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Herbal therapies for pain management: a scoping review of the current evidence

Md. Kamrul Hasan · Khwaja Zohura Zanzabil · Iffat Ara · Tania Rahman · Alexander Kieu · Linda Östlundh · Sameeha Junaidi · Moien AB Khan

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Abstract Pain is a common symptom which can result in disability and lower quality of life. The current review covers the use of medicinal plants as an alternative therapy for pain relief, as traditional painkillers like NSAIDs, opioids, and antidepressants can have serious side effects. Medicinal plants are effective, easily available, low-cost, and have fewer side effects. The review examines commonly used medicinal plants, their active components, their pharmacological activity, and their mechanism of

Khwaja Zohura Zanzabil and Iffat Ara have been contributed equally to this work.

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Md. K. Hasan · I. Ara
Department of Biochemistry and Molecular Biology, Tejgaon College, National University, Dhaka, Gazipur 1704, Bangladesh
e-mail: kamrul.hasan11@northsouth.edu; hasanm57@mcmaster.ca

I. Ara
e-mail: ara041135@gmail.com

Md. K. Hasan
Department of Public Health, North South University, Dhaka 1229, Bangladesh

Present Address:
Md. K. Hasan
Department of Health Research Methods, Evidence, and Impact, McMaster University, 1280 Main St. W., Hamilton L8S 4K1, Canada

K. Z. Zanzabil
Department of Mathematics and Natural Sciences, Biotechnology Program, School of Data and Sciences, BRAC University, Dhaka, Bangladesh
e-mail: zohurazanzabil@gmail.com

T. Rahman
Department of Biochemistry and Molecular Biology, University of Dhaka, Dhaka 1000, Bangladesh
e-mail: tania.rahman@du.ac.bd

A. Kieu
Health and Wellness Research Group, Department of Family Medicine, College of Medicine and Health Sciences, United Arab Emirates University, Al Ain, United Arab Emirates
e-mail: akieu@uaeu.ac.ae

L. Östlundh
Örebro University, Orebro, Sweden
e-mail: linda.ostlundh@oru.se

S. Junaidi
RAK Medical & Health Sciences University, Ras Al Khaimah, United Arab Emirates
e-mail: sameeha.19901068@rakmhsu.ac.ae

M. AB. Khan (✉)
Health and Wellness Research Group, Department of Family Medicine, College of Medicine and Health Sciences, United Arab Emirates University, Al-Ain, United Arab Emirates
e-mail: moien.khan@uaeu.ac.ae

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action for different types of pain in humans and animal models. The review also discusses the use of herbal therapies for pain in various conditions, such as rheumatoid arthritis, neuropathies, osteoarthritis, dysmenorrhea, headache, migraine, wounds, low back pain, and chest pain, and weighs the advantages and disadvantages of using herbal therapies in light of recent research.

Keywords Pain management · Analgesic herbs · Alternative medicine · Complementary therapies · Phytomedicine · Herbal pharmacology

Abbreviations

NSAIDs	Non-steroidal anti-inflammatory drugs
IASP	International association for the study of pain
IBS	Irritable bowel syndrome
PRISMA-ScR	Preferred reporting items for systematic reviews and meta-analyses extension for scoping reviews
PICOS	Population, intervention, comparison, outcome, study design
PRISMA	Preferred reporting items for systematic reviews and meta-analyses
RA	Rheumatoid arthritis
IL	Interleukin
TNF	Tumor necrosis factor
MMPs	Matrix metalloproteinases
PGE2	Prostaglandin E2
COX-2	Cyclooxygenase-2
DMARDs	Disease-modifying anti-rheumatic drugs
NO	Nitric oxide
NF-kB	Nuclear factor kappa B
MAPK	Mitogen-activated protein kinase
OA	Osteoarthritis
BMI	Body mass index
ICAM-1	Intercellular adhesion molecule-1
iNOS	Inducible nitric oxide synthase
PI3K	Phosphoinositol 3 kinase
TLR	Toll-like receptor
LPS	Lipopolysaccharide
ROS	Reactive oxygen species
SOD	Superoxide dismutase
CFA	Complete freund's adjuvant
IKB	Inhibitor of NF-κB
LOX	Lipoxygenase
hs-CRP	High sensitivity C-reactive protein
VAS	Visual analog scale
LBP	Low back pain
NMDA	N-methyl-D-aspartate
cAMP	Cyclic adenosine monophosphate
LPA	Lysophosphatidic acid
NGF	Nerve growth factor
SNRIs	Serotonin and non-adrenaline reuptake inhibitors
TCAs	Tricyclic antidepressants
CNS	Central nervous system
5-HT1A	5-Hydroxytryptamine receptor 1A
GABA	Gamma-aminobutyric acid
TRPA-1	Transient receptor potential ankyrin 1
KATP channels	ATP-sensitive potassium channels
TTH	Tension-type headaches
TXB2	Thromboxane B2
PAF	Platelet-activating factor
TRPM8	Transient receptor potential melastatin 8
THC	Tetrahydrocannabinol
TRPV1	Transient receptor potential vanilloid 1
EMS	Emergency medical services
ED	Emergency departments
STAT-3	Signal transducer and activator of transcription-3
ECGS-T segment	Electrocardiography ST segment
CAT	Chloramphenicol acetyltransferase
GSH	Glutathione
CBD	Cannabidiol
FDA	Food and drug administration
SJW	St. Johns wort
P gp	P Glycoprotein
RCTs	Randomized controlled trials
HDF	Human dermal fibroblasts
CCI	Chronic critical illness
Iba1	Ionized calcium-binding adaptor molecule 1
GFAP	Glial fibrillary acidic protein
PDGF	Platelet-derived growth factor
SPE	Solid phase extraction

Introduction

Pain is described as "An unpleasant sensory and emotional experience connected with actual or potential tissue damage, or described in terms of such damage," according to the International Association for the Study of Pain (IASP) (Lewis 2003). Pain is one of the fundamental human health problems and can lead to significant suffering and disability (Vos et al. 2012) and remains one of the significant reasons people visit physicians. It is associated with many medical conditions created by intense or damaging stimuli, which lowers quality of life and puts a financial strain on healthcare (Williams and Craig 2016).

Generally, the sensation of pain is transmitted by afferent neurons from the periphery to the spinal cord (Peirs and Seal 2016). Although pain is a response to tissue injury, it can sometimes become chronic, leading to biological changes to the central nervous system or peripheral tissue. Additionally, pain can give rise to fear, anxiety, and increased hypothalamic stress response through cortical stimulation that eventually increases blood viscosity and platelet accumulation (Ahmad and Zakaria 2015). Every year, the prevalence of pain rises, especially among the elderly, as a result of longer life expectancies (Scurrah et al. 2018). The prevalence of pain is two times higher in older persons than in younger people, especially those over 60 years (Middaugh and Pawlick 2002). More than 100 million Americans are thought to be impacted by pain (Simon 2012), and 25% of Americans report experiencing pain every day (Gedin et al. 2017).

Pain can be neuropathic, visceral, visceral-chronic, inflammatory, or acute. Neuropathic pain is brought on by damage to the neurological system, whereas inflammatory pain is connected to tissue damage and immune cell infiltration (Pranay et al. 2023; Sommer 2016; Woolf 2010). Although there are numerous ways to categorize pain, it is frequently done so using time. Traditionally, pain can be classified as either being acute or chronic.

Acute pain typically results from damage or injury, lasts less than three months, and has no negative effects on the patient's quality of life. When pain is acute, its source and location are obvious. Acute pain (Apkarian et al. 2011) brought on by improper care can manifest as increased sympathetic nervous system activity, tachycardia, tachypnea, etc. Trauma and surgical procedures are two instances of acute pain (Noroozian et al. 2018). In contrast, chronic pain might persist for three to six months or longer. The likelihood of acquiring chronic pain increases with age, previous pain experience, anxiety, stress, and depression, with females more likely to experience it (Apkarian et al. 2011). Mild chronic pain can occasionally become acute, episodic, or ongoing.

Sometimes mild to severe, episodic or persistent chronic pain might develop. It is a nociceptive or neuropathic pain-related public health issue (Noroozian et al. 2018). By activating somatic or visceral pain receptors, nociceptive pain is felt. Fractures of the bones and illnesses of the joints are a few examples of somatic discomfort. Irritable bowel syndrome (IBS), gastritis, and visceral discomfort are gastrointestinal conditions that cause pain. Neuropathic pain develops as a result of nerve injury brought on by radiotherapy or surgery (Noroozian et al. 2018).

Analgesic medications work differently to relieve pain by affecting both the peripheral and central neural systems. Typically, narcotics (opioids) and non-narcotics are used as analgesics (non-opioids). Pain treatment techniques typically involve the use of opiates like morphine, codeine, heroin, oxycodone, etc. and non-steroidal anti-inflammatory medicines (NSAIDs) such salicylates, COX-2 inhibitors, ibuprofen, etc. NSAIDs that are anti-inflammatory and analgesic are excellent treatments for mild to moderate pain. Opioid drug use, however, might result in adverse consequences such nausea, vomiting, respiratory depression, constipation, physical dependence, tolerance, etc. (Martyn et al. 2019). In recent years, medicinal plants have become more and more popular as a form of pain management due to the potential negative side effects and ineffectiveness of chemical medications (Bahmani et al. 2014).

Numerous studies have demonstrated the value of several herbal plants for treating pain (Bahmani et al. 2012; Bahmani and Eftekhari 2012; Jahromi et al. 2021; Kopustinskiene et al. 2022; Pranay et al. 2023; Song et al. 2023). Herbal remedies have historically been utilized as analgesic treatments due to their easy accessibility, low cost, little side effects, and potential to improve quality of life (Ayaz et al. 2016; Narwade et al. 2023; Ullah et al. 2015). Nearly 80% of people worldwide rely on plant-based medicines, according

to the World Health Organization (WHO) (Bahmani et al. 2014). Approximately 20 million Americans use herbal medicines in the United States (Bent 2008). Alkaloids, flavonoids, terpenoids, and steroids are among the active phytoconstituents extracted from these plants that inhibit the COX and LOX pathways, which have an impact on eicosanoid metabolism (Weiner and Ernst 2004). When taken in the right dosages, the active components of these plants have analgesic and anti-inflammatory properties, which can effectively relieve pain and have a positive impact on the course of the disease (Akhtar et al. 2011a). The main purpose of this scoping review is to evaluate the effectiveness and safety of medicinal plants in treating various pain related conditions. By examining both animal studies our aim is to understand the mechanisms through which these herbal remedies provide pain relief and reduce inflammation. Moreover we strive to contribute to the body of evidence based knowledge on pain management by synthesizing existing research findings.In essence, our goal is to provide healthcare professionals and researchers with an well informed perspective on the use of plants, for treating pain.

Materials and methods

An exploratory review design was employed to examine several medicinal plants' safety, efficacy, and potential uses for treating rheumatoid arthritis, osteoarthritis, dysmenorrhea, headaches, migraines, wounds, low back pain, and chest pain. We conducted this study based on the Arksey and O'Malley framework (Arksey and O'Malley 2007) and the Preferred Reporting Items for Systematic Reviews and Meta-Analyses extension for scoping reviews (PRISMA-ScR) (Tricco et al. 2018). In this exploratory review, five steps were followed: (i) Defining the eligibility criteria; (ii) identifying relevant studies through search strategy; (iii) selecting studies; (iv) extracting data; and (v) compiling and summarizing the findings.

Eligibility criteria

For this scoping review we have reported based on the PICOS (Population, Intervention, Comparison, Outcome, Study Design) methodology (Higgins et al. 2008). We have reported the findings utilising PRISMA-ScR methodology (Tricco et al. 2018).

Inclusion criteria

We will consider studies that involve both animal and human subjects that experience types of pain such as rheumatoid arthritis, neuropathic pain, osteoarthritis, dysmenorrhea, headache, migraine, wounds, low back pain or chest pain. There are no restrictions based on age or gender. Our focus will be on research that examines the use of plants for managing pain. We aim to include information on plant details including compounds and administration methods as well as outcomes related to pain relief. Studies comparing interventions will also be included. We will only consider research articles published in English that follow the PRISMA guidelines and can be both qualitative and quantitative.

Exclusion criteria

Our review excludes studies that do not involve animal or human subjects experiencing the specified types of pain. Additionally, studies that do not explore plant interventions for pain management or lack details about the intervention will not be included. Irrelevant studies unrelated to plant use for managing pain will also be excluded. Furthermore, studies where pain relief is not the primary focus will not be considered. We will exclude research articles that are not original publication in languages other than English.

Search strategy

A medical librarian (LÖ) conducted a systematic literature search in the four electronic databases: PubMed, EMBASE, Scopus and Web of Science. The search was conducted from time of inception to October 2022. Search terms relevant to the research question were systematically developed after discussing with subject matter experts. The search included PubMed and PubMeds' MeSH for the best possible search outcome. A combination of the search fields title, abstract and MeSH/Thesaurus and relevant truncation were applied to all search terms for the best possible search results: ((herb[Title/Abstract] OR herbs[Title/Abstract] OR herbal[Title/Abstract] OR herbals[Title/Abstract] OR "Herbal Medicine"[Mesh] OR "Plants, Medicinal"[Mesh] OR "Medicinal Plant*"[Title/Abstract] OR "Medical Plant*"[Title/Abstract] OR "Pharmaceutical Plant*"[Title/Abstract]

OR "Healing Plant*"[Title/Abstract]) AND ("Pain"[Mesh:NoExp] OR "Neuralgia"[Mesh] OR "Arthritis, Rheumatoid"[Mesh] OR "Osteoarthritis"[Mesh] OR "Dysmenorrhea"[Mesh] OR "Low Back Pain"[Mesh] OR "Migraine Disorders"[Mesh] OR "Headache"[Mesh] OR "Chest Pain"[Mesh] OR "Pain"[Title/Abstract] OR "Osteoarthritis"[Title/Abstract] OR "Dysmenorrhea*"[Title/Abstract] OR "Low Back Pain"[Title/Abstract] OR "Migraine*"[Title/Abstract] OR "Headache*"[Title/Abstract] OR "Chest Pain"[Title/Abstract] OR Neuralgia*[Title/Abstract] OR Neurodynia*[Title/Abstract] OR "Rheumatoid Arthrit*"[Title/Abstract] OR Osteoarthritides[Title/Abstract] OR Osteoarthros*[Title/Abstract] OR Arthritis[Title/Abstract] OR Arthritides[Title/Abstract] OR Arthros*[Title/Abstract] OR dysmenorrhea*[Title/Abstract] OR Ache[Title/Abstract] OR Aches[Title/Abstract]. A detailed search can be found in online Appendix Table 1.

Data extraction

From the article, we extracted the following information: Scientific name, common name, family name, disease treated by the plant, bioactive phytochemicals, part of the plant used for treatment, and mode of administration. Additionally, we extracted scientific names for the plants, bioactive compounds, mechanisms of action of bioactive compounds, extracts that had an effect, extract dose, and human or experimental animal models with pain as outcomes (Table 1, Fig. 2).

Study selection and characteristics

The results of the search strategy are shown in Fig. 1. We include 378 published articles in the write-up. We have used a thematic analysis of the disease, the pathological disease process, extract dosage and the pain response as outcomes.

Rheumatoid arthritis

Rheumatoid Arthritis (RA) is a multifaceted autoimmune disease known for its progressive joint inflammation and a range of systemic complications, including extra-articular manifestations like rheumatoid nodules, pericarditis, and more (Cojocaru et al. 2010; Marcucci et al. 2018). This debilitating condition affects approximately 1% of the global population, with a higher prevalence in North America and Europe, and a notable predilection for women (Gibofsky 2012; Köhler et al. 2019).

The etiology of RA is complex, involving genetic, hormonal, environmental, and immune factors. Factors such as smoking have been strongly associated with an increased risk of RA, with smokers being three to four times more likely to develop the disease (Lahiri et al. 2012; Sparks and Karlson 2016). Immune dysregulation plays a central role in RA, with activated CD4+T cells producing pro-inflammatory cytokines like interleukin IL-1, IL-6, and tumor necrosis factor (TNF)-alpha, leading to autoantibody production and joint damage (Choy and Panayi 2001; Mateen et al. 2016).

In the pathogenesis of RA, joint-damaging cytokines contribute to cartilage degradation by activating proteolytic enzymes like MMPs and collagenases (Jeong et al. 2016a, b; Moelants et al. 2013). Additionally, the activation of the p38 kinase signaling pathway by inflammatory cytokines further exacerbates joint pain and cartilage destruction (Ding et al. 2010; Ma et al. 2019). Arachidonic acid metabolism, specifically the conversion of arachidonic acid into prostaglandin E2 (PGE2) by COX-2 enzymes, plays a crucial role in the formation of pannus in synovial joints, contributing to synovial fibroblast apoptosis and joint inflammation (Amin et al. 2017; Farzaei et al. 2016; Linden et al. 2009).

Treatment strategies for RA encompass a spectrum of medications, including NSAIDs, immunosuppressants, pain relievers, disease-modifying anti-rheumatic drugs (DMARDs), and anti-TNF alpha agents, all aimed at alleviating pain, swelling, and joint damage (Hochberg et al. 2012; Hyrich et al. 2006; Soliman et al. 2012). However, long-term use of NSAIDs can lead to toxic side effects, and TNF-alpha inhibitors may induce hypersensitivity reactions and autoimmune responses (Cabral et al. 2016; McAlindon et al. 2014).

As a result, alternative therapies utilizing medicinal plant extracts have gained attention for their potential benefits in managing RA-related pain and inflammation pain (Table 1, Fig. 2, online Appendix Fig. 1).

1. *Arnica Montana*, a member of the Asteraceae family, has a long history of traditional use in treating RA and inflammation-related

Table 1 Plant based interventions for Rheumatoid arthritis

Plant (Scientific name)	Bioactive compounds	Mechanism of action	Extract	Dose	Experimental model	Results
1. *Arnica montana*	1,8 cineol, linalool, alpha-cadinol (Kowalski et al. 2015; Pljevljakušić et al. 2012; Sugier et al. 2017; Weremczuk-Jeżyna et al. 2011)	Anti-inflammatory Inhibits the cytokine induced airway mucus hypersecretion effectively	Methanolic extract (Sharma et al. 2016)	75 mg/kg body weight (Sharma et al. 2016)	Rat (Sharma et al. 2016)	Lessens histological and radiological changes in affected joints, reduces NO, IL-6, IL-12, IL-beta, TNF-alpha concentrations (Sharma et al. 2016)
2. *Curcuma spp.*	Curcumin (Nonose et al. 2014)	Improves inflammatory conditions in joint (Nonose et al. 2014)	Essential oil extract (Funk et al. 2010)	56 mg/kg/day (Funk et al. 2010)	Rat (Funk et al. 2010)	Inhibits joint swelling and arthritis induced by streptococcal cell wall (Funk et al. 2010)
3. *Equisetum arvense*	Kynurenic acid (Zgrajka et al. 2013)	Inhibits synoviocytes proliferation (Parada-Turska et al. 2006)	Root	15.89 pmol/ml	Human (Parada-Turska et al. 2006)	Inhibits proliferation of synoviocytesml
4. *Salix spp.*	Salicin (Bonaterra et al. 2010; Drummond et al. 2013; Khayyal et al. 2005; Shara and Stohs 2015)	Decreases proinflammatory mediators and inhibits COX 2 activity (Bonaterra et al. 2010; Drummond et al. 2013; Khayyal et al. 2005; Shara and Stohs 2015)	Bark extract (Biegert et al. 2004)	240 mg/day (Biegert et al. 2004)	Human (Biegert et al. 2004)	Relieves pain of Ra (Biegert et al. 2004)
5. *Aloe barbadensis*	Anthraquinone (Sharma et al. 2014a, b)	Inhibits PGE2 and iNO (Budai et al. 2013; Kshirsagar et al. 2014)	Methanolic extract (Kshirsagar et al. 2014)	25, 50, and 75 mg/kg of aloe emodin (Kshirsagar et al. 2014)	Rat (Kshirsagar et al. 2014)	Inhibits PGE2, IL-8, IL-6, IL-3, TNF-alpha production and translocation of NF-KB kinases, p^{38}, JNK and ERK
6. *Andrographis paniculata*	Andrographolide (Gupta et al. 2017; Li et al. 2017a, b)	Reduces PGE2 production (Wang et al. 2004; Yan et al. 2012)	Ethanolic, Dried	10, 20, and 30 μM) of		andrographolide (Yan et al. 2012)
Human (Yan et al. 2012)	induces cell cycle arrest and apoptosis (Yan et al. 2012)					
7. *Berberis* orthrobotrys	Beta-sitosterol (Mehmood et al. 2018)	Inhibits NF-KB and regulates genes for increased inflammatory mediators (Valerio and Awad 2011)	Aqueous methanolic extract (Alamgeer et al. 2017)	150 mg/kg (Alamgeer et al. 2017)	Rat (Alamgeer et al. 2017)	Exhibits anti-arthritic activity by inhibiting IFN-alpha, PDGF, IL-1, IL-6, TNF-alpha etc. cytokine production (Alamgeer et al. 2017)
8. *Celastrus paniculatus*	Celastrine, celapagine, beta-sitosterol, beta-amyrin (Shashank et al. 2017; Shimizu et al. 2015)	Inhibits TNF-alpha and IL-6 (Kulkarni et al. 2015)	Ether seed extract (Kulkarni et al. 2015)	(500 and 400) mg/kg (Kulkarni et al. 2015)	Mice (Kulkarni et al. 2015)	Inhibits TNF-alpha, IL-6 and inflammatory mediators involved in swelling, joint devastation (Kulkarni et al. 2015)
9. *Oenothera biennis*	Gamma linolenic acid (Voukeng et al. 2016)	Reduces COX 2 gene expression and modulates NO, TNF-alpha, IL-1 beta, TXB2 pathway (Voukeng et al. 2016)	Seed oil	1.4 g/day	Human	Exhibits antiinflammatory and immunoregulatory properties

