for pain. The ingredients of Shoolprashaman Mahakashaya are Katu & Tikta Rasa, Laghu, Tikshna, Ruksha & Snigdha guna, Ushna Virya, Katu Vipaka, Shothaghna, and Shoolghna karma in nature with obvious alleviating action on all Dosha, especially Vata and Kapha, due to which it can act on pain actively. Similarly, all the ingredients of Shoolprashaman Mahakashaya and their chemical constitutes such as fruit and root of *P. longum Linn.* & *P. zeylanica Linn.* contain piperine, *Z. officinale Roscoe*. Contain Gingerol, Shogaol, and Piperine fruit extract and ethanol extract inhibit prostaglandins and other inflammatory mediators thus showing analgesic and anti-inflammatory action. Hydro-alcoholic extract of *P. zeylanica Linn.* leaf and methanolic extract of the leaves of *C. gynandra Linn.* shows anti-inflammatory activity. In-vivo and In-vitro studies on ginger oil, black pepper & *C. gynandra Linn.* and seeds of *A. graveolens* shows marked anti-inflammatory and analgesic actions. Clinical study on the fine powder of *P zylanica Linn.* and *Z Officinale Roscoe*. supplementation also shows anti-inflammatory and analgesic actions. Aqueous and hydro-alcoholic extract and oil of *C. cyminum Linn.* possess analgesic and anti-inflammatory activity. Among these studies, most of the ingredients in their hydro-alcoholic, ethanolic, and methanolic extracts have marked

anti-inflammatory and analgesic activity which confirms and verify the categorization of these drugs in Shoolprashaman mahakashaya. These all Aushadh Dravyas show analgesic and anti-inflammatory activities.

## Conclusion

This article concludes that the ingredients of Shoolprashman mahakashaya mentioned in Charak Samhita possess anti-inflammatory and analgesic activities as already established by various researches and studies which have been reviewed in this article. These Aushadh Dravyas individually as a single herb and in a combination of polyherbal or herbomineral formulation can act as an analgesic and anti-inflammatory drug. Further Pre-clinical and Clinical studies should be conducted on these Aushadh Dravyas, and on other effective Yoga mentioned in Ayurvedic literature by which a fast-acting pain-killer can be developed, and Ayurvedic, Vaidyas community may have safe and effective analgesic formulation.

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