INTERNATIONAL RESEARCH JOURNAL OF PHARMACY
www.irjponline.com
ISSN 2230 – 8407

Review Article

REVIEW OF PAIN: AN AYURVEDIC APPROACH

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Article Received on: 10/06/19 Approved for publication: 18/07/19

DOI: 10.7897/2230-8407.1009256

ABSTRACT

Pain is a serious problem globally due to its high prevalence and is regarded as the fifth vital sign. The standard methods comprising of NSAID and opioid group, interventional methods and implantable methods; although often very effective, have known adverse effects on gastrointestinal, renal and cardiovascular systems and surgical risks. Ayurvedic pain management comprises of pharmacological and non-pharmacological approaches. In this review, we have discussed pain management using herbal and herbomineral formulations. We began with comparison of Ayurvedic concept of pain with that of Biomedicine to arrive at concurrence and then systematically searched the databases PubMed and Scopus using search terms 'pain management, animal models of pain, Ayurveda and herbal medicine'. Out of 160 initial papers, 16 studies involving a total of 1591 participants befitting inclusion criteria were analyzed for the type of pain, intervention, outcome measures and results and others were rejected. PRISMA is followed to report the findings. Studies on Ayurvedic medicines were conducted in three different countries. Eight of them were RCT's with five multi-centered studies. Three single herbs, six polyherbal formulation, one herbomineral formulation and various external therapies were identified. The studies used standard scales like VAS or WOMAC index for analyzing the intensity of pain and showed statistically significant results to Ayurvedic medications in various pain conditions without any adverse effects. This review gives a comprehensive understanding of the concept of pain and its management from both Biomedicine and Ayurveda. It also highlights the unexplored potential of many herbomineral formulations to treat pain.

Keywords: Pain management; Ayurveda; Yoga; Herbomineral; Nanomedicine; Analgesic.

INTRODUCTION

Pain is the most common symptom of the disease which grows with an increase in average life span. It is regarded as the fifth vital sign which should be addressed as important as other vital parameters[1]. It is also a protective mechanism of the body to response to a harmful stimulus[2]. Chronic pain is considered a health crisis due to its high prevalence and associated physical and emotional incapacity. It affects 30 to 50 percent of the world population[3]. The major conditions predominantly related to pain are cancer, osteoarthritis, rheumatoid arthritis, spinal pain, injuries and surgeries. Classification of pain as a disease may help to reduce its global burden and co-morbid conditions[4]. Ayurveda, gives a profound understanding of pain, types of pain and its treatment. Sula is the term used for pain and is a cardinal symptom attributed to Vatadosha. Vata disorders arise out of two main mechanisms either due toocclusion of vata (avarana) or due to depletion of body tissues (dhatus). Pain can appear as a disease (roga), prodromal symptoms (poorvaroopa) of a disease or as a complication of a disease (upadrava). The main principle of pain management in Ayurveda is to bring back the balance of vatadosha and also to increase the pain threshold of the individual.

The conventional chronic pain management comprises of drug therapy with opioid analgesics and NSAIDs, behavioural approaches, interventional methods and implantable methods[5]. NSAIDs have a range of adverse effects mainly affecting the GI, renal and CV systems[6,7]; which with longer duration of treatment and in the presence of comorbidities pose a higher risk. Hence the quest for better options continues. Ayurveda has an extensive pharmacopoeia of herbal and mineral ingredients used for the management of pain and inflammation. Herbs are used as a single candidate or as a formulation. The raw metals and minerals are converted into potent medicines known as bhasmas by using various well-controlled physicochemical processes[8]. In spite of a large amount of literature in the Ayurveda samhitas, very few drugs and therapies are studied scientifically providing evidence. It would be interesting to take a review of the concept of pain and various treatment options from samhitas of Ayurveda and also from published research works on the background of Biomedicine. The objective of this systematic review is to identify various leads for pain management through Ayurveda.

Overview of pain

The concept of pain and pain management in Biomedicine

Task force on the taxonomy of the International Association for the Study of Pain (IASP) had defined pain as 'An unpleasant sensory and emotional experience associated with actual or potential tissue damage, or described in terms of such damage'. Considering the duration of symptoms, pain can be divided into Acute pain: (duration < 3 months) and Chronic pain (duration > 3 months). According to aetiology, pain can be classified into nociceptive pain which is due to the stimulation of nociceptors by noxious stimuli and neuropathic pain is the result of dysfunction of the nervous system[1].