Table 1 continued

Plant (Scientific name)	Bioactive compounds	Mechanism of action	Extract	Dose	Experimental model	Results
10 *Uncaria tomentosa*	Pentacyclic oxindole, proanthocyanidins (Navarro et al. 2019)	Inhibits IL-1 alpha, IL-1 beta, IL-4, IL-17 and TNF-alpha (Navarro et al. 2019)	Krallendorn® capsule contains 20 mg of aqueous acid-extracted dry extract of U. tometosa (Mur et al. 2002)	(2386.5 µg/g)	Human (Mur et al. 2002)	reduction of the number of painful joints (Mur et al. 2002)
11. *Withania somnifera*	Withanolides, withaferin A (Khan et al. 2015; Singh et al. 2007)	Inhibits TNF-alpha, IL-1beta, IL-12, NF-KB (Ganesan et al. 2011; Grover et al. 2010; Heyninck et al. 2014; Singh et al. 2007)	Aqueous root extract (Ramakanth et al. 2016)	500 mg/day (Ramakanth et al. 2016)	Human (Ramakanth et al. 2016)	Reduces pain, stiffness and deformities in patients with knee joint pain (Ramakanth et al. 2016)
12. *Caragana pruniosa*	Purinosanone D and E, butin, scutellaprostin C and 2,4-dihydroxy flavanone (Meng et al. 2009; Peng et al. 2016; Sun et al. 2015; Zaka et al. 2017)	Downregulates TNF-alpha, IL-1beta, IL-6 and CRP (Meng et al. 2009; Peng et al. 2016; Sun et al. 2015)	Ethanolic root extract (Peng et al. 2016; Zhang et al. 2019)	(130, 260 and 520) mg/kg (Peng et al. 2016; Zhang et al. 2019)	Rat (Peng et al. 2016; Zhang et al. 2019)	Suppresses TNF-alpha, IL-1beta, IL-6, IL-10 and CRP levels elevated in RA (Peng et al. 2016; Zhang et al. 2019)
13. *Eysenhardita polystachya*	Stigmasterol, isoduartin, cuneatin and 3,4-dimethoxy-8,9 pterocarpan (Alonso-Castro et al. 2018; Pablo-Pérez et al. 2018)	Reduces serum IL-6 and TNF-alpha etc. proinflammatory cytokines (Alonso-Castro et al. 2018; Pablo-Pérez et al. 2018)	Ethanolic extract (Pablo-Pérez et al. 2018)	(25,50,100 and 200) mg/kg/day (Pablo-Pérez et al. 2018)	Rat (Pablo-Pérez et al. 2018)	Reduces arthritic pain by decreasing serum IL-6, TNF-alpha, GM-CSF etc. proinflammatory cytokines production (Pablo-Pérez et al. 2018)
14. *Inula helenium*	Alantolactone, isoalantolactone (Chun et al. 2012; Gao et al. 2017)	Inhibits TNF-alpha, MCP1, MCP3, IL-1, IL-6, MCP2 expression (Younis et al. 2016)	Root extract (Gao et al. 2017)	(12.5–50) mg/kg (Gao et al. 2017)	Rat (Gao et al. 2017)	Reduces RA symptoms by inhibiting TNF-alpha induced NF-KB and MAPK pathway activation (Gao et al. 2017)
15. *Nigella sativa*	Thymoquinone (Umar et al. 2012; Vaillancourt et al. 2011)	Hinders IL-1beta, TNF-alpha, IL-10, IFN-gamma, PGE2, IL-6 expression (Umar et al. 2012)	Capsules containing *Nigella sativa* essential oil (Hadi et al. 2016)	1000 mg/day (Hadi et al. 2016)	Human (Hadi et al. 2016)	Improves inflammation by increasing IL-10 and reduces oxidative stress in RA (Hadi et al. 2016)
16. *Strychnos nux-vomica*	Brucine, Brucine-N-oxide (Yin et al. 2003)	Suppress PGE2 production and decrease vascular permeability (Chaurasia 2009; Ekambaram et al. 2010)	aqueous extract (SPE),whole seed powder	200 mg/kg/p.o (Ekambaram et al. 2010)	Rat model (Ekambaram et al. 2010)	Reduces paw edema volume (Ekambaram et al. 2010)

conditions. Its active compounds, including 1,8 cineol, linalool, and alpha-cadinol, have shown promise in reducing inflammation and improving joint health (Sharma et al. 2016). Studies on a collagen-induced arthritic rat model demonstrated that phenolic and flavonoid compounds from Arnica Montana extracts could effectively mitigate histological and biochemical changes

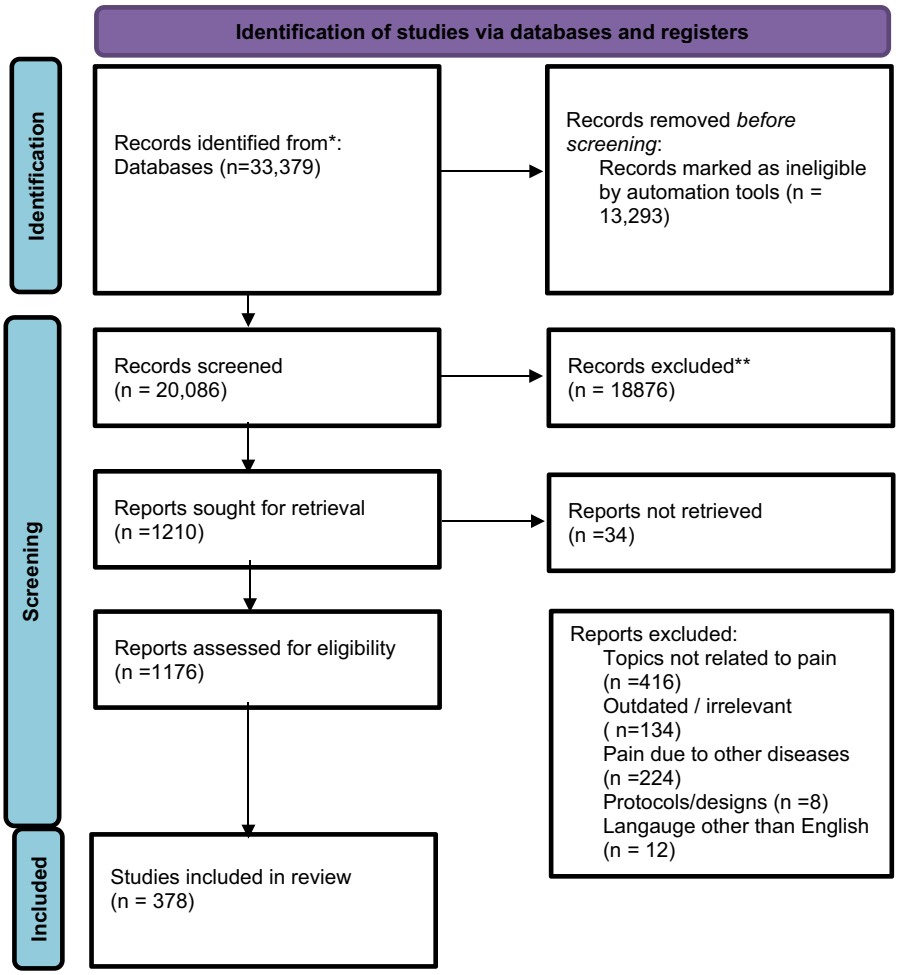

Fig. 1 PRISMA

in affected joints. These compounds also reduced levels of pro-inflammatory cytokines such as nitric oxide (NO), IL-6, IL-12, IL-1beta, and TNF-alpha, while enhancing antioxidant defenses and reducing peroxidative injury (Sharma et al. 2016).

2. *Curcuma species*, particularly Curcuma longa or turmeric, have gained popularity for their anti-inflammatory properties. Curcumin, a phenolic compound found in turmeric, has shown efficacy in suppressing joint damage and inflammation by inhibiting various inflammatory mediators (Prasad and Aggarwal 2011). It also prevents destructive changes in joints and bones (Gründemann et al. 2014; Li et al. 2013). Notably, curcumin exhibited superior efficacy to prednisone in reducing neutrophil infiltration in rat models of zymosan-induced arthritis (Nonose et al. 2014). Coumarin, another active compound, contributes to systemic oxidative stress reduction (Panahi et al. 2016). Beta-element, derived from Curcuma wenyujin, has been used traditionally in China for RA treatment due to its anti-proliferative activity against fibroblast-like synoviocytes (Zou et al. 2016).
3. *Equisetum arvense*, commonly known as horsetail, has been employed in European ethnomedicine for its anti-inflammatory properties. Clinical trials have indicated its potential in reducing TNF-alpha levels in RA patients (Jiang et al. 2014). Kynurenic acid, an active

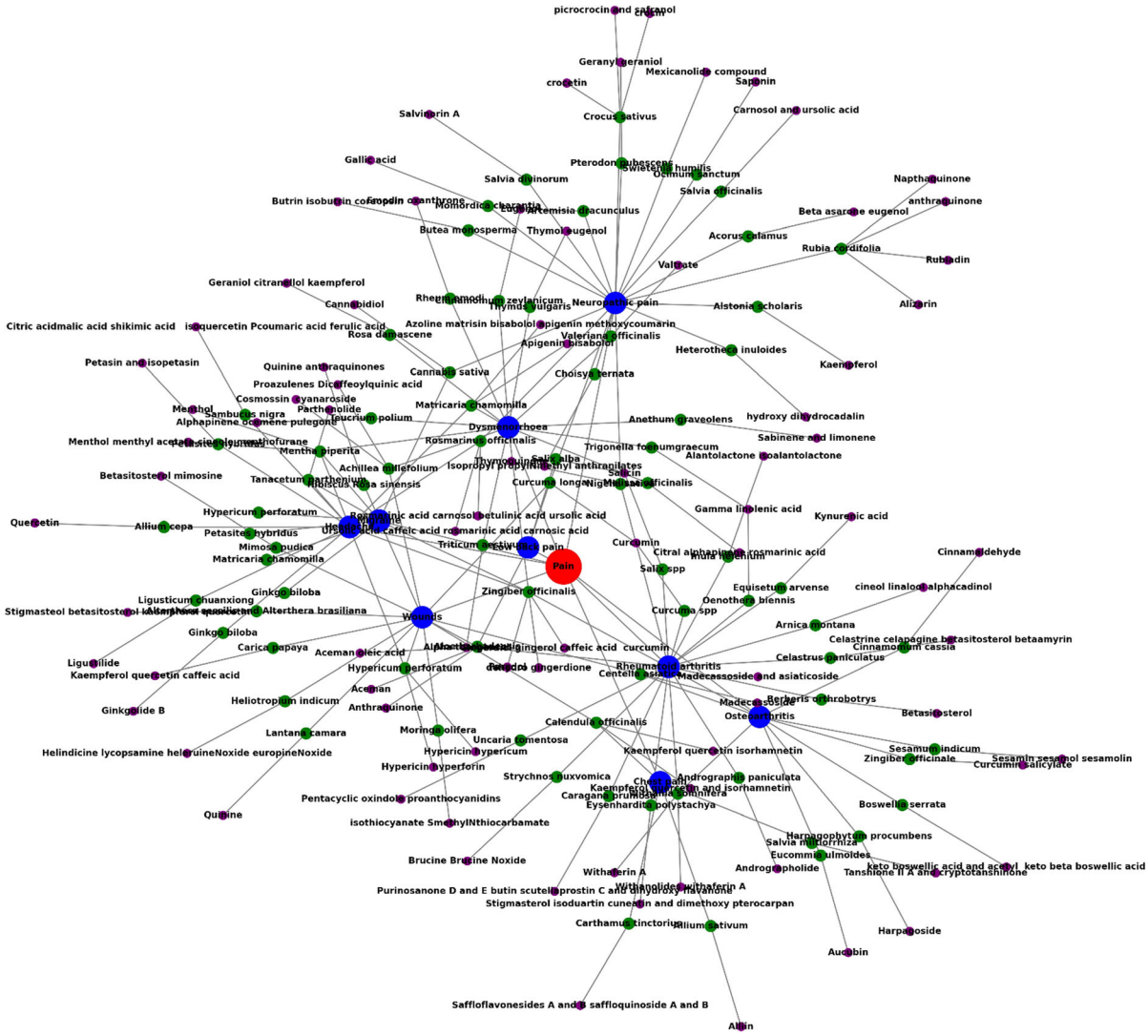

Fig. 2 Network visualization of the role of herbal therapy in pain management. The visualization aims to illustrate the relationships between pain, treated diseases, and herbal remedies This network visualization represents herbal therapy for pain management. The central node, 'Pain', in red, connects to various diseases treated (blue nodes). Each disease is linked to specific plant species (green nodes), which are further connected to their bioactive compounds (purple nodes).

compound from horsetail, has demonstrated analgesic and anti-inflammatory effects (Zgrajka et al. 2013). These findings suggest that *Equisetum arvense* may have a role to play in managing RA-related inflammation.

4. *Salix species,* commonly known as willow, have been used traditionally for pain relief. Active ingredients such as salicin, polyphenols, and flavonoids have been found to inhibit the synthesis of pro-inflammatory mediators, particularly cyclooxygenase-2 (COX-2) (Bonaterra et al. 2010; Drummond et al. 2013; Khayyal et al. 2005). Additionally, willow bark extracts have been shown to block the activity of TNF-alpha and NF-kB, further supporting their anti-inflammatory properties (Bonaterra et al. 2010). Clinical trials have demonstrated the effectiveness of willow bark extract in relieving RA pain, with results comparable to the nonsteroidal anti-inflammatory drug (NSAID) diclofenac (Biegert et al. 2004)

5. *Aloe barbadensis,* commonly known as aloe vera, contains various chemical constituents with anti-inflammatory properties, including anthraquinone alkaloids (Jales et al. 2021). These compounds have demonstrated effectiveness in treating arthritis and rheumatic conditions (Budai et al. 2013). Aloe vera extract has been found to inhibit the production of pro-inflammatory cytokines such as PGE2, IL-8, IL-6, IL-1, and TNF-alpha, as well as the activation of signaling pathways involved in inflammation (Yagi and Yu 2018).
6. *Andrographis paniculata*, an herbaceous plant of the Acanthaceae family, contains andrographolide and its derivatives, which exhibit anti-rheumatoid activity by inhibiting NF-kB activation (Gupta et al. 2017). Clinical trials have demonstrated the potential of andrographolide in reducing RA symptoms (Wang et al. 2004; Yan et al. 2012). This plant offers a potential avenue for RA management.
7. *Berberis arthrobotrys*, a member of the Berberidaceae family, contains active phytoconstituents such as beta-sitosterol that regulate genes associated with inflammation and inhibit NF-kB in rheumatoid arthritis (Uttra et al. 2019). Aqueous methanolic extracts of this plant have shown anti-arthritic activity by suppressing the production of pro-inflammatory cytokines in animal models (Valerio and Awad 2011). These findings suggest a potential role for Berberis arthrobotrys in RA treatment.
8. *Celastrus paniculatus,* locally known as black oil, possesses anti-inflammatory, antioxidant, and antipyretic properties due to compounds like sesquiterpenoids and alkaloids (Shashank et al. 2017). This plant has demonstrated the ability to inhibit pro-inflammatory mediators, including TNF-alpha and IL-6, in animal models (Kulkarni et al. 2015). It shows promise as a natural remedy for RA.
9. *Oenothera biennis,* or evening primrose, contains gamma-linolenic acid, which has been shown to reduce the pathogenesis of RA by modulating inflammatory mediators (Voukeng et al. 2016). This compound can suppress the expression of genes associated with inflammation, including COX-2, and reduce oxidative stress in RA (Voukeng et al. 2016).
10. *Uncaria tomentosa*, commonly known as cat's claw, contains active compounds like pentacyclic oxindole and proanthocyanidins with anti-inflammatory properties. It has been found to alleviate pro-inflammatory cytokines and improve RA symptoms in animal models (Sordi et al. 2019). Clinical trials have shown its potential in reducing joint pain in RA patients (Mur et al. 2002). Uncaria tomentosa may offer a natural approach to RA management.
11. *Withania somnifera*, known as ashwagandha, contains active compounds called withanolides, including Withaferin A, with antioxidant properties (Singh et al. 2011). These compounds inhibit the production of pro-inflammatory cytokines like TNF-alpha and IL-1 beta, as well as NF-kB activation (Singh et al. 2007). Withania somnifera has shown promise in reducing pain, stiffness, and deformities in RA patients (Ramakanth et al. 2016).
12. *Caragana pruinosa*, a member of the Leguminosae family, contains active constituents like flavonoids and purinosanones that downregulate pro-inflammatory cytokines such as TNF-alpha and IL-6 (Zaka et al. 2017). Preclinical studies have demonstrated its effectiveness in improving RA symptoms (Peng et al. 2016; Sun et al. 2015).
13. *Eysenhardtia polystachya*, known as Palo Azul, has been used traditionally for its anti-inflammatory properties. Studies have shown that its ethanolic extract can reduce arthritic pain and levels of pro-inflammatory cytokines in animal models (Huang et al. 2014a, b). This plant extract may hold promise as a natural remedy for RA.
14. *Inula helenium*, a member of the Asteraceae family, contains active compounds like alantolactone and isoalantolactone, which inhibit TNF-alpha-induced NF-kB and MAPK pathway activation (Gao et al. 2017). Inula helenium has shown potential in reducing pro-inflammatory cytokines and may have a role in RA management (Younis et al. 2016).
15. *Nigella sativa*, known as kalonji or black caraway, contains thymoquinone, which inhibits the expression of pro-inflammatory cytokines like IL-1beta, TNF-alpha, and IL-6 (Umar et al. 2012; Vaillancourt et al. 2011). Clinical trials have demonstrated its effectiveness in reducing inflammation and oxidative stress in RA patients (Hadi et al. 2016).

Table 2 Plant based interventions for Osteoarthritis

Plant (Scientific name)	Bioactive compounds	Mechanism of action	Extract	Dose	Experimental model	Results
1. *Boswellia serrata*	11 keto boswellic acid and acetyl 11 keto beta boswellic acid (Hamidpour et al. 2013; Sharma et al. 1989; Wang et al. 2014)	Improves synovial fluid protein pattern and recduces the leukocyte infiltration (Hamidpour et al. 2013; Sharma et al. 1989; Wang et al. 2014)	Acetone extract (Wang et al. 2014)	34.14 mg/gKBA and 74.62 mg/g AKBA	Rat (Wang et al. 2014)	Improves arthritic conditions (Wang et al. 2014)
2. *Harpagophytum procumbens*	Harpagoside (Boje et al. 2003; Mncwangi et al. 2012)	Inhibits iNOS and COX2 expression (Huang et al. 2006)	Aqueous extract (Wegener and Lüpke 2003)	2400 mg/day (Wegener and Lüpke 2003)	Human (Wegener and Lüpke 2003)	Reduces knee and hip osteoarthritis pain (Wegener and Lüpke 2003)
3. *Eucommia ulmoides*	Aucubin (He et al. 2014a, b, c)	Decreases cell apoptosis, ROS production and caspase-3 activity (Young et al. 2017)	Aqueous extract (Lu et al. 2013)	6 ml/kg/day (Lu et al. 2013)	Rat (Lu et al. 2013)	Reduces the serum MMP-13, MMP-1, MMp-3 and protects articular cartilage (Lu et al. 2013)
4. *Cinnamomum cassia*	Cinnamaldehyde (Zhou et al. 2019)	Increases glutathione peroxidase, SOD and catalase activity (Zhou et al. 2019)	Hydroalcoholic bark extract (H. Sharma et al. 2018)	250 mg/kg (H. Sharma et al. 2018)	Rat (H. Sharma et al. 2018)	Reduces formaldehyde and CFA induced arthritis (H. Sharma et al. 2018)
5. *Centella asiatica*	Madecassoside (Moqbel et al. 2020)	Suppresses NF-Kb activation pathway (Cao et al. 2010)	Nuclear extracts	300 μM	Rat	Prevention of hypotension, Protects cardiovascular and inflammatory agent
6. *Withania somnifera*	Withaferin A (Grover et al. 2010; Heyninck et al. 2014)	Suppresses NF-KB activation (Grover et al. 2010; Heyninck et al. 2014)	Aqueous root extract (Ramakanth et al. 2016)	(120 and 250)mg (Ramakanth et al. 2016)	Human (Ramakanth et al. 2016)	Reduces pain, disability, stiffness and knee swelling index (Ramakanth et al. 2016)
7. *Zingiber officinalis*	6-dehydro gingerdione (Ji et al. 2017; Schadich et al. 2016)	Alleviates iNOS, COX-2, IL-beta, IL-6 and TNF-alpha expression (S.-H. Huang et al. 2014a, b, p. 264)	Methanol	40 μg/m	Qiagen Kits	Activate NRF2 & expression of GSTP1

Table 2 continued

Plant (Scientific name)	Bioactive compounds	Mechanism of action	Extract	Dose	Experimental model	Results
8. *Sesamum indicum*	Sesamin, sesamol, sesamolin (Rangkadilok et al. 2010)	Inhibits LOX, TNF-alpha, IL-1 beta, IL-6, MMP-13 and MMP-9 activity (Hsu et al. 2013, 2016; Sotnikova et al. 2009)	Sesame seed powder (Haghighian et al. 2015)	40 g (Haghighian et al. 2015)	Human (Haghighian et al. 2015)	Reduces serum inflammation and oxidative stress in patients with knee OA (Haghighian et al. 2015)

16. *Strychnos nux-vomica*, commonly known as poison nut, contains brucine and brucine N-oxide, which have anti-inflammatory properties (Yin et al. 2003). Preclinical data suggests that Strychnos nux-vomica can suppress PGE2 and decrease vascular permeability, providing potential relief from arthritic pain (Chaurasia 2009; Ekambaram et al. 2010).These medicinal plant extracts and their active constituents offer promising alternatives for managing RA-related pain and inflammation, providing potential relief with fewer adverse effects than conventional medications. Table 1 summarizes the plant extracts and their mechanisms of action, which have shown promise as complementary therapies for RA (Table 1, Fig. 2).