Pain pathways

In order for a stimulus to be perceived as pain, four different physiological processes are necessary.

a. Transduction- the stimulus is converted into electrical activity at the nerve ending. b. Transmission- it is the spread of electrical activity. c. Modulation- changes in nociceptive transmission. d. Perception[9]

Assessment of pain

The assessment and measurement of pain are fundamental to the process of assisting in the diagnosis of the cause of a patient's pain, selecting an appropriate analgesic therapy and evaluating then modifying that therapy according to response[1]. SOCRATES is a useful mnemonic acronym commonly used by healthcare professionals to evaluate pain, i.e. Site and radiation, Onset, Character, Radiation, Associated symptoms and signs, Time course and Treatment, Exacerbating/Relieving factors and Severity. Multiple pain rating scales are available to assess the intensity of pain like Visual Analogue Scale (VAS), Western Ontario and McMaster University Osteoarthritis Index (WOMAC),Fibromyalgia Impact Questionnaire (FIQ) etc. [1,9]

Management of Pain

For acute pain[1,10,11]- The Acute Pain Service (APS) plays an important part in acute pain management after surgery. Normally for treating the acute pain, the 'analgesic ladder' introduced for the treatment of cancer pain by the World Health Organization (WHO) consisting of three steps is used[12]. Non-opioid ± adjuncts (e.g. paracetamol, aspirin, NSAIDs) are used in the first step. If the pain is still unsettled or there is increasing intensity, along with first step medicine, weak opioids (e.g. codeine, tramadol) can be added. For moderate to severe pain or persistent or increasing pain in spite of step two treatment, stronger opioids (e.g.oxycodone, diamorphine, fentanyl, and alfentanil) are considered in addition.

For Chronic pain[5]- It includes pharmacological approaches (e.g. NSAIDs, Opioid analgesics, antidepressants, anticonvulsants), behavioural approaches (e.g. relaxation techniques, hypnotic techniques, cognitive behavioural therapies), interventional methods (e.g. trigger point injections, nerve block therapy, epidural steroid injections) and implantable methods (epidural and intrathecal drug delivery).

The concept of pain and pain management in Ayurvedic medicine

Terminologies in Ayurveda literature regarding various pain sensations

Different types of pain were explained in Ayurveda in the context of vitiated vatadosha (one of the three basic elements of the body). Pricking pain (toda), splitting pain (bheda), piercing type pain (vyadha), binding type pain (veshtana), pain during joint movements (prasaranaakunchanavedana), severe pain (maharuja) are different terminologies in the literature[13] (Table 1). Type of pain in biomedicine is explained with some examples from Ayurveda treatises (Table 2).

Assessment of pain

Trividhapareeksha (Patient examination method) consists of inspection (darshana), palpation (sparshan) and interrogation (prashna)[14] are very relevant in understanding the causes, symptoms and etiopathogenesis of disease in Ayurvedic point of view. They are almost similar to the current clinical methods like history taking, general and systemic examinations. Pain is always assessed using these three tools of examinations. Acute pain in joint dislocations and fractures explained in Ayurveda classics with symptoms which are very good tools for analyzing the pain. For example, the pain in dislocation is assessed by checking tenderness (sparshasahatvam), unbearable pain (ugraruja) and inability to perform flexion and extension of joints (prasaranaakunchanaashakti)[15]. Other than these no specific scales are found.

Pain management through Ayurveda

The main stages of Ayurvedic management of pain include determination of the causative factors (hetu), analyze the etiopathogenesis (samprapti) and select the suitable treatment. Ayurvedic treatment can be classified as pharmacological and non-pharmacological. Pharmacological treatment comprises of drug therapy using various single drugs and formulations, external therapies like oil massage (abhyanga), hot fomentation (swedana), application of paste of drug on affected areas, thermal cauterization (agni karma), chemical cauterization (kshara karma), medical leech therapy (jalookavacharana), bloodletting (rakta moksha) and non-pharmacological approach using trigger point pressure massage (marma therapy), various yoga postures, lifestyle modifications and dietary advice (Table 3). Many dosage forms are available in Ayurvedic Pharmacopeiaand Formulary for the management of pain. They are single herbs and polyherbal formulations like decoctions, powders, tablets, medicated oils and ghee, hydro alcoholics, herbo mineral preparations as shown in Table 4. Table 4 contains a list of plants and formulations which are published in various indexed journals. Formulations recommended for pain which contains many ingredients from column one from the treatise Rasa Yoga Sagara (*) and Charaka Samhita (*) without specific studies. Future studies need to be carried out to find out whether all these herbo-mineral formulations are indicated for a similar type of pain or each has a specific target and do they have common ingredients or not.

Exploratory systematic review of published articles

An attempt is made to review the published data on Ayurvedic formulations and therapies for pain management. We used the following methods.

Search strategy

PubMed and Scopus were searched to assess the data. The keywords used for the purpose of search include 'Pain management, animal models for pain, Ayurveda, Herbal medicine. No limits were adopted such as; journals, years of publication, types of articles, or authors except articles published in the English language until February 2019 were included for the purpose of review. Titles, abstracts, and full texts for compliance with eligibility criteria were reviewed.

Inclusion and exclusion criteria for the papers

Valid references, proper methodology, the specification of pain types and its description, Ayurvedic intervention (internal medication, therapy or both), dose and duration of treatment and adoption of international guidelines were the criteria's for inclusion. The studies fulfilling the selection criteria were selected and remaining were excluded.

Results of the search

Total of 160 articles were identified related to pain and pain management, out of which 50 duplicates were removed and 110 papers were screened by title and abstract. Total 20 articles were selected for full-text examination, from which 16 articles full filling the inclusion criteria were selected and the remaining studies were excluded (Figure 1).

Quality assessment

The first author reviewed the included papers and the second review was performed by one of three authors also assessed these selected papers. Critical Appraisal Skills Programme (CASP)[16] checklist was used for assessing the quality of the selected papers.

Data analysis

Since we do not find a large number of studies on pain management using Ayurveda medicines and therapies, the methods were kept simple, and no statistical technique was applied to the selected papers. Articles were then analyzed for the type of pain, intervention, outcome measures and results. Detailed description regarding the features of included studies is explained in Table 5.

The brief overview of the studies as follows.

Study design

Among the 16 studies, 8 studies were randomized double-blind clinical trials and 5 of them were multicentered. Most trials employed a parallel group design and only one with cross over design. The duration of studies from the first dose of drug administration until following up ranges from 10 days to 180 days (Table 5).

Settings

Studies were conducted in three different countries, with eleven of the studies conducted in India, Four in Germany, and one in Iran (Table 5).

Types of studies

The review considered all quantitative study designs including randomized controlled trials, non-randomized controlled trials, before and after studies, prospective matched control and single group clinical studies (Table 5).

Participants

A total of 1591 participants were used in the sixteen trials. Sample sizes ranged from a minimum of 21 to a maximum of 182 participants. All studies recruited participants of either sex with various kinds of pain conditions and the age of participant ranges from 18 to 75 years.

Interventions

Nine out of the selected studies compared Ayurvedic interventions against a placebo control. Among the 16 studies oral Ayurvedic single herbs were used in three studies, polyherbal formulations in five studies, herbo-mineral preparations in two studies, orally administered Ayurvedic herbal medicine along with various therapies was used in five studies[17–21] and external therapy was used as an intervention in only one study [22].

Outcomes

Most of the studies used Pain visual analogue scale (VAS) and WOMAC index (The Western Ontario and McMaster Universities Osteoarthritis Index for pain and disability) for analyzing the outcomes like the intensity of pain, stiffness, crepitus, swelling, Ritchie's index for pain and swelling is used in two studies, Fibromyalgia impact questionnaire (FIQ), German version of the Pain Perception scale were used in one study and Comprehensive Headache related Quality of Life Questionnaire (CHQQ) in one study to test the outcomes.

Various pain conditions in selected articles

Among the sixteen included trials, 8 are osteoarthritic pain, 3 are Rheumatoid arthritis while others include Polyarthritis, Fibromyalgia, Migraine, Low backache and Dysmenorrhea.

DISCUSSION

The evidence for the efficacy of Ayurveda medicines in the management of various pain conditions was examined by this systematic review. Total 16 studies were identified, involving 1591 participants with various pain conditions like osteoarthritis, rheumatoid arthritis, low backache etc. Single herbal drugs, compound herbal formulations, herbo mineral formulations, various external therapies combined with internal Ayurvedic interventions show statistically significant results or equivalent results with the comparative group as shown in Table 5.

Some findings need specific attention which is discussed below. Studies by Sander O *et al* (1998), Chopra A *et al* (2000) and Chopra A *et al* (2012) showed no statistically significant results in the reduction of pain. According to Sander O *et al* (1998)[23], there was no significant change in subjective, clinical or laboratory parameter from baseline or difference between both groups. But the mean NSAID dose reduction reached levels of 5.8% (H15) when compared to placebo. The results are questionable because the drug Boswellia serratta[24,25] has proven analgesic and anti-inflammatory effects and hence this study points the need for the greater patient population to confirm or reject the result. According to Chopra et al (2000)[26], RA-1, a plant extract formulation shows some results in joint swelling, but none of the differences was statistically significant. Interestingly the serum haemoglobin count was statistically increased in the treatment group. All the single drugs in RA-1 formulation (*Withania somnifera, Boswellia serrata, Zingiber officinale* and *Curcuma longa*[27–29] had proven analgesic and anti-inflammatory effects. According to Chopra et al (2012)[30], the study was conducted with B formulation (extracts of *Zingiber officinale, Tinospora cordifolia, Withania somnifera* and *Tribulus terrestris*) and monoherb formulation BPRT (extract of *Semecarpus anacardium*) as treatment groups with oral Hydroxychloroquine sulphate (HCQS) as the comparative group. B formulation and HCQS had comparable and better results than BPRT for several efficacy measures. HCQS long-term therapy had proven adverse effects[31] and the possibility of adverse effects in Ayurvedic herbal drugs was less. All three interventions showed an impressive fall in serum IL-1β. B formulation and HCQS showed a modest reduction in the RF titer. According to Gajendrakumar *et al*[32], RA factor was significantly reduced in treatment group while treated with *Withania somnifera* powder (5 g/daily) with the herbomineral preparation known as Siddha makaradhwaja (100 mg/daily). Hence we may say that herbal interventions may not be better but equally effective with lesser or no adverse reactions for long term use.