Osteoarthritis

Osteoarthritis (OA) is one of the most common types of joint disorder which is associated with joint pain. OA is a long-term, chronic musculoskeletal disorder that affects 15% of the population (Hsu et al. 2016). Joint pain is a significant symptom of OA that reduces the patient's quality of life (Owens and Conaghan 2016), with the knee and back being the most commonly affected joints (Yudoh et al. 2017). Eighty percent of the human population suffering from OA are over 65 years old (Mahdavi et al. 2018). OA affects women more than men and is the leading cause of pain and disability in older people (Wang et al. 2015). The risk of developing osteoarthritis is increased by increased body mass index (BMI), older age, genetics, obesity, diet, and physical activities that cause stress across joints (Murphy et al. 2016). Traumatic joint injuries, particularly knee injuries, can lead to a five–sixfold increase in the risk of developing OA (Lane et al. 2017). OA is characterized by bone erosion, increased pro-inflammatory cytokines including IL-1, IL-6, and TNF-alpha, and irreversible articular cartilage degeneration (Hsu et al. 2016), leading to increased synthesis of collagenase, degradation of matrix metalloproteinase (MMP), and decreased collagenase inhibitor synthesis (Park et al. 2009). Breakdown of the extracellular matrix stimulates the accumulation of innate immune cells leading to inflammation and tissue destruction (Mora et al. 2018). Signaling pathways such as mitogen-activated protein kinase (MAPK) play a role in OA (Mobasheri & Batt 2016). Il-8, IL-17, IL-18, IL-21 diffuse into the synovial fluid, act on chondrocytes and impair matrix synthesis (Khalid et al. 2017). OA is associated with bone thickening, ligament degeneration, and synovial inflammation (Kolasinski et al. 2020). Both peripheral and central mechanisms contribute to OA pain. Peripheral pain is observed in the early stage of osteoarthritis, while central pain is observed in the late and chronic stages (Arendt-Nielsen et al. 2010). NSAIDs, acetaminophen, opioids, intraarticular injections are used in OA treatment. Acetaminophen, NSAIDs, and opioids inhibit the synthesis of prostaglandins and cyclooxygenase enzyme, which helps in pain relief. However, these drugs have adverse effects as well. Long-time use of NSAIDs is associated with nephrotoxicity gastrointestinal and cardiovascular effects (Solomon et al. 2018). Numerous herbs offer alternative approaches to alleviate the pain and symptoms associated with OA. Below, is a list of medicinal

plant extracts and their active phytoconstituents that are employed in the treatment of OA-related pain (Table 2, Fig. 2, online Appendix Fig. 2).

1. *Boswellia serrata*, a plant with a history in Ayurvedic medicine for treating arthritis, exhibits anti-inflammatory and cartilage-protective properties. In vitro studies revealed its ability to resist cartilage degradation by inhibiting MMP-3 and blocking ICAM-1 (Sengupta et al. 2010). Moreover, it hinders collagen and cartilage breakdown by reducing MMP-9, MMP-13, COX-2, NO, and PGE2 production (Blain et al. 2010). Boswellic acids, such as 11-keto boswellic acid and acetyl 11-keto-beta boswellic acid, improve synovial fluid proteins and reduce joint inflammation (Sharma et al. 1989; Wang et al. 2014). This herb also suppresses NF-kB activation and pro-inflammatory cytokines (Ammon 2010; Khajuria et al. 2008). Combining Boswellia with other herbs like Zingiber officinale, Tinospora cordifolia, and Phyllanthus emblica further protects cartilage (Sumantran et al. 2011). Boswellia extract enhances antioxidant status by reducing NO, myeloperoxidase, and lactoperoxidase (Umar et al. 2014). Additionally, a mixture of Boswellia, Withania somnifera, Zingiber officinale, and Curcuma longa alleviates arthritis symptoms by decreasing TNF-alpha and NO production (Dey et al. 2014). The combination of Uncaria tomentose, Boswellia serrata, Lepidium meyenii, and leucine protects articular cartilage, inhibits NF-kB activation, and enhances aggrecan and type II collagen production in OA chondrocytes (Akhtar et al. 2011b). Phytopreparations from Boswellia resin have shown efficacy in relieving pain and improving functionality in knee and hand OA patients without severe toxicity (Belcaro et al. 2015). Furthermore, a combination of Curcuma longa and Boswellia appears more effective and safe in managing OA symptoms than the COX-2 inhibitor celecoxib (Kizhakkedath 2013).
2. *Harpagophytum procumbens*, commonly known as devil's claw, exhibits chondroprotective activity by reducing the release of pro-inflammatory cytokines like TNF-alpha and IL-1beta and inhibiting the synthesis of MMP and esterase (Fiebich et al. 2001). Clinical studies have supported the use of aqueous extracts of Harpagophytum procumbens (at 2400 mg/day) in reducing pain associated with knee and hip osteoarthritis (Chantre et al. 2000; Chrubasik et al. 2002; Wegener and Lüpke 2003). Harpagoside, a compound found in the plant, inhibits iNOS and COX-2 expression by blocking NF-kB activation (Huang et al. 2006).
3. *Eucommia ulmoides*, a member of the Eucommiaceae family, shows promise in osteoarthritis treatment. It reduces the production of pro-inflammatory cytokines such as IL-6, IL-17, TNF-alpha, and IL-1beta in an OA rat model by suppressing the phosphoinositol 3 kinase (PI3K)/Akt signaling pathway activation (Wang et al. 2015). In murine macrophages, Eucommia ulmoides modulates COX-2 and inhibits toll-like receptor (TLR)4, TNF-alpha, IL-1beta, iNOS, and IL-6 production induced by LPS (Koh et al. 2017). Aucubin, an active compound from this plant, reduces cell apoptosis, ROS production, and caspase-3 activity (Young et al. 2017). When used in combination with meloxicam, Eucommia ulmoides has demonstrated better pain relief compared to meloxicam monotherapy (Hu et al. 2020). Additionally, an aqueous extract (6 mg/kg/day) of Eucommia ulmoides protects articular cartilage by reducing serum MMP-13, MMP-1, and MMP-3 levels in an OA animal model (Lu et al. 2013).
4. *Cinnamomum cassia*, a traditional Chinese medicine, is employed for osteoarthritis treatment due to its anti-inflammatory effects and low toxicity (Cross et al. 2014). It influences apoptosis, cell proliferation, differentiation, and the balance of osteoblasts and osteoclasts (Hootman et al. 2016). Cinnamaldehyde, an active compound, inhibits chondrocyte oxidation by increasing the activity of enzymes like glutathione peroxidase, SOD, and catalase (Zhou et al. 2019). The hydroalcoholic bark extract of Cinnamomum cassia, at a dose of 250 mg/kg, reduces arthritis induced by formaldehyde and CFA (Sharma et al. 2018).
5. *Centella asiatica*, commonly known as 'Gotu kola,' is distributed widely in Asia and is utilized for its antioxidant and anti-inflammatory activities in OA treatment (Prakash et al. 2017). The plant contains various phytochemicals, including

tannins, polyphenols, beta-carotene, vitamin C, and flavonoids, which contribute to its antioxidant activity (Chandrika and Prasad Kumara 2015). Madecassoside, a major phytoconstituent, suppresses the NF-kB activation pathway and protects cartilage by inhibiting the effects of IL-1beta on bone marrow cells (Moqbel et al. 2020). Centella asiatica also inhibits NO production and exhibits disease-modifying activity in OA patients (Hartog et al. 2009). Oral administration of Centella asiatica attenuates collagen-induced arthritis by reducing NO and pro-inflammatory cytokine production (Sharma et al. 2014a, b).

6. *Withania somnifera*, known for its analgesic and anti-inflammatory properties in Ayurvedic medicine, inhibits NF-kB activation, ROS production, and the secretion of pro-inflammatory cytokines such as IL-6, TNF-alpha, MMP-8, IL-1beta, and IL-10 (Khan et al. 2019). Withaferin A, an active ingredient, suppresses NF-kB activation by reducing the IKB association complex (Grover et al. 2010; Heyninck et al. 2014). Withania somnifera also inhibits collagenase activity and improves joint disease (Ganesan et al. 2011). In collagen-induced arthritic rats, it alleviates symptoms such as redness, ankylosis, swelling, and deformity (Gupta and Singh 2014). Compared to a placebo, a 250 mg aqueous root extract of Withania somnifera taken once daily reduces pain, disability, stiffness, and knee swelling index (Ramakanth et al. 2016).
7. *Zingiber officinale*, known for its anti-inflammatory properties, inhibits COX-1, COX-2, and LOX in vitro (Huang et al. 2014a, b; Van Breemen et al. 2011). Human clinical studies have demonstrated that the administration of 1 g/day of Zingiber officinale powder for three months improves knee osteoarthritis by reducing serum nitric oxide, high sensitivity reactive protein (hs-CRP), and other inflammatory markers (Naderi et al. 2016). Other studies have supported its effectiveness in improving the clinical condition of OA patients as evaluated by the VAS scale (Alipour et al. 2017). In combination with glucosamine, Zingiber officinale effectively reduces pain in knee and hip OA patients (Drozdov et al. 2012). Active compounds such as 1-dehydrogingerdione and 6-dehydrogingerdione inhibit NF-kB activation and reduce inflammatory gene expression (Lee et al. 2012; Yang et al. 2012).
8. *Sesamum indicum*, commonly known as sesame, has been used in traditional Asian medicine for its anti-inflammatory properties. Sesame oil inhibits inflammation by blocking NF-kB activation and reducing the levels of TNF-alpha, IL-1beta, and IL-6 in arthritic rats (Hsu et al. 2013). It also reduces joint pain by blocking lipid peroxidation and superoxide production (Hsu et al. 2016). Sesame seeds have been shown to lower serum inflammation markers in knee OA patients (Haghighian et al. 2015). Active phytochemicals in sesame, such as sesamin, sesamolin, and sesamol, inhibit LOX, TNF-alpha, IL-1beta, IL-6, MMP-13, and MMP-9 activity (Hsu et al. 2013, 2016; Sotnikova et al. 2009). Sesamol has been found to reduce joint inflammation, cartilage degradation, and bone resorption in arthritic animals (Hemshekhar et al. 2012).

In summary, these natural remedies offer promising avenues for osteoarthritis treatment, with potential benefits in reducing inflammation, protecting cartilage, and alleviating pain. However, further research and clinical trials are necessary to confirm their efficacy and safety in clinical practice.

Low back pain

Low back pain (LBP) is a prevalent public health issue, ranking as the second most common reason for physician visits, the fifth major cause of hospitalization, and the third most frequent indication for surgery (Goetzel et al. 2015). The consequences of LBP extend to limitations in daily activities, including the inability to work (Natour et al. 2014). Chronic LBP exacerbates individuals' suffering and escalates treatment costs (Liao et al. 2009). In response to this complex health issue, diverse treatment strategies have been employed, encompassing physical therapy, surgical interventions, NSAIDs, and early resumption of regular physical activity (Last and Hulbert 2009). In developed countries, additional approaches such as injections, opioid therapy, spinal imaging, and surgical fusions are employed in the management of LBP (Madden et al. 2013). Beyond conventional treatments, some plant-based remedies and their active components have gained attention for their efficacy, minimal side effects, and accessibility in LBP

Table 3 Plant based interventions for Low back pain

Plant (scientific name)	Bioactive compounds	Mechanism of action	Extract	Dose	Experimental model	Results
1. *Aloe barbadensis*	Acemannan, oleic acid (Salehi et al. 2018)	Inhibition to COX enzymes	Petroleum ether, water, upper steam, young bark, mature bark, Leaves & Roots, Acetone	1.0 ml/kg bodyweight, 1.56 mg/ml	Rats, Agar plate	Phagocytic and proliferative activity, Antimicrobial
2. *Salix alba*	Salicin (Bonaterra et al. 2010; Drummond et al. 2013; Khayyal et al. 2005; Shara & Stohs 2015)	Inhibits COX activity and reduces pro-inflammatory mediators synthesis (Bonaterra et al. 2010; Drummond et al. 2013; Khayyal et al. 2005; Shara & Stohs 2015)	Bark extract (Chrubasik et al. 2000)	(120 and 240) mg (Chrubasik et al. 2000)	Human (Chrubasik et al. 2000)	Reduces the pain intensity (Chrubasik et al. 2000)
3. *Zingiber officinale*	Curcumin, salicylate (Altman and Marcussen 2001)	inhibition of cyclooxygenase and lipooxygenase pathways (Lem and Lee 2017)	Ginger compress (Lem and Lee 2017)	255 mg	Human (Lem and Lee 2017)	Reduced symptoms of backpain
4. *Curcuma longa*	Curcumin (Abdel-Lateef et al. 2016; Altman & Marcussen 2001)	Inhibits COX and LOX synthesis, NF-KB, TNF-alpha etc. pro-inflammatory cytokines (Ramadan et al. 2010)	200 mg/kg body weight turmeric powder in 1.0 ml distilled water (Ramadan et al. 2010)	200 mg/kg (Ramadan et al. 2010)	Rat model (Ramadan et al. 2010)	Suppressed severity of arthritis (Ramadan et al. 2010)

management. Various plants and their active ingredients have gained attention in the management of low back pain due to their perceived efficacy, minimal side effects, and accessibility (Table 3, Fig. 2, online Appendix Fig. 3).

1. *Aloe barbadensis*, commonly known as Aloe vera, has been employed for its medicinal properties in the treatment of conditions like arthritis, radiation burns, diabetes, and ulcers (Eshghi et al. 2010; Guha et al. 2014; Hashemi et al. 2015). Aloe vera possesses anti-bacterial, anti-diabetic, and anti-inflammatory activities (Attah et al. 2016). This plant is rich in various vitamins, enzymes, and naturally active ingredients, including glycosides, acemannan, anthraquinones, saponins, and oleic acid (Salehi et al. 2018). Notably, the enzymes in aloe vera contribute to pain and inflammation reduction, while salicylic acid, a key compound, exhibits pain-relieving properties akin to aspirin (Ahlawat and Khatkar n.d.; Gupta and Malhotra 2012; Hajhashemi et al. 2012).
2. *Salix alba*, or willow, has a historical reputation for pain relief. The bark extract of this plant contains salicin, which inhibits COX-2 activity and reduces the synthesis of pro-inflammatory mediators (Bonaterra et al. 2010; Drummond et al. 2013; Khayyal et al. 2005; Nahrstedt et al. 2007; Shara and Stohs 2015). Clinical evidence from a randomized, double-blind study suggests

that salicin, isolated from willow bark extract, can effectively alleviate low back pain (Chrubasik et al. 2000).

3. *Zingiber officinale*, commonly known as ginger, is a rich source of bioactive compounds like beta-carotene, curcumin, capsaicin, gingerols, caffeic acid, and salicylate (Altman and Marcussen 2001). Traditionally, ginger has found use in the treatment of various ailments, including rheumatism, gastrointestinal issues, and pain (Lantz et al. 2007). Research has shown that daily consumption of zingiber officinale can reduce pain and muscle injury induced by exercise (Black et al. 2010). Furthermore, a randomized controlled trial demonstrated the efficacy of ginger essential oil in reducing the intensity of low back pain when used in Swedish massage (Sritoomma et al. 2014).
4. *Curcuma longa*, commonly known as turmeric, has a long history of use as a spice, coloring agent, and flavoring agent. Its anti-inflammatory properties have made it a traditional remedy for conditions like arthritis (Al-Reza et al. 2010) curcumin, a key ingredient in curcuma longa, inhibits the synthesis of enzymes like LOX and COX, as well as various inflammatory cytokines and joint-destructive enzymes (Ramadan et al. 2010). Additionally, curcumin exhibits antioxidant properties by reducing plasma malondialdehyde levels and enhancing the activity of catalase and superoxide dismutase (Yuliani et al. 2018). Clinical studies have shown that daily intake of curcumin, in combination with other natural substances, can effectively reduce chronic low back pain without adverse effects (Qu et al. 2017).

Neuropathic pain

Neuropathic pain is a chronic condition characterized by sensory abnormalities, including hyperalgesia, dysesthesia, and allodynia (Amin et al. 2015). It affects a significant portion of the population, with a prevalence of 13–17%, particularly among women aged 50–64 and individuals in rural areas (Van Hecke et al. 2014). Factors contributing to neuropathic pain range from metabolic disorders like peripheral diabetic neuropathy to viral infections and inflammatory disorders (Colloca et al. 2017).

The etiology of neuropathic pain involves nociceptor sensitization, with alterations leading to neuroplasticity and central sensitization (Julius and Basbaum 2001). Receptors such as N-methyl-D-aspartate (NMDA) and glutamic metabotropic receptors play crucial roles in intracellular changes (Attal 2012). Various signaling pathways, including cAMP, protein kinases, and nitric oxide, are implicated in functional and structural alterations (Hucho and Levine 2007). Lipid metabolites like lysophosphatidic acid (LPA) released after tissue injury contribute to neuropathic pain through G-protein coupled LPA receptors (Ueda 2008). Inflammatory mediators such as interleukin, TNF-alpha, and nerve growth factor (NGF) further intensify hyperalgesia and allodynia (Sommer and Kress 2004). Treatment options for neuropathic pain encompass a range of drugs, including antidepressants, NSAIDs, opioids, serotonin and non-adrenaline reuptake inhibitors (SNRIs), anti-COX2 inhibitors, and gabapentin (Finnerup et al. 2015). Tricyclic antidepressants (TCAs) like amitriptyline are particularly effective due to their ability to block NMDA receptors, interfering with central sensitization (Kremer et al. 2016).

However, long-term use of certain medications can lead to adverse effects, such as weight gain, dizziness, and somnolence with TCAs and SNRIs, local irritation and pain with lidocaine and capsaicin, and cardiovascular and gastrointestinal issues with NSAIDs (Carter et al. 2014; Finnerup et al. 2010). Opioids may cause constipation, addictive behavior, and tolerance (Garland 2014).

Alternative approaches involve the use of medicinal plants and secondary metabolites with antioxidant and anti-inflammatory properties. These substances modulate protein kinases and CNS neurotransmitter systems, contributing to neuropathic pain management (Alonso-Castro et al. 2017; Juárez-Vázquez et al. 2013). Various medicinal plants and their active phytoconstituents have shown promise in alleviating neuropathic pain (Moreno-Salazar et al. 2008; Robles-Zepeda et al. 2011; Sanadgol et al. 2017).

In summary, neuropathic pain is a complex condition with diverse etiological factors and treatment options. While conventional medications can be effective, their long-term use may lead to adverse effects. Exploring alternative therapies, including medicinal plants and their active compounds, presents a promising avenue for pain management.

Table 4 Plant based interventions for Neuropathic pain

Plant (scientific name)	Bioactive compounds	Mechanism of action	Extract	Dose	Experimental model	results
1. *Acorus calamus*	Beta asarone, eugenol (Balakumbahan et al. 2010; Raja et al. 2009)	Improvement of neuron organelles and synaptic structure (Li et al. 2017a, b)	Saponin rich extract (Muthuraman and Singh 2012)	(200 and 40)mg/kg (Muthuraman and Singh 2012)	Rat (Muthuraman and Singh 2012)	Improves CCI induced sciatic functional changes, electrophysiological changes and nociceptive threshold levels (Muthuraman and Singh 2012)
2. *Alstonia scholaris*	Kaempferol (Khyade and Vaikos 2011)	Inhibits ROS and inflammatory cytokines production (H. Singh et al. 2017)	Methanolic extract (Singh et al. 2017)	10 mg/kg (Singh et al. 2017)	Rat (Singh et al. 2017)	Reduces the painful condition of heat and mechanical hyperalgesia and cold allodynia (Singh et al. 2017)
3. *Butea monosperma*	Butrin, isobutrin, coreopsin (Kasture et al. 2002; Surin and Ananthaswamy 2011)	Exhibits anti-oxidant, neuroprotective action and modulates and cellular calcium (Thiagarajan et al. 2012a)	Ethanolic extract (Thiagarajan et al. 2012a)	(200, 300 and 400) mg/kg (Thiagarajan et al. 2012a)	Rat (Thiagarajan et al. 2012a)	Decreases CCI induced histopathologica, biochemical and behavioral changes (Thiagarajan et al. 2012a)
4. *Curcuma longa*	Curcumin (X. Zhao et al. 2012)	Decreases serum COX2 concentrations (Zanjani et al. 2014)	Curcumin suspended in ethyloleate (Zanjani et al. 2014)	(50 mg/kg (Zanjani et al. 2014)	Rat (Zanjani et al. 2014)	decreased mechanical and cold allodynia (Zanjani et al. 2014)
5. *Salvia divinorum*	Salvinorin A (McCurdy et al. 2006)	Activates kappa-opioid receptors (McCurdy et al. 2006)	Acetonic extract (Simón-Arceo et al. 2017)	(30, 100 and 200) mg/kg (Simón-Arceo et al. 2017)	Rat (Simón-Arceo et al. 2017)	Activates kappa-opioid receptors (Simón-Arceo et al. 2017)
6. *Crocus sativus*	Crocin (Alavizadeh and Hosseinzadeh 2014)	Decreases Glutamate, Aspertate in extra cellular space	Ethanolic and aqueous extract (Amin and Hosseinzadeh 2015)	200 mg/kg (Amin and Hosseinzadeh 2015)	Rat (Amin and Hosseinzadeh 2015)	Attenuates CCI induced hyperalgesia and allodynia (Amin and Hosseinzadeh 2015)
7. *Nigella sativa*	Thymoquinone (Forouzanfar et al. 2014; Kanter 2007)	Improves behavioral signs and oxidative effect of neuropathic pain (Amin et al. 2014)	Ethanolic extract (Tewari et al. 2015)	(500 and 1000) mg/kg (Tewari et al. 2015)	Rat (Tewari et al. 2015)	Exhibit analgesic effect on cisplatin induced neuropathic pain (Tewari et al. 2015)
8. *Ocimum sanctum*	Saponin (Kaur et al. 2015)	Attenuates the amount of nerve injury inciting agent induced calcium and free radicals (KAUR et al. 2015)	Methanolic leave etract (Muthuraman et al. 2008)	(100 and 200) mg/kg (Muthuraman et al. 2008)	Rat (Muthuraman et al. 2008)	Reduces thermal and mechanical hypernociception and allodynia (Muthuraman et al. 2008)
9. *Momordica charantia*	Gallic acid (Grover and Yadav 2004)	Reduces total calcium, GSH and superoxide ion (Kaur and Muthuraman 2019)	Fruit extract (Jain et al. 2015)	(400 and 800) mg/kg (Jain et al. 2015)	Rat (Jain et al. 2015)	Improves vincristine induced neuropathic pain (Jain et al. 2015)
10. *Rosmarinus officinalis*	Ursolic acid, caffeic acid, rosmarinic acid, carnosic acid (Yu et al. 2013)	Reduced activation markers (Iba1, GFAP), inflammatory factors - (TNF-α, iNOS, toll-like receptor 4), apoptosis-related mediators (Bax, cleaved caspase-3, and 9) (Ghasemzadeh et al. 2016)	Alcoholic extract (Ghasemzadeh et al. 2016)	(100, 200 and 400) mg/kg (Ghasemzadeh et al. 2016)	Rat (Ghasemzadeh et al. 2016)	Reduces hyperalgesia,, mechanical and cold allodynia (Ghasemzadeh et al. 2016)
10 *Rubia cordifolia*	Napthaquinone, anthraquinone (Devi Priya and Siril 2014)	GABA or Antioxidant inhibition	Alcoholic root and rhizome extract (Diwane et al. 2015)	(100, 200 and 400) mg/kg (Diwane et al. 2015)	Rat (Diwane et al. 2015)	Decreases the withdrawal latency in cold allodynia (Diwane et al. 2015)

Table 4 continued

Plant (scientific name)	Bioactive compounds	Mechanism of action	Extract	Dose	Experimental model	results
11. *Salvia officinalis*	Carnosol and ursolic acid (Rodrigues et al. 2012)	Shows modulatory effects on TRPA-1 receptors (Rodrigues et al. 2012)	Butanol and aqueous extract (Qnais et al. 2010)	(10, 31.6, 100, 316, 1000) mg/kg (Qnais et al. 2010)	Rat (Qnais et al. 2010)	Increases the latency on hot plate assay (Qnais et al. 2010)
12. *Choisya ternata*	Isopropyl, propyl-N-methyl anthranilates (Pinheiro et al. 2014)	Activates adrenergic and nitergic pathways, K^+ ATP channels and serotonergic pathways (Pinheiro et al. 2014)	Essential oil extracts (Pinheiro et al. 2015)	(3,10 and 30) mg/kg (Pinheiro et al. 2015)	Mice (Pinheiro et al. 2015)	Reduces NO, IL-1 beta and TNF alpha production (Pinheiro et al. 2015)
13. *Heterotheca inuloides*	7-hydroxy-3,4 dihydrocadalin (Rodríguez-Chávez et al. 2015)	Activates $5HT_{1A}$, $5HT_{1D}$ receptors (Rocha-González et al. 2010)	Hexane extract (Rocha-González et al. 2010)	1–1000 μg/paw	Rat (Rocha-González et al. 2010)	Inhibited inflammation and arthritis (Rocha-González et al. 2010)
14. *Artemisia dracunculus*	Eugenol (Obolskiy et al. 2011)	Improvement of neuron organelles and synaptic structure (Li et al. 2017a, b)	Ethanolic extract (Obrosova et al. 2010)	500 mg/kg/day (Obrosova et al. 2010)	Rat (Obrosova et al. 2010)	Upregulates 12/15 LOX and expression of nitrated protein in peripheral nervous system (Obrosova et al. 2010)
15. *Pterodon pubescens*	Geranyl geraniol (Hoscheid and Cardoso 2015)	Acts on $5HT_3$ receptors (Spindola et al. 2011)	Ethanolic fruit extract (Nucci-Martins et al. 2015)	(30–300) mg/kg (Nucci-Martins et al. 2015)	Mice (Nucci-Martins et al. 2015)	Prevents PSNL induced thermal and mechanical hyperalgesia (Nucci-Martins et al. 2015)
16. *Cannabis sativa*	Cannabidiol (Russo and Guy 2006)	Reduces NO, PGE2, GSH related enzymes and lipid peroxides (Costa et al. 2007)	*Cannabis sativa* extract (Comelli et al. 2008)	cannabis extract d 64.5% CBD (Comelli et al. 2008)	Rat (Comelli et al. 2008)	Attenuates vanilloid and TRPV1 induced thermal hyperalgesia (Comelli et al. 2008)
17. *Swietenia humilis*	Mexicanolide compound (Ovalle-Magallanes et al. 2017)	Activates GABAergic, NO, opiodergic and serotonergic pathways, guanylyl cyclase, K_{ATP} channels and inhibits hyperalgesia (Ovalle-Magallanes et al. 2017)	Aqueous extract (Ovalle-Magallanes et al. 2017)	(10, 31.6, 56.2, 100 and 177) microgram/paw (Ovalle-Magallanes et al. 2017)	Mice (Ovalle-Magallanes et al. 2017)	Activates GABAergic, NO, opiodergic and serotonergic pathways, guanylyl cyclase, K_{ATP} channels and inhibits hyperalgesia (Ovalle-Magallanes et al. 2017)

Various medicinal plants and their active phytoconstituents have shown promise in alleviating pain and addressing related symptoms. These natural remedies offer potential alternatives to conventional medications, which often come with adverse effects (Table 4, Fig. 2, online Appendix Fig. 4).

1. *Acorus calamus*, a member of the Araceae family, has been traditionally used in Indian medicine to manage severe inflammatory disorders. It contains phytoconstituents like beta asarone and eugenol, which have demonstrated benefits in reducing neuropathic pain and associated oxidative stress (Balakumbahan et al. 2010; Mittal et al. 2009). Additionally, hydroalcoholic extracts of Acorus calamus have been found to mitigate thermal hyperalgesia and allodynia in neuropathic pain models (Muthuraman et al. 2010).
2. *Alstonia scholaris*, known as the 'Indian devil tree,' has shown anti-nociceptive and anti-inflammatory properties due to its bioactive constituents, including coumarin, alkaloids, and flavonoids (Khyade and Vaikos 2011). Methanolic extracts of this plant have demonstrated effectiveness in reducing neuropathic pain symptoms and oxidative stress (Singh et al. 2017).
3. *Butea monosperma*, also known as the 'Flame of the forest,' Butea monosperma has exhibited neuroprotective effects, particularly in vincristine-induced neuropathic pain. Its bioactive compounds, such as butrin and isobutrin, contribute to the reduction of hyperalgesia and allodynia, possibly through their antioxidant properties (Thiagarajan et al. 2012b).

4. *Curcuma longa* with its active phenolic ingredient Curcumin, has been effective in alleviating neuropathic pain, including allodynia and hyperalgesia, while reducing COX-2 levels (Zanjani et al. 2014). This plant has shown potential as a natural remedy for neuropathic pain management.
5. *Salvia divinorum,* a native Mexican plant, has demonstrated efficacy in relieving neuropathic pain. Salvinorin A, one of its phytoconstituents, activates kappa-opioid receptors, providing analgesic effects in various animal models (McCurdy et al. 2006). Ethyl acetate extracts from Salvia divinorum have also shown antinociceptive properties through the activation of opioid and 5-HT1A receptors (Tlacomulco-Flores et al. 2020).
6. *Crocus sativus,* Crocus sativus, commonly known as saffron, contains bioactive constituents like crocin and safranal, which have demonstrated potential in reducing neuropathic pain behavioral symptoms (Amin and Hosseinzadeh 2012). These extracts have also exhibited anti-inflammatory effects by reducing pro-inflammatory cytokines (Safakhah et al. 2016).
7. *Nigella sativa,* known for its volatile oil containing thymoquinone, has shown promise in improving neuropathic pain symptoms and oxidative effects (Amin et al. 2014). Ethanolic extracts of Nigella sativa have also demonstrated analgesic effects in cisplatin-induced neuropathic pain (Tavakkoli et al. 2017).
8. *Ocimum sanctum,* widely distributed in India, has been found to reduce neuropathic pain by decreasing calcium levels and oxidative stress induced by nerve injury (Kaur et al. 2015). Saponin, isolated from Ocimum sanctum, also plays a role in reducing painful neuropathic conditions (Kaur et al. 2015).
9. *Momordica charantia,* known as bitter melon, has shown neuroprotective actions, reducing hyperalgesia and allodynia, possibly through its anti-inflammatory and antioxidative activity (Jain et al. 2014).
10. *Rosmarinus officinalis* also known commonly as Rosemary, rich in phytoconstituents like rosmarinic acid, has demonstrated anti-inflammatory effects by reducing COX-2 and pro-inflammatory cytokines in neuropathic pain models (Ghasemzadeh Rahbardar et al. 2017).
11. *Rubia cordifolia,* an ayurvedic herb, exhibits anti-inflammatory and analgesic activities, possibly through GABAergic or antioxidant mechanisms (Diwane et al. 2015).
12. *Salvia officinalis,* garden sage, containing carnosol and ursolic acid, has strong antinociceptive effects and may modulate TRPA-1 receptors (Rodrigues et al. 2012).
13. *Choisya ternata,* has antinociceptive effects due to its active constituents, such as isopropyl, methyl, and propyl-N-methyl anthranilate, which activate various pathways (Pinheiro et al. 2014).
14. *Heterotheca inuloides*, also known as 'Arnica Mexicana,' has shown anti-neuropathic action by activating opioid and serotonergic receptors, as well as guanylyl cyclase (Rocha-González et al. 2014).
15. *Artemisia dracunculus,* exhibits anti-nociceptive and anti-inflammatory activity, possibly through eugenol and other phytoconstituents (Abad et al. 2011).
16. Pterodon pubescens, prevents thermal and mechanical hyperalgesia by acting on 5HT3 receptors (Spindola et al. 2011).
17. *Cannabis sativa,* commonly known as marijuana, contains cannabidiol, which alleviates neuropathic pain and reduces oxidative stress (Costa et al. 2007; Serpell et al. 2014).
18. *Swietenia humilis,* grown in Mexico, inhibits hyperalgesia by activating GABAergic, NO, opioidergic, and serotonergic pathways, as well as guanylyl cyclase and KATP channels (Ovalle-Magallanes et al. 2017).

Dysmenorrohea

Dysmenorrhea is a common menstrual disorder that affects approximately 50% of women of reproductive age (Bernardi et al. 2017). The pain experienced during dysmenorrhea can range from mild to severe and is often accompanied by symptoms such as diarrhea, nausea, vomiting, and constipation (Edmonds 2012). Dysmenorrhea can significantly impact a woman's quality of life and social activities (Mrugacz et al. 2013).

In the treatment of dysmenorrhea, inhibitors of prostaglandin synthesis and NSAIDs like aspirin, ibuprofen, and mefenamic acid are commonly used due to their ability to inhibit thromboxane and prostaglandins (García-Martínez et al. 2015). However, it's important to note that these drugs can have adverse effects, including hepatotoxicity and bone loss (Williams et al. 2013) and gastrointestinal and liver issues (Moll et al. 2011).

In addition to conventional medications, many medicinal plants have been explored as alternative treatment strategies for dysmenorrhea due to their anti-spasmodic, analgesic, and prostaglandin inhibitory effects. These natural remedies offer potential options for managing this common and often debilitating condition. Further research and critical appraisal of the literature are essential to assess the effectiveness and safety of these alternative treatments in the management of dysmenorrhea.

Various medicinal plants have been explored for their potential in alleviating dysmenorrhea, a common and often debilitating condition in women. These plants offer promising anti-spasmodic, analgesic, and prostaglandin inhibitory effects. Here, we summarize the key findings from the literature on selected plants, their active compounds, mechanisms of action, and recommended doses (Table 5, Fig. 2, online Appendix Fig. 5).

1. *Zingiber officinalis* (Ginger), containing compounds like gingerol and gingerdiol, has been shown to inhibit the synthesis of prostaglandins and inflammatory cytokines. It effectively relieves pain, including primary dysmenorrhea. A dose of 1500 mg/day of Zingiber officinalis root powder has been found to effectively alleviate severe pain associated with primary dysmenorrhea (Rahnama et al. 2012). Additionally, a mixture of 750 mg/day Zingiber officinalis powder and zinc sulfate showed significant pain relief compared to a placebo (Kashefi et al. 2014).
2. *Foeniculum vulgare* (Fennel, with active compounds like estragole and trans-anethole, reduces uterine contractions by inhibiting prostaglandins. A 2% fennel oil drop has shown effectiveness in reducing primary dysmenorrhea pain when compared to mefenamic acid (Bokaie et al. 2013). Combining Foeniculum vulgare with vitex has been found to be more effective in reducing dysmenorrhea symptoms than mefenamic acid (Zeraati et al. 2014).
3. *Cinnamomum zeylanicum* (Cinnamon), contains eugenol, which inhibits prostaglandin synthesis and inflammation. It has been shown to reduce dysmenorrhea pain as effectively as ibuprofen when taken at a dose of 1260 mg/day (Jaafarpour, Hatefi, Khani, et al., 2015). Cinnamon also reduces nausea, menstrual bleeding, and vomiting in primary dysmenorrhea without adverse effects (Jaafarpour et al. 2015a, b).
4. *Trigonella foenum-graecum* (Fenugreek), contains gamma-linolenic acid, which inhibits prostaglandin synthesis and cyclooxygenase pathway, reducing pain. A dose of 6 g/day of Trigonella foenum-graecum has been found to be as effective as mefenamic acid in reducing the severity of dysmenorrhea (Inanmdar et al. 2016). Capsules prepared from fenugreek seed powder at a dose of 2700 mg/day have also shown efficacy in relieving dysmenorrhea symptoms (Younesy et al. 2014).
5. *Mentha piperita* (Peppermint), contains menthol, which inhibits prostaglandin synthesis and myometrium contractions. Peppermint oil has been shown to be safer and more effective than mefenamic acid in relieving dysmenorrhea pain (Masoumi et al. 2016). A dose of 990 mg/day of Mentha piperita capsules has been effective in reducing the pain of primary dysmenorrhea (Heshmati et al. 2016).
6. *Teucrium polium,* has anti-inflammatory and antispasmodic properties. The aqueous extract of Teucrium polium at a dose of 1000 mg/day during menstruation reduced the pain and severity of primary dysmenorrhea as effectively as mefenamic acid (Abadian et al. 2016).
7. *Triticum aestivum* (Wheat Germ), contains vitamins that attenuate pain in primary dysmenorrhea patients. An extract dose of 1200 mg/day taken during the menstrual cycle's specified days has been shown to alleviate the symptoms of primary dysmenorrhea (Ataollahi et al. 2014).
8. *Rosa damascene* (Rose), with its high vitamin C and flavonoid content, has analgesic and anti-inflammatory effects. A dose of 600–800 mg/day of Rosa damascene has been found to be as effective as mefenamic acid in reducing

Table 5 Plant based interventions for Dysmenorrhoea

Plant (Scientific name)	Bioactive compounds	Mechanism of actions	Extract	Dose	Experimental model	Results
1. *Zingiber officinalis*	Gingerdiol, gingerol, caffeic acid (Semwal et al. 2015), curcumin (Daily et al. 2015)	Inhibit prostaglandin, inflammatory cytokines, leukotriene synthesis and thromboxane activity (Chen et al. 2016; Mirabi et al. 2014)	Powder of *Zingiber* root (Rahnama et al. 2012)	1500 mg/kg (Rahnama et al. 2012)	Human (Rahnama et al. 2012)	Relieves severe pain of primary dysmenorrhoea (Rahnama et al. 2012)
2. *Foeniculum vulgare*	Essential oil (Badgujar et al. 2014; Mirabi et al. 2014; Rather et al. 2016)	Inhibit prostaglandin and circulatory oxytocin levels and reduces uterine contraction (Badgujar et al. 2014; Mirabi et al. 2014; Rather et al. 2016)	Capsules of *Foeniculum* (Moslemi et al. 2012)	184 mg/day (Moslemi et al. 2012)	Human (Moslemi et al. 2012)	Reduces pain intensity of primary dysmenorrhea (Moslemi et al. 2012)
3. *Cinnamomum zeylanicum*	Eugenol (Mirabi et al. 2014; Nabavi et al. 2015)	Inhibits prostaglandin synthesis and inflammation (De Smet et al. 1993)	capsule containing 420 mg Cinnamon (Jaafarpour et al. 2015)	1260 mg/day (Jaafarpour et al. 2015)	Human (Jaafarpour et al. 2015)	Reduced severity score and duration of pain (Jaafarpour et al. 2015)
4. *Trigonella foenum-graecum*	Gamma linolenic acid (Inanmdar et al. 2016)	Inhibits prostaglandin synthesis and cyclooxygenase pathways (Inanmdar et al. 2016)	Capsules of seed powder (Younesy et al. 2014)	2700 mg/day (Younesy et al. 2014)	Human (Younesy et al. 2014)	Relieves the severity and symptoms of primary dysmenorrhoea (Younesy et al. 2014)
5. *Mentha piperita*	Menthol, menthyl acetate, cineole, menthofurane (Heshmati et al. 2016; Kamatou et al. 2013)	Inhibits prostaglandin, leukotriene and interleukine synthesis (Heshmati et al. 2016; Kamatou et al. 2013)	Peppermint capsule (Heshmati et al. 2016)	990 mg/day (Heshmati et al. 2016)	Human (Heshmati et al. 2016)	Alleviates the severity of dysmenorrhea (Heshmati et al. 2016)
6. *Teucrium polium*	Alpha-pinene, ocemene, pulegone (Abadian et al. 2016)	inhibiting acetylcholine-induced muscle contraction (Bahramikia & Yazdanparast 2012)	*Teucrium polium* capsule (Abadian et al. 2016)	1000 mg/day (Abadian et al. 2016)	Human (Abadian et al. 2016)	Decreases the pain of primary dysmenorrhea (Abadian et al. 2016)
7. *Triticum aestivum*	Alpha tocopherol (Güven & KARA, 2016)	uses pro -inflammatory activities to activate neuropeptides, cytokines, and macrophages and reduces inflammation (Ataollahi et al. 2014)	Capsules of germ extract (Ataollahi et al. 2014)	1200 mg/day (Ataollahi et al. 2014)	Human (Ataollahi et al. 2014)	Alleviates the symptoms of primary dysmenorrhoea (Ataollahi et al. 2014)
8. *Rosa damascene*	Geraniol, citranellol, kaempferol (Bani et al. 2014)	Regulating acetylcholine release or Stimulating GABAergic and putative neurons	*Rosa damascene* capsule (Bani et al. 2014)	800 mg/day (Bani et al. 2014)	Human (Bani et al. 2014)	Reduces the intensity of primary dysmenorrhea (Bani et al. 2014)
9. *Melissa officinalis*	Citral, alpha-pinene, rosmarinic acid (Miraj et al. 2016)	Through cholinergic system and L-Arginine-nitric pathway	*Melissa officinalis* capsule (Mirabi et al. 2018)	990 mg/day (Mirabi et al. 2018)	Human (Mirabi et al. 2018)	Decreases the severity of dysmenorrhea (Mirabi et al. 2018)
10. *Thymus vulgaris*	Thymol, eugenol (Assiri et al. 2016)	Inhibits prostaglandin synthesis and inflammation (De Smet et al. 1993)	Essential oil (Salmalian et al. 2014)	25 drops (Salmalian et al. 2014)	Human (Salmalian et al. 2014)	Reduces pain severity (Salmalian et al. 2014)
11. *Valeriana officinalis*	Valtrate (Bone & Mills 2013)	Inhibits calcium ion binding to smooth muscle (Mirabi et al. 2011, 2014)	Powder of valerian root (Mirabi et al. 2011)	765 mg/day (Mirabi et al. 2011)	Human (Mirabi et al. 2011)	Decreases primary dysmenorrhea intensity (Mirabi et al. 2011)

Table 5 continued

Plant (Scientific name)	Bioactive compounds	Mechanism of actions	Extract	Dose	Experimental model	Results
12. *Rheum emodi*	Emodin, oxanthrone (Rehman et al. 2015; Takeoka et al. 2013)	Arachiodonic acid release and COX2 enzyme expression	Capsules of *Rheum emodi* powder (Rehman et al. 2015)	840 mg/day (Rehman et al. 2015)	Human (Rehman et al. 2015)	Capable of reducing pain of dysmenorrhea (Rehman et al. 2015)
13. *Achillea millefolium*	Cosmossin 1, cyanaroside 1 (Saeidnia et al. 2011)	Flavonoids (spasmolytic agent) relaxes smooth muscle of mammals	*A.millefolium* powder (Jenabi and Fereidoony 2015)	4 g powder/ 300 ml water (Jenabi and Fereidoony 2015) 3 days/month	Human (Jenabi and Fereidoony 2015)	Minimises pain in primary dysmenorrhoea
14. *Anethum graveolens*	Sabinene and limonene (Jana and Shekhawat 2010; Kazemi 2015b)	Inhibits NO synthesis (Kazemi 2015a)	Capsules of seed powder (Heidarifar et al. 2014)	2000 mg/day (Heidarifar et al. 2014)	Human (Heidarifar et al. 2014)	Reduces pain intensity of primary dysmenorrhea (Heidarifar et al. 2014)
15. *Matricaria chamomilla*	Azoline, matrisin, bisabolol, apigenin, methoxy-coumarin (Gosztola et al. 2010; Orav et al. 2010; Srivastava et al. 2010)	Reduces prostaglandins (Radfar et al. 2018)	*Matricaria* capsule (Radfar et al. 2018)	750 mg/day (Radfar et al. 2018)	Human (Radfar et al. 2018)	Reduces pain intensity of dysmenorrhea (Radfar et al. 2018)

pain sensitivity during primary dysmenorrhea (Bani et al. 2014).