External therapies without internal medication like Anuvasanabasti (enema) treatment (Pradeep *et al*)[22] for 10 days showed statistically significant ($P < 0.05$) reduction in pain and swelling. Ayurvedic massage therapy with sahacharaditaila (Syalkumar *et al*)[20] in low backache condition showed significant reduction in mean back pain. Only external therapies prove effective and can be used when the patient cannot be put on long term NSAID's. Further drugs used through skin route or external routes also reach the systemic circulation. Specific studies may be conducted to know the needs for external treatments. Internal medication along with yoga shows significant results in Fibromyalgia[21] and Migraine[18]. Hence a combination of internal medication along with external therapies has shown more promising results in various pain conditions. This approach is not the standard approach of RCT's, but it is concurrent with evidence-based medicine which is very patient-centric.

Table 1: Classification of pain in Ayurveda with examples

S. No.	Classification criteria	Type of sula (pain)	Condition
1.	Duration of pain	1.Acute pain (ashukarisula)	Acute spreading eruptions (visarpa)[39]
		2.Chronic pain (chirakarisula)	Rheumatism due to rakta (vatarakta) [40] Vitiated vata in sandhi/joint- Osteoarthritis (sandhigatavata)[39]
2.	Site of pain	1.Localized pain (ekangasula)	Pain over low back region
		2.Generalized pain (sarvangasula)	Whole body pain
3.	Severity of pain	1.Superficial pain (uttana) 2.Deep pain (gambeera)	Seen in vataraktadisorders[39]
4.	Predominance of Dosha	1.Vatika	Sciatica (gridhrasi)[39]
		2.Paittika	Acute spreading eruptions (visarpa)[39]
		3.Kaphaja	Vata vitiation in mamsa/muscle (mamsagatavata)[39]
		4.Tridoshaja	
5.	Pain related to organs	Visceral pain as a symptom of a disease	Stomach pain (udarasula) Cardialgia (hritsula)[39]
6	Nature of pain	Pain similar to scorpion bite (vrischikaivasula)	Rheumatism due to ama(amavata)[40]
		Slicing pain (Krakachanivadaaryathe / bheda)	Heart disease (hridroga)[39]
		Profound pain (avagadaruja), cutting pain (todabahulam)	Diabetic carbuncles (pramehapitaka)[39]

Table 2: Types of Pain in Biomedicine with examples from Ayurveda

Types of pain[41]	Definition	Examples from Ayurvedic literature	
Musculoskeletal pain	Chronic musculoskeletal pain is defined as persistent or recurrent pain that arises as part of a disease process directly affecting bone(s), joint(s), muscle(s), or related soft tissue(s).	Muscular pain	Vata vitiation in 1. Muscle tissue (mamsadhatu), adipose tissue (medadhatu)- Pricking pain (toda)[39] 2. Entire body- Pricking pain(toda) and splitting pain (bheda)[39].
		Pain related to bone and joints	1.Vata vitiation in Bone (asthi)- Severe pain (teevrasula)[39] 2. Vitiated vata in sandhi/joint-(sandhigatavata)- Pain during joint movements (Prasaranaakunchanavedana)[39] 5. Knee synovitis (kroshtukasheersha)[39] 6. Calcaneal spur (vatakandakam)[39] 7. Low backache (Kateesula)[39]
Postsurgical and post-traumatic pain	Pain that develops after a surgical procedure or a tissue injury (involving any trauma, including burns) and persists at least three months after surgery or tissue trauma.	1. Post-partum pain syndrome (pain in sootikavataroga)[40] 2. Post-surgical pain in haemorrhoids (arsas), fistula in-ano (bhagandara)[40]	
Neuropathic pain	It is caused by a lesion or disease of the somatosensory nervous system.	Shooting and radiating pain in sciatica (gridhrasi)[39]	
Headache and orofacial pain	It includes primary (idiopathic), secondary (symptomatic) headache, and orofacial pain including cranial neuralgias	Severe pain at half part of the body or head in facial paralysis (arditaroga)[39]	
Visceral pain	A persistent or recurrent pain that originates from the internal organs of the head and neck region and the thoracic, abdominal, and pelvic cavities	1.Abdominal pain (udarasoola) 2.Cardialgia (hritsoola)	

Table 3: Pharmacological and non-pharmacological strategies of pain management in Ayurveda

Pharmacological approach	Applying the paste of herbal drugs in the affected area (lepa) [42–46]	Satapushpaadilepa, Ellumnishaadilepa, Manjishtaadilepa are used as paste along with water and applied over the affected area and removed before the paste dries completely
	Oil massage (abhyanga)[47]	Oil massage of the affected areas with suitable medicated oils according to the condition of the patient.
	Hot fomentation (swedana) [22]	Hot fomentation by the steam of various medicinal plants decoction.
	Thermal cauterization (agnikarma)[48–50]	It is one of the para-surgical procedures to give instant relief from pain in musculoskeletal and arthritic conditions using metal probes.
	Chemical cauterization (ksharakarma)[51–53]	Herbal alkali application on warts.
	Bloodletting (rakta moksha)[51]	Venepuncture (siravedha) and cupping (sringa) are used in neurological or muscular pain.
	Medical leech therapy (jalookavacharana)[54]	Leech is applied to the affected painful part. It has also been reported that the leeches have an analgesic effect in osteoarthritic pain which may be due to the salivary secretion of analgesic agents, such as inhibitors of kallikrein and anti-inflammatory agents, including protease inhibitors[55].
	Enema (basti)[22]	It is advocated in vata predominant type of pain. According to Grampurohit et al (2014)[22], Basti showed good results in osteoarthritis joint pain.
Non pharmacological approach	Marma therapy[56]	Pressing and manipulating the vital points named marma to reduce the pain.
	Yoga postures[57–59]	Yoga postures have emerged as an important treatment modality for chronic pain recently.

Table 4: Some of the Formulations used in Ayurvedic pain management

Herbal Single drugs	Herbal formulations	Herbo-mineral formulations[60]*
1.*Nelsonia canescens* Spreng. (badarasna)[61] 2. *Grewiaasiatica* Linn. (parusaka) [62] 3.*Terminalia chebula* Retz.(bibeetaki)[63] 4.*Inula racemosa* Hook. f. (pushkaramoola)[64] 5.*Mangifera indica* L. (amra)[65] 6.*Alangium salvifolium* L.f.(ankola) [66] 7.*Pavonia zeylanica* L. (bala)[66] 8.*Saraca asoca* Roxb.(asoka) [67] 9.*Acorus calamus* L. (vacha)[68] 10.*Pentatropis capensis* Linn. f.(kakanasa)[69] 11.*Embelia ribes* Burm (vidanga)[70] 12.*Cassia occidentalis* Linn (kasamarda)[71] 13.*Withania somnifera* L. (ashwagandha)[72] 14. *Terminalia arjuna* Roxb. (arjuna)[73] 15. *Lepidium sativum* (chandrasoora) [74] 16. *Holoptelea integrifoli*a Planch.**(**chiribilva)[75] 17.*Tinospora cordifolia* L. (guduchi)[76] 18.*Cyclea peltata* Burm.f. (pada)[77] 19.*Schleichera oleosa* (Lour.) Oken.(koshamra)[78] 20.*Melia azedarach* Linn.(mahanimba) [79] 21.*Phyllanthus amarus* (bhumyaamalaki) [80] 22.*Dalbergia latifolia* (shinshapa)[81] 23.*Bulbophyllum neilgherrense* Wight. [82]	1. Vedanasthapana decoction [83]* 2.Dashamoola decoction[84] 3.Maharasnadhi decoction[19,85] 4.Amalakyadi powder[86] 5.Triphala powder[87] 6.Manjishtaadi lepa powder [44] 7.Ellumnishaadi lepa powder[43] 8.Yoga raja guggulu tablet[88] 9.Murivenna oil[89] 10.Narayan oil[19] 11. Guggulutiktaghrita[90] 12.Dasamooolahta[84]	1.Vatavidhvamsana Rasa 2.Sula kootara rasa 3.Sula gajakesari rasa 4.Sula gajaankura rasa 5.Sulaghni vati 6.Suladhavaanala rasa 7.Sula dhvamsi rasa 8.Sula nirmoolana rasa 9.Sula raja loham 10.Sula vajrinivati 11.Sulavidhvamsani vati 12.Sula simha rasa 13.Sulahari vati 14.Sula anthaka rasa 15.Sulari rasa 16.Sulebha simhinirasa 17.Vataantaka rasa 18.Vata sulahara rasa 19.Vatavisphothara rasa 20.Vata rakshasa rasa 21.Vata raja vati 22.Sophaarirasa 23.Sodhakaalanala rasa