9. *Melissa officinalis* (Lemon Balm), possesses antispasmodic, anti-inflammatory, and analgesic effects. Capsules containing 990 mg/day of Melissa officinalis have been shown to decrease the severity of dysmenorrhea (Mirabi et al. 2018). The use of Melissa officinalis tea bags every 8 h after menstruation has been effective in alleviating dysmenorrheal symptoms (Safdari Dehcheshmeh and Parvin 2016).
10. *Thymus vulgaris* (Thyme), contains thymol and other compounds with antispasmodic and anti-inflammatory properties. Essential oil from Thymus vulgaris, taken at a specified dose, significantly improved primary dysmenorrhea pain compared to ibuprofen (Salmalian et al. 2014).
11. *Valeriana officinalis* (Valerian), has sedative and antispasmodic effects. A dose of 765 mg/day of valerian root has been shown to be more effective in treating primary dysmenorrhea than a placebo (Mirabi et al. 2011).
12. *Rheum emodi,* has analgesic and anti-inflammatory effects. Capsules prepared from the plant powder, taken at a dose of 840 mg/day during specified days of the menstrual cycle, have been found to be as effective as mefenamic acid in reducing dysmenorrhea pain (Rehman et al. 2015).
13. *Achillea millefolium* (Yarrow), has antispasmodic and anti-prostaglandin effects. Tea made from Achillea millefolium has been effective in improving primary dysmenorrhea symptoms (Jenabi and Fereidoony 2015).
14. *Anethum graveolens* (Dill), has been shown to relieve the pain and severity of primary dysmenorrhea as effectively as mefenamic acid when taken at a dose of 2000 mg/day (Heidarifar et al. 2014).
15. *Matricaria chamomilla* (Chamomile), contains active compounds like bisabolol and apigenin, which have anti-inflammatory and antispasmodic effects. A dose of 250 mg of Matricaria chamomilla taken three times daily has been shown to reduce primary dysmenorrhea pain (Radfar et al. 2018).

Headache

Headache is a prevalent neurological problem that affects a substantial portion of the global population, making it one of the most common reasons for

Table 6 Plant based interventions for Headache

Plant (Scientific name)	Active compounds	Mechanism of actions	Extract	Dose	Experimental model	Result
1. *Sambucus nigra*	Citric acid,malic acid, shikimic acid (Dulf et al. 2013; Ma and Wu 2012), isoquercetin, P-coumaric acid, ferulic acid (Bhattacharya et al. 2013b)	Activation to hypothalamic-pituitary-axis. Releases adrenocortical hormone	Hydroalcoholic leave extract (Neekhra et al. 2021)	(200 and 400) mg/kg (Neekhra et al. 2021)	Male Wistar rats (Neekhra et al. 2021)	Reduces chronic stress induced perturbations (Neekhra et al. 2021)
2. *Allium cepa*	Quercetin (Sagar et al., 2020b)	Downregulates NF-KB levels, inhibits PGE2 and TXB2 levels derived from arachidonic acid (Moslemi et al. 2012)	Methanolic extract	(50, 250 and 500) microgram/ml	LPS-induced BV-2 microglial cells	Decreases the level of TNF-alpha, Il-6, IL-beta etc. proinflammatory cytokines
3. *Ligusticum chuanxiong*	Ligustilide (Zhao et al., 2014b; Zhu et al. 2014a, b)	Inhibits pro-inflammatory cytokines, NF-KB induced chemotaxis (L. X. Zhao et al., 2014b; Zhu et al. 2014a, b)	Ethanolic extract (Yuan et al. 2010)	32 mg/kg (Yuan et al. 2010)	Rat (Yuan et al. 2010)	Reduces headache by adjusting monoamine neurotransmitter (Yuan et al. 2010)
4. *Rosmarinus officinalis*	Rosmarinic acid, carnosol, betulinic acid, ursolic acid (Borrás-Linares et al., 2014b)	Inhibits uptake of monoamines and monoamine oxidase activity (Waggas and Balawi 2008)	Leaf extract (Waggas and Balawi 2008)	100 mg/kg (Waggas and Balawi 2008)	Rat (Waggas and Balawi 2008)	Show neuroprotective effects by decreasing dopamine, epinephrine, norepinephrine and catecholamine content (Waggas and Balawi 2008)

seeking medical treatment (Stovner et al. 2007). According to the third edition of the International Headache Society, headache is classified into primary and secondary. Cephalalgias, cluster headache, tension-type headaches (TTH), external pressure headache where cold stimulus headache, etc., are primary headaches and headaches caused by underlying diseases including vascular disorders or tumors, head injuries, and infections are secondary headaches (Headache Classification Committee of the International Headache Society 2013). Primary headaches, including TTH and migraine, are the most frequent in childhood (Genizi et al. 2013). Nonsteroidal anti-inflammatory drugs (NSAIDs) (Krishnasamy et al. 2020), including aspirin and ibuprofen (Hasnaoui et al. 2003), triptans (Kassem & Labib 2016), and ergot alkaloids (Krishnasamy et al. 2020), are used in the treatment of headaches, but none of these can fully recover the recurrent attacks (Table 6, Fig. 2, online Appendix Fig. 6).

1. *Sambucus nigra*: Elderberry, known as Sambucus nigra, is rich in vitamins, essential oils, and various minerals. It possesses antioxidant and anti-inflammatory properties. Elderberry tea is traditionally used for pain relief, and studies have shown that its methanolic fruit extract can reduce headache severity (Ulbricht et al. 2014). The plant possesses anti-oxidant (Jimenez et al. 2014a; Topoľská et al. 2015) and anti-inflammatory (Ulbricht et al. 2014) properties. The plant shows antidiabetic potential by promoting insulin secretion and glucose uptake (Bhattacharya et al. 2013a). The plant is effective in headache treatment.. The plant inhibits the synthesis of COX- and 10 µg/ml of its methanolic fruit extract reduces the severity of headache compared to an indomethacin control group (Thole et al. 2007).
2. *Allium cepa*: *Allium cepa*, commonly known as onion, is a plant of the Liliaceae family cultivated worldwide, particularly in countries with moderate climates (Bisen and Emerald 2016). *Allium cepa* possesses anti-tumor, antiarthritic, antimicrobial, anti-hyperlipidaemic, and anticarcinogenic properties (Upadhyay 2017). Active phytoingredients such as vitamins, quercetin, luteonin, kaempferol, etc., are present in onion (Sagar et al. 2020a) that downregulate NF-KB

levels, inhibit PGE2 and TXB2 levels derived from arachidonic acid (Lesjak et al. 2018), as well as chalcones, isoflavones, flavanones, and anthocyanins (Liguori et al. 2017).

3. *Ligusticum chuanxiong*: *Ligusticum chuanxiong* is a plant of the Umbelliferae family used in traditional Korean, Chinese and Japanese folk medicine systems (Kemper 2011). The plant has anti-inflammatory (Or et al. 2011), antioxidant (Ramalingam and Yong-Ki 2010) (J. B. Jeong et al. 2009) and neuroprotective effects (Shu et al. 2009) (Lin et al. 2009). Ligustilide isolated from this plant inhibits the production of pro-inflammatory cytokines, Nf-kB induced chemokines and thus helps in inflammatory pain reduction (Zhao et al., 2014a; Di Zhu et al. 2014a, 2014b).
4. *Rosmarinus officinalis*: *Rosmarinus officinalis* has been used to treat numerous diseases such as rheumatic pain, dysmenorrheal, epilepsy, stomachache, depression, and mental fatigue in folk medicine (Heinrich et al. 2006). The perennial shrub has anti-inflammatory (Benincá et al. 2011), neuroprotective (Hou et al. 2013), antioxidant (Bakirel et al. 2008) and memory-enhancing effects (Sasaki et al. 2013). The active ingredients f the plant include rosmarinic acid, carnosol, carnosic acid, betulinic acid, rosmanol and ursolic acid (Borrás-Linares et al. 2014a). Carnosol, betulinic acid, and ursolic acid isolated from *Rosmarinus officinalis* aerial crude extract inhibit leukocyte, IL-1beta, TNF-alpha, etc., pro-inflammatory mediators in carrageenan-induced murine pleurisy model (Benincá et al. 2011).

Migraine

Migraine, is characterized by recurrent headaches with or without aura, often beginning in childhood and peaking between the ages of 22 and 55 years, with a higher prevalence in women (Burstein et al. 2015). These debilitating headaches are associated with pulsating pain of moderate to severe intensity, often leading to impaired daily physical activity (Olesen 2018). Common accompanying symptoms include nausea, vomiting, sensitivity to light and sound, all localized to one-half of the head (Charles and Hansen 2015). The headache itself is typically unilateral, throbbing, and can last for hours to days (Olesen 2018).

The etiology of migraine is multifactorial, involving lifestyle, environmental, and genetic factors (Durham and Papapetropoulos 2013). External triggers include alcoholic and caffeinated beverages (Millichap and Yee 2003), smoking and stress (Martin 2010). Additionally, sex hormones, particularly estradiol and progesterone, play a role in menstrual migraines (Gupta et al. 2007). Treatment options for migraines encompass a range of pharmaceuticals. Aspirin, acetaminophen, ergot derivatives (Monteith and Goadsby 2010), beta-blockers like propranolol and metoprolol, and anticonvulsants such as valproate and topiramate are commonly employed (Goadsby and Sprenger 2010).

There is growing interest in alternative treatments for migraines, with numerous medicinal plants showing promise due to their safe and effective phytoingredients (Table 7, Fig. 2, online Appendix Fig. 7).

1. *Tanacetum parthenium* (Feverfew): Feverfew, widely distributed in North America, Europe, and South America, has been traditionally used for various ailments, including nausea and allergies. It contains parthenolide, a sesquiterpene lactone, which has anti-inflammatory and anti-platelet aggregation properties. Parthenolide inhibits histamine release, reduces nitroglycerin-induced Fos expression, and targets the TRPA1 channel, all contributing to its potential to prevent migraines (Pareek et al. 2011; Rios and Passe 2004; Sun-Edelstein and Mauskop 2011).
2. *Petasites hybridus* (Butterbur): Butterbur, found in Europe and Asia, has been traditionally used for various ailments, including asthma and fever. Its active compounds, petasin and isopetasin, inhibit leukotriene synthesis and COX2-mediated prostaglandin E2 release, offering relief from migraines. Additionally, isopetasin activates the TRPA1 channel, providing antinociceptive effects (Lipton et al. 2004; Sun-Edelstein and Mauskop 2011; Taylor 2011).
3. *Hypericum perforatum* (St. John's Wort): Known for its effectiveness in treating mild to moderate depression, Hypericum perforatum also

Table 7 Plant based interventions for Migraine

Plant (scientific name)	Bioactive compounds	Mechanism of actions	Extract	Dose	Experimental model	Results
1. *Tanacetum parthenium*	Parthenolide (Rajapakse and Pringsheim 2016)	Inhibits histamine release (Pareek et al. 2011) and NO synthesis (Aviram et al. 2012)	Water extract (Recinella et al. 2020)	(10–100) microgram/ml (Recinella et al. 2020)	Mice (Recinella et al. 2020)	Reduces inflammatory pathways and inhibits hypothalamic dopamine release (Recinella et al. 2020)
2. *Petasites hybridus*	Petasin and isopetasin (Prieto 2014; Taylor 2011)	Inhibits leukotriene synthesis and release of COX2 mediated PGE2 (Taylor 2011)	Root extract (Lipton et al. 2004)	50 mg/day (Lipton et al. 2004)	Human (Lipton et al. 2004)	Reduces the number of monthly migraine attacks (Lipton et al. 2004)
3. *Hypericum perforatum*	Hypericin, hypericum (Wölfle et al. 2013)	Counteracts NO donor induced by blocking NF-KB, STAT1 and CREB etc. protein kinase C mediated pathway (Galeotti & Ghelardini 2013)	*Hypericum perforatum* dried extract (Galeotti & Ghelardini 2013)	t(5 mg/kg p. o) (Galeotti and Ghelardini 2013)	Mouse (Galeotti and Ghelardini 2013)	Counteracts pain hypersensitivity (Galeotti and Ghelardini 2013)
3. *Ginkgo biloba*	Ginkgolide B (Zhou et al. 2013)	Modulates brain glutamatergic transmission and antagonize PAF receptor (Tulsulkar and Shah 2013)	Leaf extract (Tulsulkar and Shah 2013)	100 mg/kg (Tulsulkar and Shah 2013)	Mice (Tulsulkar and Shah 2013)	Reduces hippocampal neuronal death (Tulsulkar and Shah 2013)
4. *Mentha piperita*	Menthol (Heshmati et al. 2016)	Inhibits prostaglandin, leukotriene and interleukin synthesis (Heshmati et al. 2016)	ethanol solution (Haghighi et al. 2010)	10% ethanol solution (Haghighi et al. 2010)	Human (Haghighi et al. 2010)	Alleviated symptoms of migraine without aura
5. *Zingiber officinalis*	6-Paradol (Gaire et al. 2015)	Attenuates neuroinflammation in microglia (Gaire et al. 2015)	Ginger rhizome powder (Gaire et al. 2015)	250 mg/day (Gaire et al. 2015)	Human (Gaire et al. 2015)	Reduces the common migraine attack (Gaire et al. 2015)
6. *Matricaria chamomilla*	Apigenin, bisabolol (Gosztola et al. 2010)	Inhibits iNOS expression, NO synthesis and PGE2 release (Zargaran et al. 2014)	Aqueous extract in sesame oil (Zargaran et al. 2014)		Human (Zargaran et al. 2014)	Pain relief in migraine patients (Zargaran et al. 2014)
7. *Cannabis sativa*	Cannabidiol (Izzo et al. 2009)	Inhibits cytokines, chemokines and ROS production (Zou and Kumar 2018)	Ethanol 96%	5 mg/day up to 12 days	Human (18–64) years old	Relief muscle stiffness, sensitivity, sleep quality, relief body pain and spasm

possesses analgesic properties. Its major active compounds, hypericin and hyperforin, exhibit anti-inflammatory effects and can counteract nitric oxide-induced pain hypersensitivity (Galeotti et al. 2010a, b; Kasper et al. 2010).

4. *Ginkgo biloba* leaf extracts contain terpene lactones and flavonoids, with ginkgolide B being particularly noteworthy. Ginkgolide B has antioxidant and anti-inflammatory effects, reducing neuronal damage and modulating platelet-activating factor (PAF) release. This modulation can be especially beneficial in migraine management (Ahlemeyer and Krieglstein 2003; Choi et al. 2019; D'Andrea et al. 2009; Tulsulkar & Shah 2013).
5. *Mentha piperita* (Peppermint) active compound, menthol, inhibits prostaglandin and interleukin synthesis, acting as a pain reliever. Menthol also activates TRPM8 receptors, providing relief from meningeal inflammation-induced pain (Haghighi et al. 2010; Heshmati et al. 2016; Jimenez et al. 2014b; Kamatou et al. 2013).
6. *Zingiber officinales* (Ginger) contains gingerols, diterpenoids, and flavonoids that inhibit the synthesis of prostaglandins and inflammatory cytokines. It also offers anti-inflammatory and antibacterial effects. 6-paradol, a compound found in ginger, attenuates neuroinflammation, making it a potential treatment option (Maghbooli et al. 2014; Mintah et al. 2019; Nour et al. 2017).
7. *Matricaria chamomilla* (Chamomile): Chamomile has been used traditionally for various purposes, including pain relief. It contains active compounds like bisabolol and apigenin, which inhibit iNOS expression and PGE2 release, providing anti-inflammatory effects. Chamomile gel has shown efficacy in reducing migraine symptoms (Miraj and Alesaeidi 2016; Zargaran et al. 2014, 2018).
8. *Cannabis sativa* (Cannabis), contains various phytocannabinoids like CBD and THC. CBD has anti-inflammatory properties, modulating pain perception and reducing cytokine release. It interacts with receptors like TRPV1 and 5-HT1A, providing relief from inflammatory and neuropathic pain. Additionally, CBD reduces nitroglycerin-induced neuronal activation and central sensitization (Russo et al. 2008; Stevens et al. 2016; Zou & Kumar 2018).

Chest pain

The chest is an important part of our body and is located between the ribs from which various problems of our body can occur (Goodacre et al. 2005). Chest pain is one of the most frequent symptoms for which patients contact emergency medical services (EMS) and emergency departments (ED) (Mockel et al. 2013; Burman et al. 2011). Chest pain can be caused due to cardiac causes, chest wall diseases, gastrointestinal symptoms, pulmonary causes, mental and psychological causes, and non-cardiac chest pain (das Virgens et al. 2017; Webster et al. 2014). Few medicinal plants and their mechanism of action to prevent chest pain are discussed in Table 8, Fig. 2, online Appendix Fig. 8).

1. *Salvia miltiorrhiza*: *Salvia miltiorrhiza*, commonly known as red sage, is a perennial plant of the Lamiaceae family (Yuan Fang et al. 2008). Traditionally, this plant is used in the treatment of cardiovascular diseases (Luo et al. 2015) such as thrombosis (Wu & Wang, 2012a), atherosclerosis, and angina pectoris (Yang et al. 2006). The primary active compounds of this plant include salvianolic acid and diterpenoid tanshinones that are hydrophilic and lipophilic, respectively (Guo et al. 2014; Ho & Hong 2011; Zhao et al. 2008; Fan et al. 2009a, b). Other active compounds include Tanshinone II-A and cryptotanshinone (Tian et al. 2017a). By inhibiting the STAT-3 pathway and expressing MMP-9, cryptotanshinone reduces the heartbeat at a dose of 10 mg/kg/d for 28 days in diabetic rats (Tian et al. 2017a). In this way, the plant prevents cardiovascular disease-related chest pain.
2. *Carthamus tinctorius*: Commonly known as Safflower, *Carthamus tinctorius* is a member of the Asteraceae family (Sciences and 2010, n.d.). Flavonoids such as saffloflavonesides A, saffloflavonesides B (He et al. 2014a), alkaloids including guanosine (Fan et al. 2009a, b), safloquinoside A and saffloquinoside B, and two

Table 8 Plant based interventions for Chest pain

Plant (Scientific name)	Bioactive compounds	Mechanism of actions	Extract	Dose	Experimental model	Results
1. *Salvia miltiorrhiza*	Tanshione II A and cryptotanshinone (Tian et al. 2017b)	Inhibits STAT 3 pathway and MMP-9 expression (Tian et al. 2017b)	cryptotanshinone	10 mg/kg/d cryptotanshinone	Rats	Reduces cardiac fibrosis
2. *Carthamus tinctorius*	Saffloflavonesides A and B, saffloquinoside A and B (Chen et al. 2013; He et al. 2014b)	Suppresses c-Jun N-terminal kinase and inhibits lipopolysaccharide (LPS)-induced apoptosis in cardiomyoblast cells (He et al. 2014b)	ethanolic extract (He et al. 2014b)	31.25, 62.5,and 125 µg/mL	H9c2 cardiomyoblast cells	Dilating coronary artery, Myocardial Ischemia improvement, Antithrombosis, Immune system modulating
3. *Allium sativum*	Alliin (Zeng et al. 2017b)	Inhibits plaque atherosclerosis and increases vasodialator (Ilmawati et al. 2017b)	Methanolic extract (Jeong et al. 2016b)	1000 µg/ml (Jeong et al. 2016b)	RAW 264.7 cells (Jeong et al. 2016b)	Prevents COX2 and PGE 2 production (Jeong et al. 2016b)
4. *Calendula officinalis*	Kaempferol, quercetin and isorhamnetin (Re et al., 2009b)	downregulation of pro-inflammatory cytokines like TNF-, IL-1, IL-6 (Ray et al. 2010)	*Calendula officinalis* in KHB buffer solution (Ray et al. 2010)	50 mM (Ray et al. 2010)	Rat (Ray et al. 2010)	Stimulates left ventricular pressure and aortic flow, reduces myocardial infraction size and apoptosis of cardiomyocytes (Ray et al. 2010)

quinochalcones (Jiang et al. 2010) have been isolated from this plant and have numerous biological activities. *Carthamus tinctorius* injection at a dose of 2.5 and 0.625 g/kg for 5 days inhibits the elevation of the typical ECGS-T segment, reduces serum IL-6 and TNF-alpha concentration, and suppresses the overexpression of Bax protein and Bcl-2 in rat (Han et al. 2009).

3. *Allium sativum*: *Allium sativum* or garlic is a plant of the Amaryllidaceae family. The major active phytoconstituents are allicin, E-ajoene, Z-ajoene (Sendl 1995), and alliin (Zeng et al. 2017a). By inactivating NF-kB, the methanolic extract of aged black garlic prevents the production of COX-2 and PGE-2 (Jeong et al. 2016a). Alliin inhibits plaque atherosclerosis and increases vasodilation (Ilmawati et al. 2017a).
4. *Calendula officinalis*: The major active ingredients of *calendula officnalis* are flavonoids such as kaempferol, quercetin, isorhamnetin, terpenoids, steroids, phenolic acids, carotenoids, etc. (Re et al. 2009a), which exhibit anti-inflammatory and antioxidant effects (Moghaddasi Mohammad and Kashanisup 2012). By activating protein kinase B and B-cell lymphoma 2 and decreasing TNF-alpha, *Callendula officinalis* changes the death signal from ischemic reperfusion into a survival signal and thus protects the heart (Lecour et al. 2005).