Table 5: Characteristics of included studies

Author	Condition	Study design	Sample Population	Outcome	Intervention	Results
R.R.Kulkarni *et al* (1991)[91]	Osteoarthritis	Double-blind, placebo-controlled, cross-over study	42 patients	The severity of pain, morning stiffness, disability score and Ritchie articular index.	Herbomineral formulation containing *Withania somnifera, Boswellia serrata, Curcuma longa* and a zinc complex (Articulin-F) or placebo for 3 months	A significant drop in severity of pain ($P < 0.001$) and disability score ($P < 0.05$).
Sander o *et al* (1998)[23]	Chronic polyarthritis	a multicenter double-blind pilot study	78 patients	VAS, Ritchie's Index for swelling and pain, ESR, CRP,	Resinous extracts of *Boswellia serrata* (H15, indish incense) - 9 tablets of active drug (3600 mg) or placebo daily or placebo for 12 weeks.	No subjective, clinical or laboratory parameter showing a significant or clinically relevant change from baseline or difference between both groups at any time point of observation.
Chopra A *et al* (2000)[26]	Rheumatoid arthritis	Randomized, double-blind, placebo-controlled, parallel efficacy clinical drug trial	182 patients	Tenderness, swelling, and Pain using VAS scale.	RA-1, a standardized plant extract formulation or identical placebo tablets, 2 tablets thrice daily (total daily dose of 444 mg extract) for 16 weeks	The active Ra 1 group remained numerically superior at all evaluation timepoints. The increased proportion with 50% reduction in swollen joint count (95% CI approximately 1.52, 29.90) and swollen joint score (95% CI approximately 0.91, 28.73)
Chopra *et al* (2004)[92]	Osteoarthritis of knee joint	Randomized, double-blind, placebo-controlled, single-centre drug trial	90 patients-age ≤ 35 years, and subjects with osteoarthritis	Pain assessed using VAS scale, WOMAC modified index	RA-11 (standardized multi-plant Ayurvedic drug) Dose: Two capsules twice a day for 32 weeks	Efficacy: Compared with placebo, the mean reduction in pain VAS at week 16 and week 32 in the active group was significant ($P<0.05$) and the improvement in the WOMAC scores at week 16 and week 32 was also significant.
Gajendra kumar *et al* (2012)[32]	Rheumatoid arthritis	Prospective, open-label, non-randomized, outpatient-based, single centred study	86 patients of both sex between the age group of 18 to 60.	Physician global assessment score, patient global assessment score, pain assessment score	5 g of Ashwagandha powder twice a day for three weeks with lukewarm water or milk and Sidhaakardhwaj powder(100mg) with honey for the next four weeks	RA factor was decreased and a significant change in post-treatment scores of tender joint counts, swollen joint counts, physician global assessment score, patient global assessment score, pain assessment score, patient self assessed disability index score
Shabnam omldvar *et al* (2012)[93]	Dysmenorrhea	Placebo controldouble-blind trial	50 female, 15-24 age with moderate or severe dysmenorrhea	Pain- VAS	Study group administered withcapsules containing 30 mg fennel extract four times a day for three days from the first day of the menstrual period.	The study group showed more effective results than placebo in pain relief ($P<0.05$)
Arvind chopra *et al* (2012)[30]	Rheumatoid arthritis	Randomized single-blind, multi center, parallel efficacy study	121 patientsof either sex (17 to 70 years).	Pain-VAS and the health assessment questionnaire	B formulation and BPRT formulation Dose: two capsules twice a day (750 mg daily) and HCQS- one tablet twice daily (200mg) for 24 weeks	Did not show significant differences by treatment groups. Several efficacy measures improved significantly in the HCQS and polyherb groups with no difference between the groups
Sanjay U *et al* (2012)[94]	Osteoarthritis	Open-label, single centre, prospective, clinical study.	36 patients of both sexes of age between 40 to 70 years	VAS, WOMAC pain sub-scale score, and WOMAC stiffness sub-scale score	Ayurveda test drug, named TLPL/AY/03/2008. Dose- two capsules twice daily orally after meals for 180 days.	The mean joint pain reduced significantly (59.85%; $P< 0.05$ and the mean WOMAC combined score, WOMAC pain sub-score, WOMAC stiffness sub-score reduced significantly.
Christian S Kessler *et al* (2013)[21]	Fibromyalgia	Non-randomized Controlled Clinical Pilot Study	21 patients Of both sex and age between 18 to 65 years.	Fibromyalgia Impact Questionnaire(FIQ) and German version of the Pain Perception Scale (SES)	Ayurvedic treatment including two weeks yoga treatment	At 2 weeks, there were comparable and significant improvements in the FIQ and for most of the secondary outcomes in both groups with no significant in-between-group differences.

Aswinkum arraut *et al* (2013)[95]	Osteoarthritis	Randomized open comparative study of 24 weeks	112 patients of both sex and age between 40 to 75 years	VAS and WOMAC index	ABFNO2 tab 750mg twice/day for two weeks, 1500 mg for the next two weeks, 2250 mg for the next two weeks and ABFNO2 750mg twice daily /day for 24 weeks in the next group	ABFNO2 and GS demonstrated, adherence to treatment of 87.75% and 74.3%, reduction in Pain-VAS at rest 61.05% and 57.1%, reduction in pain-VAS on activity 57.4% and 59.8%, WOMAC score drop 62.8% and 59.1% respectively.ABFN02 has significant activity in OA.
Pradeep *et al* (2014)[22]	Osteoarthritis	Single group clinical study with pre-test and post-test design.	30 patients with persistent pain for 3 months	Pain, swelling, tenderness, crepitus.	Anuavasanabasti (enema) with Ksheerabala Taila 120 ml for 10 days	Significant reduction ($P < 0.05$) in subjective symptoms such as pain, swelling, tenderness. In the overall effect of the therapy, 56% had mild improvement, 48% had moderate improvement and12% had no improvement.
Syalkumar *et al* (2016)[20]	Low back pain	Randomized Controlled Trial	64 patients of both sexes and age 18–70 years,	VAS, Roland Disability Questionnaire, the Hanover Functional Ability Questionnaire	Two weeks of external Ayurvedic treatment group with 6 treatments or to a group receiving standard local physical therapy	Mean back pain at week 2 was significantly reduced from 53.4 – 18.5 to 21.6 – 18.2 in the massage group and from 55.3– 12.9 to 41.8 – 19.8 in the standard thermal therapy group; $p < 0.001$.
Ramakanth *et al* (2016)[72]	Knee joint pain	Randomized, double-blind, placebo-controlled clinical study	60 patients	Modified WOMAC, KSI, VAS- Pain	*W. somnifera* 250 mg,*W. somnifera* 125 mg and placebo, all given twice daily for 12 weeks	VAS scores for pain, stiffness and disability were significantly reduced in W. *somnifera* 250 mg ($p < 0.001$), W. *somnifera* 125 mg ($p < 0.01$) groups.
Anil Mangal *et al* (2017)[19]	Osteoarthritis	An open-label, multicenter, prospective, clinical study	142 patients	VAS, WOMAC index	VatariGuggulu (500 mg thrice daily), Maharasnadikwatha (20 ml twice daily), Narayan taila externally for 12 weeks	VAS, WOMAC score and clinical symptoms were reduced significantly from baseline to end of the treatment ($P < 0.001$).
Vasudha M Sharma *et al* (2018) [57]	Migraine headache	prospective matched controlled trial	60 patients	CHQQ and VAS	Therapeutic Purgation(virechana) and Samanachikitsa followed by Yoga therapy for 90 days	Significant reduction in Migraine symptoms including pain intensity ($p < .001$) and improvement in Headache related Quality of Life ($p < .001$).
Christian S. Kessler *et al* (2018)[17]	Osteoarthritis	A multicenter randomized, controlled, open-label trial	151 patientsof both sex, 40 to 70years of age	WOMAC index, VAS	Multi-modal Ayurvedic treatment with 15 treatments over 12 weeks	Ayurveda group (mean difference 61.0 [95%CI: 52.4;69.6]) than in 63 the conventional group (32.0 [95%CI: 21.4;42.6]) resulting in a significant between Group difference ($p<0.001$)

*VAS-Visual Analogue Scale, WOMAC index- Western Ontario and McMaster Universities Osteoarthritis Index for pain and disability, KSI - Knee Swelling Index