Wounds

Wounds, a significant cause of disability are defined as physical injuries that disrupt the skin's normal functions or anatomy (Strodtbeck 2001). They often entail pain, infection risks, disfigurement, and unpleasant odors. Wounds are categorized as open or closed based on whether the skin remains intact (Lazarus et al. 1994; Percival 2002). Furthermore, wounds are classified into acute and chronic types depending on the wound healing process (Percival 2002). Acute wounds, like surgical incisions, typically heal through regular compensatory mechanisms (Percival 2002). In contrast, chronic wounds lead to pathologic inflammation and may require extended healing periods (Menke et al. 2007). Common causes of chronic wounds include diabetes mellitus, obesity, ischemia, and venous stasis (Handbook on Hyperbaric Medicine 2006; Menke et al. 2007).

Delayed wound healing is associated with factors such as older age, elevated levels of reactive oxygen species, inflammatory cytokines, and microbial biofilms (Caley et al. 2015; Oso et al. 2018; Thakur et al. 2011). For wound healing, various treatments like antibiotic ointments, hydrocortisone, and disinfectant solutions (e.g., acetic acid and betadine) are effective (Sewall et al. 2003). Additionally, some medicinal herbs are considered safe and effective alternatives for wound healing (Table 9, Fig. 2, online Appendix Fig. 9).

1. *Achillea millefolium* (Yarrow), has anti-inflammatory, antirheumatic, antiseptic, anti-prostaglandin, antiulcer, and antidiuretic effects due to its constituents like flavonoids, essential oil, sesquiterpene lactones, and dicaffeoylquinic acid. In vivo studies have shown that it reduces wound size and scar tissue thickness, aiding in wound healing (Jalali et al. 2010).
2. *Hypericum perforatum* (St. John's Wort), known for its anti-inflammatory properties, Hypericum perforatum is rich in hypericin and hyperforin. It promotes diabetic skin wound healing by enhancing collagen synthesis, proliferation, and revascularization (Yadollah-Damavandi et al. 2015).
3. *Calendula officinalis* (Pot Marigold), contains flavonoids, terpenoids, and phenolic acids with anti-inflammatory and antioxidant effects. It has been found to effectively heal wounds, promote collagen formation, and stimulate fibroblast activity, aiding in wound healing (Shafeie et al. 2015).
4. *Aloe barbadensis* (Aloe Vera), has antibacterial, anti-diabetic, and anti-inflammatory properties due to glycosides, acemannan, and polysaccharides. These components enhance T cell activity, phagocytosis, and collagen synthesis, accelerating wound healing (Xing et al. 2015).
5. *Alternanthera sessilis and Alternanthera brasiliana*, have antibacterial and cytotoxic activities. Chloroform extracts from Alternanthera leaves can significantly reduce wound area and promote re-epithelialization in animal models (Jalalpure et al. 2008). Alternanthera brasiliana accelerates the healing process in burn wounds by increasing the content of vitamin C, SOD, CAT, protein, GSH, and hydroxyproline in damaged tissue (Barua et al. 2012).
6. *Heliotropium indicum*, contains pyrrolizidine alkaloids and has traditionally been used for various ailments. Methanolic extract of Heliotropium indicum stimulates wound healing by increasing catalase and SOD activity, granulation tissue weight, and hydroxyproline content (Dash and Murthy 2011).
7. *Curcuma longa* (Turmeric) with Curcumin, its active compound, has anti-inflammatory, antioxidant, and anti-infectious effects. Curcumin promotes wound healing by deposition of collagen, tissue remodeling, and granulation tissue formation (Joe et al. 2010).
8. *Moringa olifera* (Drumstick), promotes wound healing by enhancing cell proliferation and migration of human dermal fibroblast cells (Gothai et al. 2016). It also reduces wound size and accelerates healing in diabetic-induced rats (Muhammad et al. 2016).
9. *Lantana camara* (Lantana), exhibits wound-healing properties by increasing collagen synthesis and wound contraction rate (Nayak et al. 2009). It contains essential oils with antifungal, antibacterial, and antimicrobial activity (Deena and Thoppil 2000).
10. *Centella asiatica* (Gotu Kola), with active glycosides Madecassoside and asiaticoside enhance collagen synthesis and wound contraction, promoting wound healing (Wu and Wang 2012b). It improves chronic ulcer healing in animal models (Somboonwong et al. 2012).
11. *Carica papaya* (Papaya) latex enhances re-epithelialization and hydroxyproline content in damaged tissue, aiding in burn wound healing (Gurung and Škalko-Basnet 2009). The stem of Carica papaya accelerates wound healing in albino rats (Singh et al. 2020).
12. *Hibiscus Rosa sinensis* (Shoeblackplant), enhances cellular proliferation and collagen synthesis at the wound site, aiding in wound healing (Bhaskar and Nithya 2012).
13. Mimosa pudica, has anti-inflammatory and antinociceptive properties due to compounds like beta-sitosterol and mimosine. Methanolic extracts of Mimosa pudica stimulate wound contraction and reduce wound area in animal models (Paul et al. 2010).

Table 9 Plant based interventions for Wounds

Plant (scientific name)	Bioactive compounds	Mechanism of action	Extract	Dose	Experimental model	Results
1. *Achillea millefolium*	Proazulenes, Dicaffeoylquinic acid (Benedek et al. 2007, 2008)	Prevention of Blood loss by coagulation, Debridement of wound, tissue remodeling and collagen positioning	Alcoholic extract (Jalali et al. 2010)	5 ml/day (Jalali et al. 2010)	Rabbit (Jalali et al. 2010)	Accelerates burn-induced wound healing (Jalali et al. 2010)
2. *Hypericum perforatum*	Hypericin, hyperforin (Saddiqe et al. 2010; Wölfle et al. 2013)	Fibroblas proliferation inducing effect	Ethanol extract (Yadollah-Damavandi et al. 2015)	5% HP gel	Rat (Yadollah-Damavandi et al. 2015)	Improves tissue regeneration (Yadollah-Damavandi et al. 2015)
3. *Calendula officinalis*	Kaempferol, quercetin, isorhamnetin (Re et al., 2009b)	Enhances antioxidant defence mechanism (Chandran and Kuttan 2008)	Ethanolic extract (Chandran and Kuttan 2008)	200 mg/kg (Chandran and Kuttan 2008)	Rat (Chandran and Kuttan 2008)	Increases collagen hydroxyproline and hexosamine contents and improves wound healing (Chandran and Kuttan 2008)
4. *Aloe barbadensis*	Acemannan (Salehi et al. 2018)	Promotes T cell activity, phagocytosis and trans of IL-6, IL-alpha, TNF-alpha and IL-1beta etc. proinflammatory mRNAs (Ali et al. 2014)	Commercial Aloe vera gel	300 mg/kg mannose sugar (Ali et al. 2014)	Mouse (Davis et al. 1994)	improved wound healing process (Ali et al. 2014)
5. *Alternanthera sessilis* and *Alternanthera brasiliana*	Stigmasteol, beta-sitosterol, kaempferol, quercetin (Pereira et al. 2013)	HaCat cells & HDFs Proliferation and migration. Growth factor increasing such as KGF, PDGF, VEGF	Chloroform extract (Jalalpure et al. 2008)	200 mg/kg body weight (Jalalpure et al. 2008)	Rat (Jalalpure et al. 2008)	Reduces wound area and increases re-epithelialisation (Jalalpure et al. 2008)
6. *Heliotropium indicum*	Helindicine, lycopsamine, heleruine-N-oxide, europine-N-oxide (Dash and Abdullah 2013; Souza et al. 2005)	Increasing the formation of collagen & less macrophages	Methanolic extract (Dash and Murthy 2011)	(300, 600 and 2000) mg/kg (Dash and Murthy 2011)	Rat (Dash and Murthy 2011)	Increases SOD and catalase activity, tissue granulation weight and the hydroxyproline content (Dash and Murthy 2011)
7. *Curcuma longa*	Curcumin (Akbik et al. 2014)	Heals wounds through deposition of collagen, tissue remodeling and granulation tissue formation (Joe et al. 2010)	Ethanolic extract (Pawar et al. 2015)	150 mg/kg body weight (Pawar et al. 2015)	Rat (Pawar et al. 2015)	Heals wound (Pawar et al. 2015)
8. *Moringa olifera*	4-isothiocyanate, S-methyl-N-thiocarbamate (Cheenpracha et al. 2010)	Increases cell proliferation and migration of HDF cell (Gothai et al. 2016)	Ethyl acetate extract (Gothai et al. 2016)	(12.5 and 25) microgram/ml (Gothai et al. 2016)	Human dermal fibroblast cells (Gothai et al. 2016)	Helps in wound healing (Gothai et al. 2016)
9. *Lantana camara*	Quinine (Venkatachalam et al. 2011)	10.5402/2011/847980 (Nayak et al. 2009)	Aqueous leaf extract (Nayak et al. 2009)	100 mg/kg/day (Nayak et al. 2009)	Rat (Nayak et al. 2009)	Increases collagen synthesis and wound contraction rate, decreases healing time (Nayak et al. 2009)
10. *Centella asiatica*	Madecassoside and asiaticoside (Chandrika amd Prasad Kumara 2015; Moqbel et al. 2020)	Increased anti-oxidant levels (Jamil et al. 2007)	Alcoholic extract (Jamil et al. 2007)	100 mg/L of extract	Rat (Jamil et al. 2007)	Helps in wound healing (Jamil et al. 2007)

Table 9 continued

Plant (scientific name)	Bioactive compounds	Mechanism of action	Extract	Dose	Experimental model	Results
11. *Carica papaya*	Kaempferol, quercetin, caffeic acid (Saikia et al. 2015; Sangsoy et al. 2017; Santana et al. 2019)	Increases rate and extent of wound closure and increases hydroxyproline levels (Nayak et al. 2007)	Aqueous extract (Nayak et al. 2007)	100 mg/kg/day (Nayak et al. 2007)	Rat (Nayak et al. 2007)	Reduces wound area, enhances hydroxyproline content and weight of dry granulation tissue (Nayak et al. 2007)
12. *Hibiscus Rosa sinensis*	Quinine, anthraquinones (Kaur and Lakshmanan 2015; Kumari et al. 2015)	Increases levels of hexosamine and uronic acid (Bhaskar and Nithya 2012)	Flower ethanolic extract (Bhaskar and Nithya 2012)	5/10 g of extract in 100 g of ointment base (Bhaskar and Nithya 2012)	Rat (Bhaskar and Nithya 2012)	Enhances cellular proliferation and collagen synthesis at wound site, increases DNA, protein and collagen content, improves re-epithelialisation rate and wound contraction (Bhaskar and Nithya 2012)
13. *Mimosa pudica*	Beta-sitosterol, mimosine (Jha 2007)	Collagen progression,	Methanolic shoot extract and methanolic root extract	250 g and 250 g	Rat	Increase excisional wound contraction rate and promotes wound healing activity

Discussion

Pain is a condition that drives many patients to explore complementary therapies. Herbal medicines have gained interest as potential solutions for pain management. In this review we have delved into the effects of herbal treatments on pain relief and the underlying mechanisms at play.

Our review emphasizes the positive outcomes associated with herbal medicines in managing pain. Existing evidence suggests that these therapies may effectively alleviate pain by targeting two mechanisms; reducing inflammation and mitigating oxidative stress. These therapeutic effects can be attributed to their ability to regulate signaling pathways and modulate immune cell activity. Notably herbal remedies like turmeric (Curcuma longa) have shown anti inflammatory properties by inhibiting pro inflammatory cytokines such, as interleukin 1β (IL 1β) and tumor necrosis factor alpha (TNF α) (Ammon 2006; Chainani-Wu 2003; Grzanna et al. 2005; Han et al. 2018; Jurenka 2009; McKenna et al. 2001; Siddiqui 2011). Similarly frankincense (Boswellia serrata) has demonstrated its ability to inhibit the production of leukotrienes which are known mediators of inflammation (Ammon 2006).

Furthermore herbal treatments have also been found to exhibit antioxidant effects. For instance, Ginkgo biloba has been found to possess antioxidant properties by neutralizing free radicals and shielding against oxidative stress (McKenna et al. 2001). Similarly, Hypericum perforatum (St. Johns wort) has displayed the ability to boost the expression of antioxidant enzymes like superoxide dismutase (SOD) thereby providing defense against harm (Sánchez-Reus et al. 2007).

One of the advantages of herbal medicines for managing pain is their generally favorable tolerance, minimal side effects, affordability and some level of effectiveness (Klepser and Klepser 1999). Additionally, incorporating treatments into pain management empowers patients by allowing them to actively participate in choosing therapies they believe will be most beneficial.

The increasing popularity of complementary medicine can be attributed in part to the growing emphasis on patient autonomy and the widespread availability of online information. Dissatisfaction with therapies often stemming from a lack of confidence among both practitioners and patients (Winter and Korzenik 2017) has also contributed to this trend. It is vital for healthcare providers to stay knowledgeable about the range of pain therapies available, to their patients regardless of the underlying cause.

However it is essential for healthcare professionals to have an understanding of the risks and limitations associated with the use of herbal remedies in clinical

settings. For example cannabis, a herbal treatment for pain management contains active compounds like delta 9 tetrahydrocannabinol (THC) and cannabidiol (CBD) which interact with the body's endocannabinoid system to provide relief from pain (Russo 2008). However the use of cannabis for pain management remains a subject of controversy due to its effects, potential for misuse and varying legal status in different countries. Turmeric despite being studied for its potential benefits faces challenges such as its relatively low curcumin content and limited ability to be absorbed by the body effectively. This may require doses for therapeutic effects (Corroon and Felice 2019; Prasad et al. 2014). Moreover recommending supplements like curcumin to specific patient groups such as children or pregnant and breastfeeding women raises concerns due to limited conclusive evidence regarding their benefits. Additionally there are variations in the status of herbal medicines across different countries making it challenging to ensure their quality, safety and effectiveness—especially in regions where these therapies are not regulated by organizations like the US Food and Drug Administration (FDA).

Another significant concern relates to interactions, between herbal remedies and prescription medications that could potentially lead to adverse effects. For instance St. Johns wort (SJW) is a known herbal supplement that people often use to address depression and anxiety. It is important to note that SJW can interact with painkillers. When someone takes SJW, it triggers the activity of two enzymes called P450 3A4 (CYP3A4) and P glycoprotein (P gp). These enzymes are responsible for breaking down and eliminating prescription drugs, including opioids. This interaction can potentially speed up the metabolism and elimination of opioids which might reduce their effectiveness in providing relief from pain in cases. On the side SJW might also slow down the metabolism and elimination of opioids in specific individuals increasing the risk of respiratory depression or other adverse effects (Delgoda and Westlake 2004; Gurley et al. 2005).

Furthermore one significant challenge with medicines is the absence of standardized guidelines for dosages. Unlike prescription medications herbal remedies are not subject to regulatory oversight. As a result there is variation in terms of product composition and quality across different brands or sources. This lack of standardization can lead to inconsistencies in potency and efficacy when it comes to medicines making it difficult to achieve consistent therapeutic outcomes (Bone and Mills 2013; Tachjian et al. 2010). Both patients and healthcare practitioners often face challenges due to the absence of guidance on appropriate dosages, for these herbal remedies. This can result in situations where patients may not take enough dosage leading to inadequate pain relief or taking too much dosage causing adverse effects or toxicity concerns (Dowell et al. 2022).

Given the intricacies involved it is crucial for patients to have conversations with their healthcare providers when it comes to using herbal medicines. It is important that healthcare professionals stay updated on the research about herbal therapies and how they might interact with prescription medications (Xiong et al. 2022).

While herbal supplements have the potential to improve the quality of life for patients dealing with chronic pain there is a concern that some individuals might prioritize these therapies over conventional medicine instead of using them as complementary treatments. This approach could result in pain management and potentially harmful outcomes (Cohen et al. 2021; Gardiner et al. 2008; Jermini et al. 2019). Additionally cost can be an obstacle since insurance coverage for herbal remedies is often limited or nonexistent. As a result patients are left to navigate the market of supplements on their own increasing the risk of misuse. The lack of regulation and quality control in the industry further compounds these challenges making it difficult for patients to make decisions about which products to choose (Shaw et al. 2012).

One notable issue highlighted is the awareness among healthcare providers regarding the use of herbal supplements, in clinical practice. Many patients report that they learn about alternative therapies from sources like the Internet, friends or naturopaths rather than from their healthcare providers (Nguyen et al. 2016). It is worth noting that medical schools have historically not dedicated attention to alternative medicine and herbal therapy in their curricula. As a result healthcare professionals may not feel discussing or advising on herbal supplements. To bridge this knowledge gap academic institutions should consider incorporating training on alternative medicine into their curricula in the future.

In our review of pain management approaches we emphasize the benefits of herbal therapies. These therapies are believed to offer pain relief by reducing inflammation and modulating stress. However it is important to evaluate these findings in the context of each study's methodology. Our assessment reveals a range of research methods used including randomized controlled trials (RCTs) and observational studies. Each approach has its strengths and limitations that contribute to the overall evidence base. Significantly the sample sizes varied greatly among these studies. This highlights the need for robust research, with adequately sized samples to validate these initial findings. Furthermore the diversity observed in preparations dosing and outcome measures makes it challenging to synthesize the results. This indicates the need for standardization in research on herbal medicine. Selection and performance bias was noticeable in various forms. These biases have the potential to skew the results.

When applying these findings to practice, healthcare professionals should carefully consider efficacy and safety aspects. It is crucial to prioritize safety and follow evidence based practices when considering herbal therapies. In conclusion while herbal therapies show promise for pain management due to their inflammatory and antioxidant properties.

However, it is important to exercise caution when incorporating remedies into clinical practice taking into account the potential risks, limitations and interactions with prescription drugs. Open and honest conversations between patients and healthcare professionals are crucial to ensure effective pain management. Continuous research endeavors are necessary to address existing knowledge gaps and insurance providers may consider covering treatments if there is substantial evidence supporting their efficacy. Given the intricacies involved in this matter individuals need to be well informed, before making any decisions.

Conclusion

Pain is a common reason for seeking medical attention, and our review has identified several promising herbal therapies for pain management based on the available evidence. These medicinal herbs, containing bioactive substances, offer pain relief, anti-inflammatory, and antibacterial effects without harmful side effects. While herbal extracts hold potential as a safe and effective alternative for pain management, it's crucial to acknowledge their potential risks and limitations. Further research is essential to fully understand their mechanisms of action, determine efficacy, and optimize clinical use. Encouraging open discussions between patients and healthcare providers regarding the use of herbal supplements is a vital step toward improving pain management strategies.

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Data availability Dataset used in this study will be available as per request from the authors.

Declarations

Conflict of interest The authors report no competing interests. The authors alone are responsible for the content and writing of this article.

Ethical approval and consent to participate The review adheres to PRISMA-ScR (Preferred Reporting Items for Systematic reviews and Meta-Analyses extension for Scoping Reviews) Ethical approval was not required for the conduct of this scoping review as it involves the synthesis of published literature and does not include any primary data collection from humans or animals.

Consent for publication Not applicable.