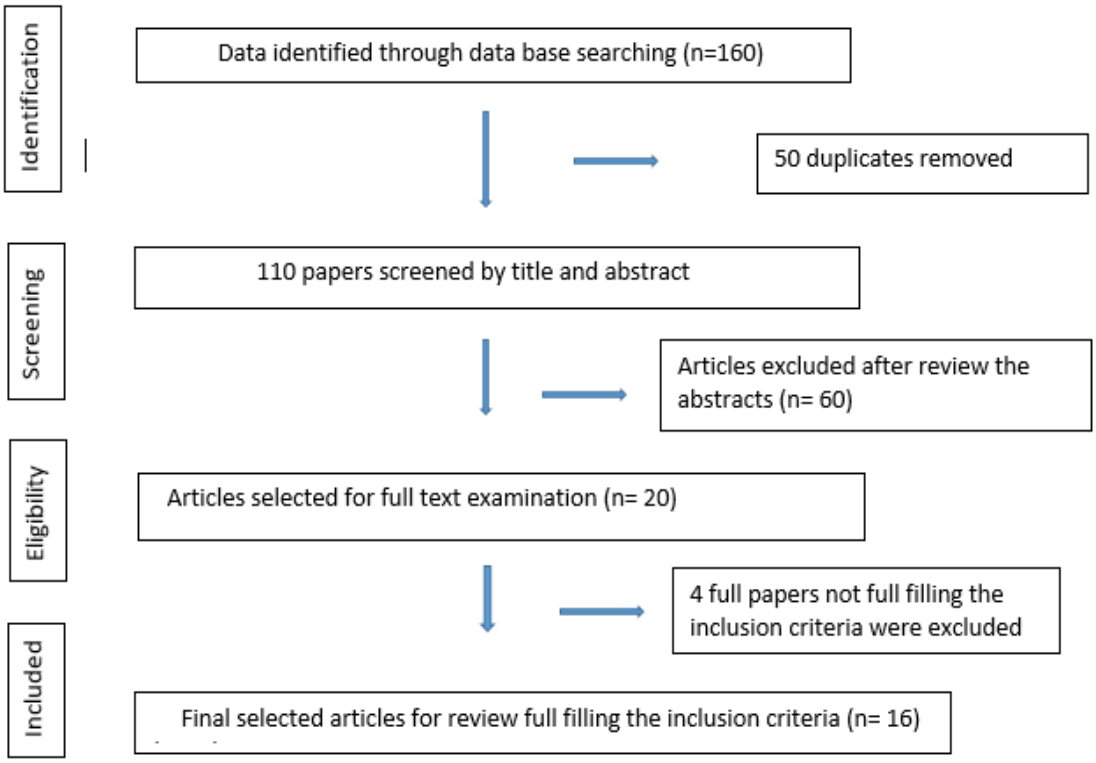

Figure 1: Flow chart showing the selection process as per PRISMA

*PRISMA - Preferred Reporting Items for Systematic Reviews and Meta-Analyses

CONCLUSION

The reviewed studies clearly showed that Ayurvedic drugs have potent analgesic and anti-inflammatory action in various pain conditions. The review also provides an understanding of the concept of pain and pain management through Ayurveda medicines and modalities. Overall an integrative approach may help to reduce symptom burden in palliative care and thereby improve the quality of life

Future possibilities in the field of Ayurvedic pain management

Pharmacological approach with herbominerals

There is a critical need for new analgesic and anti-inflammatory drugs having the efficacy of conventional NSAIDs while minimizing their associated adverse events[33]. At this point quality, herbal or herbomineral formulations explained in various Ayurvedic treatises having pain as the main indication (Table 4) should be studied systematically. Ayurvedic bhasmas are highly potent nanomedicines obtained through incineration of metals prepared along with herbs[34–36]. Nanomedicine is a novel and rapidly evolving, highly technical approach to optimizing delivery and control of medicines[37,38]. Ayurveda bhasma may provide a safe, effective and fast acting treatment option in pain conditions.

Palliative care

Each year, an estimated 40 million people are in need of palliative care, 78 percentage of the people live in low- and middle-income countries[12]. Pain is one of the most frequent and serious symptoms experienced by patients in need of palliative care. Worldwide, only about 14 percent of people who need palliative care currently receive it. Palliative care improves the quality of life of patients and their families who are facing problems associated with a life-threatening illness, whether physical, psychosocial or spiritual. There is a possibility of introducing purely herbal and non-pharmacological Ayurvedic pain management module for such patients which will help to improve the quality of life.

Non-Pharmacological approach

Nowadays many people opt for mind-body therapies like meditation and such behavioural therapies for pain management. Hence there is a huge opportunity for physicians and clinicians to introduce various non-pharmacological approaches like Marma therapy and Yoga along with internal medicine. This may bring additional benefits along with pain management.

To conclude, Ayurveda gives a specific and clear conceptual basis of pain with its types and also provides information on various herbal and herbo-mineral formulations which show the significant effect as per the studies included in the review. It may be worthwhile to take up pure studies similar to Anil mangal *et al*[19] where oral and external therapies for specific pain types may able to bring new leads for pain management.

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Cite this article as:

Mahesh S. *et al*. Review of Pain: An Ayurvedic approach. Int. Res. J. Pharm. 2019;10(9):24-34 http://dx.doi.org/10.7897/2230-8407.1009256

Source of support: Nil, Conflict of interest: None Declared