References

Abad ANA, Nouri MHK, Tavakkoli F (2011) Effect of *Salvia officinalis* hydroalcoholic extract on vincristine-induced neuropathy in mice. Chin J Nat Med 9(5):354–358. https://doi.org/10.3724/SP.J.1009.2011.00354

Abadian K, Keshavarz Z, Mojab F, Alavi Majd H, Abbasi NM (2016) Comparison the effect of mefenamic acid and *Teucrium polium* on the severity and systemic symptoms of dysmenorrhea. Complement Ther Clin Pract 22:12–15. https://doi.org/10.1016/J.CTCP.2015.09.003

Abdel-Lateef E, Mahmoud F, Hammam O, El-Ahwany E, El-Wakil E, Kandil S, Abu Taleb H, El-Sayed M, Hassenein H (2016) Bioactive chemical constituents of *Curcuma*

longa L. rhizomes extract inhibit the growth of human hepatoma cell line (HepG2). Acta Pharm 66(3):387–398
Ahlawat K, Khatkar B (2011) Processing, food applications and safety of aloe vera products: a review. J Food Sci Technol 48:525–533
Ahlemeyer B, Krieglstein J (2003) Neuroprotective effects of Ginkgo biloba extract. Cell Mol Life Sci CMLS 60 (9):1779–1792. https://doi.org/10.1007/s00018-003-3080-1
Ahmad AH, Zakaria R (2015) Pain in times of stress. Malays J Med Sci MJMS 22(Spec Issue):52
Akbik D, Ghadiri M, Chrzanowski W, Rohanizadeh R (2014) Curcumin as a wound healing agent. Life Sci 116(1):1–7. https://doi.org/10.1016/J.LFS.2014.08.016
Akhtar N, Miller MJS, Haqqi TM (2011a) Effect of a Herbal-Leucine mix on the IL-1$ß$-induced cartilage degradation and inflammatory gene expression in human chondrocytes. BMC Complement Altern Med 11:66. https://doi.org/10.1186/1472-6882-11-66
Akhtar N, Miller MJS, Haqqi TM (2011b) Effect of a Herbal-Leucine mix on the IL-1β-induced cartilage degradation and inflammatory gene expression in human chondrocytes. BMC Complement Altern Med 11:66–66. https://doi.org/10.1186/1472-6882-11-66
Alamgeer UAM, Hasan UH (2017) Anti-arthritic activity of aqueous-methanolic extract and various fractions of *Berberis orthobotrys* Bien ex Aitch. BMC Complement Altern Med 17(1):371. https://doi.org/10.1186/s12906-017-1879-9
Alavizadeh SH, Hosseinzadeh H (2014) Bioactivity assessment and toxicity of crocin: a comprehensive review. Food Chem Toxicol 64:65–80. https://doi.org/10.1016/J.FCT.2013.11.016
Ali P, Chen YF, Sargsyan E (2014) Bioactive molecules of herbal extracts with anti-infective and wound healing properties. Microbiol Surg Infect. https://doi.org/10.1016/B978-0-12-411629-0.00012-X
Alipour Z, Asadizaker M, Fayazi S, Yegane N, Kochak M, Zadeh MHH (2017) The effect of ginger on pain and satisfaction of patients with knee osteoarthritis. Jundishapur J Chronic Disease Care. https://doi.org/10.17795/JJCDC-34798
Alonso-Castro AJ, Zapata-Morales JR, Ruiz-Padilla AJ, Solorio-Alvarado CR, Rangel-Velázquez JE, Cruz-Jiménez G, Orozco-Castellanos LM, Domínguez F, Maldonado-Miranda JJ, Carranza-Álvarez C, Castillo-Pérez LJ, Solano E, Isiordia-Espinoza MA, del Carmen Juárez-Vázquez M, Argueta-Fuertes MA, González-Sánchez I, Ortiz-Andrade R (2017) Use of medicinal plants by health professionals in Mexico. J Ethnopharmacol 198:81–86. https://doi.org/10.1016/J.JEP.2016.12.038
Alonso-Castro AJ, Zapata-Morales JR, Arana-Argáez V, Torres-Romero JC, Ramírez-Villanueva E, Pérez-Medina SE, Ramírez-Morales MA, Juárez-Méndez MA, Infante-Barrios YP, Martínez-Gutiérrez F, Carranza-Álvarez C, Isiordia-Espinoza MA, Flores-Santos A (2018) Pharmacological and toxicological study of a chemical-standardized ethanol extract of the branches and leaves from *Eysenhardtia polystachya* (Ortega) Sarg. (Fabaceae). J Ethnopharmacol 224:314–322. https://doi.org/10.1016/J.JEP.2018.06.016
Al-Reza SM, Rahman A, Sattar MA, Rahman MO, Fida HM (2010) Essential oil composition and antioxidant activities of *Curcuma aromatic*a Salisb. Food Chem Toxicol 48 (6):1757–1760. https://doi.org/10.1016/J.FCT.2010.04.008
Altman RD, Marcussen KC (2001) Effects of a ginger extract on knee pain in patients with osteoarthritis. Arthritis Rheum 44(11):2531–2538. https://doi.org/10.1002/1529-0131
Amin B, Hosseinzadeh H (2012) Evaluation of aqueous and ethanolic extracts of saffron, *Crocus sativus* L., and its constituents, safranal and crocin in allodynia and hyperalgesia induced by chronic constriction injury model of neuropathic pain in rats. Fitoterapia 83(5):888–895. https://doi.org/10.1016/J.FITOTE.2012.03.022
Amin B, Hosseinzadeh H (2015) Analgesic and anti-inflammatory effects of *Crocus sativus* L. (Saffron). Bioact Nutraceuticals Diet Suppl Neurol Brain Disease Prev Ther. https://doi.org/10.1016/B978-0-12-411462-3.00033-3
Amin B, Taheri MMH, Hosseinzadeh H (2014) Effects of intraperitoneal thymoquinone on chronic neuropathic pain in rats. Planta Med 80(15):1269–1277. https://doi.org/10.1055/S-0034-1383062
Amin B, Hajhashemi V, Hosseinzadeh H (2015) Minocycline potentiates the anti-hyperalgesic effect of ceftriaxone in CCI-induced neuropathic pain in rats. Res Pharm Sci 10 (1):42–42
Amin MA, Fox DA, Ruth JH (2017) Synovial cellular and molecular markers in rheumatoid arthritis. Semin Immunopathol 39(4):385–393. https://doi.org/10.1007/S00281-017-0631-3
Ammon HPT (2006) Boswellic acids in chronic inflammatory diseases. Planta Med 72(12):1100–1116. https://doi.org/10.1055/S-2006-947227
Ammon HPT (2010) Modulation of the immune system by *Boswellia serrata* extracts and boswellic acids. Phytomedicine 17(11):862–867. https://doi.org/10.1016/J.PHYMED.2010.03.003
Apkarian AV, Hashmi JA, Baliki MN (2011) Pain and the brain: specificity and plasticity of the brain in clinical chronic pain. Pain 152:S64. https://doi.org/10.1016/J.PAIN.2010.11.010
Arendt-Nielsen L, Nie H, Laursen MB, Laursen BS, Madeleine P, Simonsen OH, Graven-Nielsen T (2010) Sensitization in patients with painful knee osteoarthritis. Pain 149 (3):573–581. https://doi.org/10.1016/J.PAIN.2010.04.003
Arksey H, O'Malley L (2007) Scoping studies: towards a methodological framework. Int J Soc Res Methodol 8 (1):19–32. https://doi.org/10.1080/1364557032000119616
Assiri AMA, Elbanna K, Abulreesh HH, Ramadan MF (2016) Bioactive compounds of cold-pressed thyme (*Thymus vulgaris*) oil with antioxidant and antimicrobial properties. J Oleo Sci 65(8):629–640. https://doi.org/10.5650/JOS.ESS16042
Ataollahi M, Amir Ali Akbari S, Mojab F, Alavi Majd H (2014) The effect of wheat germ extract on the severity of primary dysmenorrhea. J Jahrom Univ Med Sci 12(1):57–62. https://doi.org/10.29252/JMJ.12.1.57
Attah MO, Jacks T, Attah J, Otong ES, John B (2016) The effect of aloe vera (Linn) on cutaneous wound healing and

wound contraction rate in adult rabbits. Nova J Med Biol Sci 5(3):1–8. https://doi.org/10.20286/JMBS-050307

Attal N (2012) Neuropathic pain: mechanisms, therapeutic approach, and interpretation of clinical trials. Continuum (minneapolis, Minn.) 18(1):161–175. https://doi.org/10.1212/01.CON.0000411564.41709.2D

Aviram A, Tsoukias NM, Melnick SJ, Resek AP, Ramachandran C (2012) Inhibition of nitric oxide synthesis in mouse macrophage cells by feverfew supercritical extract. Phytother Res 26(4):541–545. https://doi.org/10.1002/PTR.3594

Ayaz M, Junaid M, Ullah F, Sadiq A, Subhan F, Khan MA, Ahmad W, Ali G, Imran M, Ahmad S (2016) Molecularly characterized solvent extracts and saponins from *Polygonum hydropiper* L. Show high anti-angiogenic, anti-tumor, brine shrimp, and fibroblast NIH/3T3 cell line cytotoxicity. Front Pharmacol. https://doi.org/10.3389/FPHAR.2016.00074

Badgujar SB, Patel VV, Bandivdekar AH (2014) *Foeniculum vulgare* Mill: a review of its botany, phytochemistry, pharmacology, contemporary application, and toxicology. BioMed Res Int. https://doi.org/10.1155/2014/842674

Bahmani M, Eftekhari Z (2012) An ethnoveterinary study of medicinal plants in treatment of diseases and syndromes of herd dog in southern regions of Ilam province, Iran. Comp Clin Pathol 22(3):403–407. https://doi.org/10.1007/S00580-012-1423-8

Bahmani M, Farkhondeh T, Sadighara P (2012) The anti-parasitic effects of *Nicotina tabacum* on leeches. Comp Clin Pathol 21:357–359. https://doi.org/10.1007/S00580-012-1413-X

Bahmani M, Shirzad H, Majlesi M, Shahinfard N, Rafieian-Kopaei M (2014) A review study on analgesic applications of Iranian medicinal plants. Asian Pac J Trop Med 7 (S1):S43–S53. https://doi.org/10.1016/S1995-7645(14)60202-9

Bahramikia S, Yazdanparast R (2012) Phytochemistry and medicinal properties of *Teucrium polium* L. (Lamiaceae). Phytother Res 26(11):1581–1593. https://doi.org/10.1002/PTR.4617

Bakirel T, Bakirel U, Keleş OÜ, Ülgen SG, Yardibi H (2008) In vivo assessment of antidiabetic and antioxidant activities of rosemary (*Rosmarinus officinalis*) in alloxan-diabetic rabbits. J Ethnopharmacol 116(1):64–73. https://doi.org/10.1016/J.JEP.2007.10.039

Balakumbahan R, Rajamani K, Kumanan K (2010) Acorus calamus: an overview. J Med Plants Res 4(25):2740–2745

Bani S, Hasanpour S, Mousavi Z, Garehbaghi PM, Gojazadeh M (2014) The effect of rosa damascena extract on primary dysmenorrhea: a double-blind cross-over clinical trial. Iran Red Crescent Med J. https://doi.org/10.5812/IRCMJ.14643

Barua CC, Talukdar A, Begum SA, Buragohain B, Roy JD, Pathak DC, Sarma DK, Gupta AK, Bora RS (2012) Effect of *Alternanthera brasiliana* (L) kuntze on healing of dermal burn wound. Indian J Exp Biol 50(1):56–60

Belcaro G, Feragalli B, Cornelli U, and Dugall M (2015) Hand "stress" arthritis in young subjects: effects of Flexiqule (pharma-standard Boswellia extract). A preliminary case report. Minerva Gastroenterologica e Dietologica. https://europepmc.org/article/med/26492590

Benedek B, Kopp B, Melzig MF (2007) *Achillea millefolium* L. s.l. – is the anti-inflammatory activity mediated by protease inhibition? J Ethnopharmacol 113(2):312–317. https://doi.org/10.1016/J.JEP.2007.06.014

Benedek B, Rothwangl-Wiltschnigg K, Rozema E, Gjoncaj N, Reznicek G, Jurenitsch J, Kopp B, Glasl S, Univ A, Glasl S (2008) Yarrow (*Achillea millefolium* L. sl): pharmaceutical quality of commercial samples. Ingentaconnect Com 63:23–26. https://doi.org/10.1691/ph.2008.7646

Benincá JP, Dalmarco JB, Pizzolatti MG, Fröde TS (2011) Analysis of the anti-inflammatory properties of *Rosmarinus officinalis* L. in mice. Food Chem 124(2):468–475. https://doi.org/10.1016/J.FOODCHEM.2010.06.056

Bent S (2008) Herbal medicine in the United States: review of efficacy, safety, and regulation: grand rounds at University of California, San Francisco Medical Center. J Gen Intern Med 23(6):854. https://doi.org/10.1007/S11606-008-0632-Y

Bernardi M, Lazzeri L, Perelli F, Reis FM, Petraglia F (2017) Dysmenorrhea and related disorders. F1000Research. https://doi.org/10.12688/F1000RESEARCH.11682.1

Bhaskar A, Nithya V (2012) Evaluation of the wound-healing activity of *Hibiscus rosa sinensis* L. (Malvaceae) in Wistar albino rats. Indian J Pharmacol 44(6):694–698. https://doi.org/10.4103/0253-7613.103252

Bhattacharya S, Christensen KB, Olsen LCB, Christensen LP, Grevsen K, Færgeman NJ, Kristiansen K, Young JF, Oksbjerg N (2013a) Bioactive components from flowers of *Sambucus nigra* L. increase glucose uptake in primary porcine myotube cultures and reduce fat accumulation in caenorhabditis elegans. J Agric Food Chem 61 (46):11033–11040. https://doi.org/10.1021/JF402838A

Biegert C, Wagner I, Lüdtke R, Kötter I, Lohmüller C, Günaydin I, Taxis K, Heide L (2004) Efficacy and safety of willow bark extract in the treatment of osteoarthritis and rheumatoid arthritis: results of 2 randomized double-blind controlled trials. J Rheumatol 31(11):2121–2130

Bisen SP, Emerald M (2016) Nutritional and therapeutic potential of garlic and onion (*Allium* sp.). Curr Nutr Food Sci 12(3):190–199

Black CD, Herring MP, Hurley DJ, O'Connor PJ (2010) Ginger (*Zingiber officinale*) reduces muscle pain caused by eccentric exercise. J Pain 11(9):894–903. https://doi.org/10.1016/J.JPAIN.2009.12.013

Blain EJ, Ali AY, Duance VC (2010) *Boswellia frereana* (frankincense) suppresses cytokine-induced matrix metalloproteinase expression and production of pro-inflammatory molecules in articular cartilage. Phytother Res 24(6):905–912. https://doi.org/10.1002/PTR.3055

Boje K, Lechtenberg M, Nahrstedt A (2003) New and known iridoid- and phenylethanoid glycosides from Harpagophytum procumbens and their in vitro inhibition of human leukocyte elastase. Planta Med 69(9):820–825. https://doi.org/10.1055/s-2003-43225

Bokaie M, Farajkhoda T, Enjezab B, Khoshbin A, Mojgan KZ (2013) Oral fennel (*Foeniculum vulgare*) drop effect on primary dysmenorrhea: effectiveness of herbal drug. Iran J Nurs Midwifery Res 18(2):132–132

Bonaterra GA, Heinrich EU, Kelber O, Weiser D, Metz J, Kinscherf R (2010) Anti-inflammatory effects of the willow bark extract STW 33-I (Proaktiv®) in LPS-

activated human monocytes and differentiated macrophages. Phytomedicine 17(14):1106–1113. https://doi.org/10.1016/J.PHYMED.2010.03.022

Bone K, Mills S (2013) Principles and practice of phytotherapy: modern herbal medicine, 1st edn. Elsevier, Amsterdam

Borrás-Linares I, Stojanović Z, Quirantes-Piné R, Arráez-Román D, Švarc-Gajić J, Fernández-Gutiérrez A, Segura-Carretero A (2014) Rosmarinus officinalis leaves as a natural source of bioactive compounds. Int J Mol Sci 15 (11):20585–20606. https://doi.org/10.3390/IJMS151120585

Budai MM, Varga A, Milesz S, Tozsér J, Benko S (2013) Aloe vera downregulates LPS-induced inflammatory cytokine production and expression of NLRP3 inflammasome in human macrophages. Mol Immunol 56(4):471–479. https://doi.org/10.1016/J.MOLIMM.2013.05.005

Burman RA, Zakariassen E, Hunskaar S (2011) Acute chest pain—a prospective population based study of contacts to Norwegian emergency medical communication centres. BMC Emerg Med 11(1):1–8. https://doi.org/10.1186/1471-227X-11-9

Burstein R, Noseda R, Borsook D (2015) Migraine: multiple processes, complex pathophysiology. J Neurosci 35 (17):6619–6629. https://doi.org/10.1523/JNEUROSCI.0373-15.2015

Cabral VP, Andrade CAF, Passos SRL, Martins MFM, Hökerberg YHM (2016) Severe infection in patients with rheumatoid arthritis taking anakinra, rituximab, or abatacept: a systematic review of observational studies. Rev Bras Reumatol 56(6):543–550. https://doi.org/10.1016/J.RBRE.2016.10.001

Caley MP, Martins VLC, O'Toole EA (2015) Metalloproteinases and wound healing. Adv Wound Care 4(4):225–234. https://doi.org/10.1089/WOUND.2014.0581

Cao W, Li XQ, Zhang XN, Hou Y, Zeng AG, Xie Y, hua, & Wang, S. W. (2010) Madecassoside suppresses LPS-induced TNF-α production in cardiomyocytes through inhibition of ERK, p38, and NF-κB activity. Int Immunopharmacol 10(7):723–729. https://doi.org/10.1016/J.INTIMP.2010.03.015

Carter GT, Duong V, Ho S, Ngo KC, Greer CL, Weeks DL (2014) Side effects of commonly prescribed analgesic medications. Phys Med Rehabil Clin N Am 25(2):457–470. https://doi.org/10.1016/J.PMR.2014.01.007

Chainani-Wu N (2003) Safety and anti-inflammatory activity of curcumin: a component of tumeric (*Curcuma longa*). J Alternat and Complement Med 9(1):161–168. https://doi.org/10.1089/107555303321223035

Chandran PK, Kuttan R (2008) Effect of Calendula officinalis flower extract on acute phase proteins, antioxidant defense mechanism and granuloma formation during thermal burns. J Clin Biochem Nutr 43(2):58–64

Chandrika UG, Prasad Kumara PAAS (2015) Gotu Kola (*Centella asiatica*): nutritional properties and plausible health benefits. Adv Food Nutr Res 76:125–157. https://doi.org/10.1016/BS.AFNR.2015.08.001

Chantre P, Cappelaere A, Leblan D, Guedon D, Vandermander J, Fournie B (2000) Efficacy and tolerance of *Harpagophytum procumbens* versus diacerhein in treatment of osteoarthritis. Phytomed Int J Phytother Phytopharmacol 7 (3):177–183. https://doi.org/10.1016/S0944-7113(00)80001-X

Charles A, Hansen JM (2015) Migraine aura: new ideas about cause, classification, and clinical significance. Curr Opin Neurol 28(3):255–260. https://doi.org/10.1097/WCO.0000000000000193

Chaurasia S (2009) Anti-inflammatory and antioxidant activity of strychnos nux vomica linn. Am-Eurasian J Sustain Agric 3(2):244–252

Cheenpracha S, Park EJ, Yoshida WY, Barit C, Wall M, Pezzuto JM, Chang LC (2010) Potential anti-inflammatory phenolic glycosides from the medicinal plant Moringa oleifera fruits. Bioorg Med Chem 18(17):6598–6602. https://doi.org/10.1016/J.BMC.2010.03.057

Chen Y-S, Lee S-M, Lin C-C, Liu C-Y, Wu M-C, Shi W-L (2013) Kinetic study on the tyrosinase and melanin formation inhibitory activities of carthamus yellow isolated from *Carthamus tinctorius* L. J Biosci Bioeng 115 (3):242–245

Chen CX, Barrett B, Kwekkeboom KL (2016) Efficacy of oral ginger (*Zingiber officinale*) for dysmenorrhea: a systematic review and meta-analysis. Evid-Based Complement Altern Med. https://doi.org/10.1155/2016/6295737

Choi MS, Kim JK, Kim DH, Yoo HH (2019) Effects of gut microbiota on the bioavailability of bioactive compounds from ginkgo leaf extracts. Metabolites 2019(9):132. https://doi.org/10.3390/METABO9070132

Choy EH, Panayi GS (2001) Cytokine pathways and joint inflammation in rheumatoid arthritis. N Engl J Med 344 (12):907–916. https://doi.org/10.1056/NEJM200103223441207

Chrubasik S, Eisenberg E, Balan E, Weinberger T, Luzzati R, Conradt C (2000) Treatment of low back pain exacerbations with willow bark extract: a randomized double-blind study. Am J Med 109(1):9–14. https://doi.org/10.1016/S0002-9343(00)00442-3

Chrubasik S, Thanner J, Künzel O, Conradt C, Black A, Pollak S (2002) Comparison of outcome measures during treatment with the proprietary Harpagophytum extract Doloteffin®in patients with pain in the lower back, knee or hip. Phytomedicine 9(3):181–194. https://doi.org/10.1078/0944-7113-00140

Chun J, Choi RJ, Khan S, Lee DS, Kim YC, Nam YJ, Lee DU, Kim YS (2012) Alantolactone suppresses inducible nitric oxide synthase and cyclooxygenase-2 expression by down-regulating NF-κB, MAPK and AP-1 via the MyD88 signaling pathway in LPS-activated RAW 264.7 cells. Int Immunopharmacol 14(4):375–383. https://doi.org/10.1016/J.INTIMP.2012.08.011

Cohen SP, Vase L, Hooten WM (2021) Chronic pain: an update on burden, best practices, and new advances. Lancet (london, England) 397(10289):2082–2097. https://doi.org/10.1016/S0140-6736(21)00393-7

Cojocaru M, Cojocaru IM, Silosi I, Vrabie CD, Tanasescu R (2010) Extra-articular manifestations in rheumatoid arthritis. Maedica 5(4):291–291

Colloca L, Ludman T, Bouhassira D, Baron R, Dickenson AH, Yarnitsky D, Freeman R, Truini A, Attal N, Finnerup NB, Eccleston C, Kalso E, Bennett DL, Dworkin RH, Raja SN (2017) Neuropathic pain. Nat Rev Disease Prim 3(1):1–19. https://doi.org/10.1038/nrdp.2017.2

Comelli F, Giagnoni G, Bettoni I, Colleoni M, Costa B (2008) Antihyperalgesic effect of a *Cannabis sativa* extract in a rat model of neuropathic pain: mechanisms involved. Phytother Res 22(8):1017–1024. https://doi.org/10.1002/PTR.2401

Corroon J, Felice J (2019) The endocannabinoid system and its modulation by cannabidiol (CBD). Altern Ther Health Med 25(S2):6–14

Costa B, Trovato AE, Comelli F, Giagnoni G, Colleoni M (2007) The non-psychoactive cannabis constituent cannabidiol is an orally effective therapeutic agent in rat chronic inflammatory and neuropathic pain. Eur J Pharmacol 556(1–3):75–83. https://doi.org/10.1016/J.EJPHAR.2006.11.006

Cross M, Smith E, Hoy D, Nolte S, Ackerman I, Fransen M, Bridgett L, Williams S, Guillemin F, Hill CL, Laslett LL, Jones G, Cicuttini F, Osborne R, Vos T, Buchbinder R, Woolf A, March L (2014) The global burden of hip and knee osteoarthritis: estimates from the global burden of disease 2010 study. Ann Rheum Dis 73(7):1323–1330. https://doi.org/10.1136/ANNRHEUMDIS-2013-204763

D'Andrea G, Bussone G, Allais G, Aguggia M, D'Onofrio F, Maggio M, Moschiano F, Saracco MG, Terzi MG, Petretta V, Benedetto C (2009) Efficacy of Ginkgolide B in the prophylaxis of migraine with aura. Neurol Sci 30 (1):121–124. https://doi.org/10.1007/S10072-009-0074-2

Daily JW, Zhang X, Kim DS, Park S (2015) Efficacy of ginger for alleviating the symptoms of primary dysmenorrhea: a systematic review and meta-analysis of randomized clinical trials. Pain Med 16(12):2243–2255. https://doi.org/10.1111/PME.12853

Dash GK, Abdullah MS (2013) A review on *Heliotropium indicum* L. (Boraginaceae). Int J Pharm Sci Res 4(4):1253

Dash GK, Murthy PN (2011) Studies on wound healing activity of *Heliotropium indicum* Linn. leaves on rats. Int Sch Res Not 2011:1–8. https://doi.org/10.5402/2011/847980

Davis RH, Donato JJ, Hartman GM, Haas RC (1994) Anti-inflammatory and wound healing activity of a growth substance in Aloe vera. J Am Podiatr Med Assoc 84 (2):77–81

De Smet PAGM, Keller K, Hänsel R, Chandler RF (1993) Adverse effects of herbal drugs, vol 2. Springer, Berlin, Heidelberg. https://doi.org/10.1007/978-3-642-48906-8

de Virgens CMB, Noya-Rabelo M, Carvalhal MC, Junior AMDSC, Lopes FODA, de Sá NC, Suerdieck JG, de Souza TMB, Correia VCDA, Sodré GS, da Silva AB, Alexandre FKB, Ferreira FRM, Correia LCL (2017) Accuracy of gestalt perception of acute chest pain in predicting coronary artery disease. World J Cardiol 9 (3):241–247. https://doi.org/10.4330/WJC.V9.I3.241

Deena M, Thoppil J (2000) Antimicrobial activity of the essential oil of *Lantana camara*. Fitoterapia 71(4):453–455. https://doi.org/10.1016/S0367-326X(00)00140-4

Safdari DF, Parvin N (2016) The effect of mefenamic acid and melissa officinalis on primary dysmenorrhea: a randomized clinical trial study. Int J Pharmacogn Phytochem Res 8(8):1286–1292

Delgoda R, Westlake ACG (2004) Herbal interactions involving cytochrome p450 enzymes: a mini review. Toxicol Rev 23(4):239–249. https://doi.org/10.2165/00139709-200423040-00004

Devi Priya M, Siril EA (2014) Traditional and modern use of indian madder (*Rubia cordifolia* L.): an overview. Int J Pharm Sci Rev Res 25(1):154–164

Dey D, Chaskar S, Athavale N, Chitre D (2014) Inhibition of LPS-induced TNF-$α$ and NO production in mouse macrophage and inflammatory response in rat animal models by a novel Ayurvedic formulation, BV-9238. Phytother Res 28(10):1479–1485. https://doi.org/10.1002/PTR.5151

Ding L, Heying E, Nicholson N, Stroud NJ, Homandberg GA, Buckwalter JA, Guo D, Martin JA (2010) Mechanical impact induces cartilage degradation via mitogen activated protein kinases. Osteoarthr Cartil 18(11):1509–1517. https://doi.org/10.1016/J.JOCA.2010.08.014

Diwane Patil R, Vyavahare P, Bhambar R (2015) Protective effect of Rubia cordifolia in paclitaxel-induced neuropathic pain in experimental animals. Indian J Pain 29 (3):154–154. https://doi.org/10.4103/0970-5333.165833

Dowell D, Ragan KR, Jones CM, Baldwin GT, Chou R (2022) CDC clinical practice guideline for prescribing opioids for pain—United States. MMWR Recomm Rep Morb Mortal Wkly Rep Recomm Rep 71(3):1–95. https://doi.org/10.15585/MMWR.RR7103A1

Drozdov VN, Kim VA, Tkachenko EV, Varvanina GG (2012) Influence of a specific ginger combination on gastropathy conditions in patients with osteoarthritis of the knee or hip. J Altern Complement Med 18(6):583–588. https://doi.org/10.1089/ACM.2011.0202

Drummond EM, Harbourne N, Marete E, Martyn D, Jacquier J, O'Riordan D, Gibney ER (2013) Inhibition of proinflammatory biomarkers in THP1 macrophages by polyphenols derived from chamomile. Meadowsweet Willow Bark Phytother Res 27(4):588–594. https://doi.org/10.1002/PTR.4753

Dulf FV, Oroian I, Vodnar DC, Socaciu C, Pintea A (2013) Lipid classes and fatty acid regiodistribution in triacylglycerols of seed oils of two sambucus species (S. nigra L. and S. ebulus L.). Molecules 18(10):11768–11782. https://doi.org/10.3390/MOLECULES181011768

Durham P, Papapetropoulos S (2013) Biomarkers associated with migraine and their potential role in migraine management. Headache J Head Face Pain 53(8):1262–1277. https://doi.org/10.1111/HEAD.12174

Edmonds K (ed) (2012) Dewhurst's textbook of obstetrics and gynaecology, 8th edn. Wiley, New Jersey

Ekambaram S, Perumal SS, Subramanian V (2010) Evaluation of antiarthritic activity of *Strychnos potatorum* Linn seeds in Freund's adjuvant induced arthritic rat model. BMC Complement Altern Med. https://doi.org/10.1186/1472-6882-10-56

Eshghi F, Hosseinimehr SJ, Rahmani N, Khademloo M, Norozi MS, Hojati O (2010) Effects of aloe vera cream on posthemorrhoidectomy pain and wound healing: results of a randomized, blind, placebo-control study. J Altern Complement Med 16(6):647–650. https://doi.org/10.1089/ACM.2009.0428

Fan GW, Gao XM, Wang H, Zhu Y, Zhang J, Hu LM, Su YF, Kang LY, Zhang BL (2009a) The anti-inflammatory activities of Tanshinone IIA, an active component of TCM, are mediated by estrogen receptor activation and inhibition of iNOS. J Steroid Biochem Mol Biol 113(3–

5):275–280. https://doi.org/10.1016/J.JSBMB.2009.01.011

Fan L, Zhao HY, Xu M, Zhou L, Guo H, Han J, Wang BR, Guo DA (2009b) Qualitative evaluation and quantitative determination of 10 major active components in Carthamus tinctorius L by high-performance liquid chromatography coupled with diode array detector. J Chromatogr A 1216(11):2063–2070. https://doi.org/10.1016/J.CHROMA.2008.03.046

Farzaei MH, Farzaei F, Abdollahi M, Abbasabadi Z, Abdolghaffari AH, Mehraban B (2016) A mechanistic review on medicinal plants used for rheumatoid arthritis in traditional Persian medicine. J Pharm Pharmacol 68(10):1233–1248. https://doi.org/10.1111/JPHP.12606

Fiebich BL, Fiebich BL, Heinrich M, Hiller KO, Kammerer N (2001) Inhibition of TNF-$α$ synthesis in LPS-stimulated primary human monocytes by Harpagophytum extract SteiHap 69. Phytomedicine 8(1):28–30. https://doi.org/10.1078/0944-7113-00002

Finnerup NB, Sindrup SH, Jensen TS (2010) The evidence for pharmacological treatment of neuropathic pain. Pain 150(3):573–581. https://doi.org/10.1016/J.PAIN.2010.06.019

Finnerup NB, Attal N, Haroutounian S, McNicol E, Baron R, Dworkin RH, Gilron I, Haanpää M, Hansson P, Jensen TS, Kamerman PR, Lund K, Moore A, Raja SN, Rice ASC, Rowbotham M, Sena E, Siddall P, Smith BH, Wallace M (2015) Pharmacotherapy for neuropathic pain in adults: A systematic review and meta-analysis. Lancet Neurol 14(2):162–173. https://doi.org/10.1016/S1474-4422(14)70251-0

Forouzanfar F, Bazzaz BSF, Hosseinzadeh H (2014) Black cumin (Nigella sativa) and its constituent (thymoquinone): a review on antimicrobial effects. Iran J Basic Med Sci 17(12):938–938

Funk JL, Frye JB, Oyarzo JN, Zhang H, Timmermann BN (2010) Anti-arthritic effects and toxicity of the essential oils of turmeric (*Curcuma longa* L.). J Agric Food Chem 58(2):842–849. https://doi.org/10.1021/jf9027206

Gaire BP, Kwon OW, Park SH, Chun K-H, Kim SY, Shin DY, Choi JW (2015) Neuroprotective effect of 6-paradol in focal cerebral ischemia involves the attenuation of neuroinflammatory responses in activated microglia. PLoS ONE 10(3):e0120203–e0120203. https://doi.org/10.1371/JOURNAL.PONE.0120203

Galeotti N, Vivoli E, Bilia AR, Bergonzi MC, Bartolini A, Ghelardini C (2010a) A prolonged protein kinase C-mediated, opioid-related antinociceptive effect of St John's wort in mice. J Pain 11(2):149–159. https://doi.org/10.1016/J.JPAIN.2009.06.013

Galeotti N, Ghelardini C (2013) St. John's wort reversal of meningeal nociception: a natural therapeutic perspective for migraine pain. Phytomedicine 20(10):930–938. https://doi.org/10.1016/J.PHYMED.2013.03.007

Galeotti N, Vivoli E, Bilia AR, Vincieri FF, Ghelardini C (2010b) St John's Wort reduces neuropathic pain through a hypericin-mediated inhibition of the protein kinase Cγ and ε activity. Biochem Pharmacol 79(9):1327–1336. https://doi.org/10.1016/J.BCP.2009.12.016

Ganesan K, Sehgal PK, Mandal AB, Sayeed S (2011) Protective effect of withania somnifera and cardiospermum halicacabum extracts against collagenolytic degradation of collagen. Appl Biochem Biotechnol 165(3–4):1075–1091. https://doi.org/10.1007/S12010-011-9326-8

Gao S, Wang Q, Tian XH, Li HL, Shen YH, Xu XK, Wu GZ, Hu ZL, Zhang WD (2017) Total sesquiterpene lactones prepared from Inula helenium L. has potentials in prevention and therapy of rheumatoid arthritis. J Ethnopharmacol 196:39–46. https://doi.org/10.1016/J.JEP.2016.12.020

García-Martínez O, De Luna-Bertos E, Ramos-Torrecillas J, Manzano-Moreno FJ, Ruiz C (2015) Repercussions of NSAIDS drugs on bone tissue: the osteoblast. Life Sci 123:72–77. https://doi.org/10.1016/J.LFS.2015.01.009

Gardiner P, Buettner C, Davis RB, Phillips RS, Kemper KJ (2008) Factors and common conditions associated with adolescent dietary supplement use: an analysis of the national health and nutrition examination survey (NHANES). BMC Complement Altern Med 8:9–9. https://doi.org/10.1186/1472-6882-8-9

Garland EL (2014) Treating chronic pain: the need for non-opioid options. Expert Rev Clin Pharmacol 7(5):545–550. https://doi.org/10.1586/17512433.2014.928587

Gedin F, Skeppholm M, Burström K, Sparring V, Tessma M, Zethraeus N (2017) Effectiveness, costs and cost-effectiveness of chiropractic care and physiotherapy compared with information and advice in the treatment of non-specific chronic low back pain: study protocol for a randomised controlled trial. Trials 18:613. https://doi.org/10.1186/S13063-017-2351-3

Genizi J, Srugo I, Kerem NC (2013) The cross- ethnic variations in the prevalence of headache and other somatic complaints among adolescents in Northern Israel. J Headache Pain 14(1):1–6. https://doi.org/10.1186/1129-2377-14-21

Ghasemzadeh MR, Amin B, Mehri S, Mirnajafi-Zadeh SJ, Hosseinzadeh H (2016) Effect of alcoholic extract of aerial parts of *Rosmarinus officinalis* L. on pain, inflammation and apoptosis induced by chronic constriction injury (CCI) model of neuropathic pain in rats. J Ethnopharmacol 194:117–130. https://doi.org/10.1016/J.JEP.2016.08.043

Ghasemzadeh Rahbardar M, Amin B, Mehri S, Mirnajafi-Zadeh SJ, Hosseinzadeh H (2017) Anti-inflammatory effects of ethanolic extract of Rosmarinus officinalis L. and rosmarinic acid in a rat model of neuropathic pain. Biomed Pharmacother 86:441–449. https://doi.org/10.1016/J.BIOPHA.2016.12.049

Gibofsky A (2012) Overview of epidemiology, pathophysiology, and diagnosis of rheumatoid arthritis. Am J Manag Care 18:S302–S302

Goadsby PJ, Sprenger T (2010) Current practice and future directions in the prevention and acute management of migraine. Lancet Neurol 9(3):285–298. https://doi.org/10.1016/S1474-4422(10)70005-3

Goetzel RZ, D'Arco M, Thomas J, Wang D, Tabrizi MJ, Roemer EC, Prasad A, Yarborough CM (2015) Measuring the prevalence and incidence of low back pain disorders among American workers in the aerospace and defense industry. J Occup Environ Med 57(9):998–1003. https://doi.org/10.1097/JOM.0000000000000512

Goodacre S, Cross E, Arnold J, Angelini K, Capewell S, Nicholl J (2005) The health care burden of acute chest

pain. Heart 91(2):229–230. https://doi.org/10.1136/HRT.2003.027599

Gosztola B, Sárosi S, Németh E (2010) Variability of the essential oil content and composition of chamomile (*Matricaria recutita* L.) affected by weather conditions. Nat. Product Commun. 5(3):1934578X1000500325

Gothai S, Arulselvan P, Tan WS, Fakurazi S (2016) Wound healing properties of ethyl acetate fraction of *Moringa oleifera* in normal human dermal fibroblasts. J Intercult Ethnopharmacol 5(1):1–6. https://doi.org/10.5455/JICE.20160201055629

Grover A, Shandilya A, Punetha A, Bisaria VS, Sundar D (2010) Inhibition of the NEMO/IKKβ association complex formation, a novel mechanism associated with the NF-κB activation suppression by Withania somnifera's key metabolite withaferin A. BMC Genom. https://doi.org/10.1186/1471-2164-11-S4-S25

Grover JK, Yadav SP (2004) Pharmacological actions and potential uses of *Momordica charantia*: a review. J Ethnopharmacol 93(1):123–132

Gründemann C, Lengen K, Sauer B, Garcia-Käufer M, Zehl M, Huber R (2014) *Equisetum arvense* (common horsetail) modulates the function of inflammatory immunocompetent cells. BMC Complement Altern Med 14:283–283. https://doi.org/10.1186/1472-6882-14-283

Grzanna R, Lindmark L, Frondoza CG (2005) Ginger—an herbal medicinal product with broad anti-inflammatory actions. J Med Food 8(2):125–132. https://doi.org/10.1089/JMF.2005.8.125

Guha P, Paul S, Das A, Halder B, Bhattacharjee S, Chaudhuri TK (2014) Analyses of human and rat clinical parameters in rheumatoid arthritis raise the possibility of use of crude aloe vera gel in disease amelioration. Immunome Res. https://doi.org/10.4172/1745-7580.1000081

Guo Y, Li Y, Xue L, Severino RP, Gao S, Niu J, Qin LP, Zhang D, Brömme D (2014) Salvia miltiorrhiza: an ancient Chinese herbal medicine as a source for anti-osteoporotic drugs. J Ethnopharmacol 155(3):1401–1416. https://doi.org/10.1016/J.JEP.2014.07.058

Gupta VK, Malhotra S (2012) Pharmacological attribute of Aloe vera: revalidation through experimental and clinical studies. Ayu 33(2):193–193. https://doi.org/10.4103/0974-8520.105237

Gupta S, Mehrotra S, Villalón CM, Perusquía M, Saxena PR, MaassenVanDenBrink A (2007) Potential role of female sex hormones in the pathophysiology of migraine. Pharmacol Ther 113(2):321–340. https://doi.org/10.1016/J.PHARMTHERA.2006.08.009

Gupta S, Mishra KP, Singh SB, Ganju L (2017) Inhibitory effects of andrographolide on activated macrophages and adjuvant-induced arthritis. Inflammopharmacology 26(2):447–456. https://doi.org/10.1007/S10787-017-0375-7

Gupta A, Singh S (2014) Evaluation of anti-inflammatory effect of *Withania somnifera* root on collagen-induced arthritis in rats. Pharm Biol 52(3):308–320. https://doi.org/10.3109/13880209.2013.835325

Gurley BJ, Gardner SF, Hubbard MA, Keith Williams D, Brooks Gentry W, Cui Y, Ang CYW (2005) Clinical assessment of effects of botanical supplementation on cytochrome P450 phenotypes in the elderly: St John's wort, garlic oil, Panax ginseng and Ginkgo biloba. Drugs Aging 22(6):525–539. https://doi.org/10.2165/00002512-200522060-00006

Gurung S, Škalko-Basnet N (2009) Wound healing properties of *Carica papaya* latex: in vivo evaluation in mice burn model. J Ethnopharmacol 121(2):338–341. https://doi.org/10.1016/J.JEP.2008.10.030

Güven M, Kara H (2016) Some chemical and physical properties, fatty acid composition and bioactive compounds of wheat germ oils extracted from different wheat cultivars. J Agric Sci 22:433–443

Hadi V, Kheirouri S, Alizadeh M, Khabbazi A, Hosseini H (2016) Effects of Nigella sativa oil extract on inflammatory cytokine response and oxidative stress status in patients with rheumatoid arthritis: a randomized, double-blind, placebo-controlled clinical trial. Avicenna J Phytomed 6(1):34–43

Haghighi AB, Motazedian S, Rezaii R, Mohammadi F, Salarian L, Pourmokhtari M, Khodaei S, Vossoughi M, Miri R (2010) Cutaneous application of menthol 10% solution as an abortive treatment of migraine without aura: a randomised, double-blind, placebo-controlled, crossed-over study. Int J Clin Pract 64(4):451–456. https://doi.org/10.1111/J.1742-1241.2009.02215.X

Haghighian MK, Alipoor B, Mahdavi AM, Sadat BE, Jafarabadi MA, Moghaddam A (2015) Effects of sesame seed supplementation on inflammatory factors and oxidative stress biomarkers in patients with knee osteoarthritis. Acta Med Iran 53(4):207–213

Hajhashemi V, Ghannadi A, Heidari AH (2012) Anti-inflammatory and wound healing activities of Aloe littoralis in rats. Res Pharm Sci 7(2):73–78

Hamidpour R, Hamidpour S, Hamidpour M, Shahlari M (2013) Frankincense (乳香 Rǔ Xiāng; Boswellia Species): from the selection of traditional applications to the novel phytotherapy for the prevention and treatment of serious diseases. J Tradit Complement Med 3(4):221–226. https://doi.org/10.4103/2225-4110.119723

Han SY, Li HX, Ma X, Zhang K, Ma ZZ, Tu PF (2009) Protective effects of purified safflower extract on myocardial ischemia in vivo and in vitro. Phytomedicine 16(8):694–702. https://doi.org/10.1016/J.PHYMED.2009.02.019

Han W, Zhu Y, Chen B, Liu S, Dang Y (2018) 7,8,3′-Trihydroxyflavone ameliorate oxidative stress in vivo and promotes neurite regeneration in vitro in rat retinal ganglion cells. Eur J Pharmacol 833:283–289. https://doi.org/10.1016/J.EJPHAR.2018.06.007

Hashemi SA, Madani SA, Abediankenari S (2015) The review on properties of aloe vera in healing of cutaneous wounds. BioMed Res Int. https://doi.org/10.1155/2015/714216

Hasnaoui A, ElVray M, Richard A, Nachit-Ouinekh F, Boureau F, Group FTM (2003) Assessing the severity of migraine: development of the MIGSEV Scale. Headache J Head Face Pain 43(6):628–635. https://doi.org/10.1046/J.1526-4610.2003.03105.X

He J, Yang YN, Jiang JS, Feng ZM, Zhang PC (2014a) Safflofl avonesides A and B, two rearranged derivatives of flavonoid C -glycosides with A furan-tetrahydrofuran ring from *Carthamus tinctorius*. Org Lett 16(21):5714–5717. https://doi.org/10.1021/OL502789X/SUPPL_FILE/OL502789X_SI_001.PDF

He J, Yang Y-N, Jiang J, Feng Z-M, Zhang P-C (2014b) Saffloflavonesides A and B, two rearranged derivatives of flavonoid C-glycosides with a furan-tetrahydrofuran ring from *Carthamus tinctorius*. Org Lett 16(21):5714–5717. https://doi.org/10.1021/OL502789X

He X, Wang J, Li M, Hao D, Yang Y, Zhang C, He R, Tao R (2014c) *Eucommia ulmoides* Oliv.: ethnopharmacology, phytochemistry and pharmacology of an important traditional Chinese medicine. J Ethnopharmacol 151(1):78–92. https://doi.org/10.1016/j.jep.2013.11.023

Headache Classification Committee of the International Headache Society (2013) The international classification of headache disorders, 3rd edition (beta version). Cephalalgia 33(9):629–808. https://doi.org/10.1177/0333102413485658

Heidarifar R, Mehran N, Heidari A, Tehran HA, Koohbor M, Mansourabad MK (2014) Effect of Dill (*Anethum graveolens*) on the severity of primary dysmenorrhea in compared with mefenamic acid: a randomized, double-blind trial. J Res Med Sci 19(4):326–330

Heinrich M, Kufer J, Leonti M, Pardo-de-Santayana M (2006) Ethnobotany and ethnopharmacology—interdisciplinary links with the historical sciences. J Ethnopharmacol 107 (2):157–160. https://doi.org/10.1016/J.JEP.2006.05.035

Hemshekhar M, Thushara RM, Jnaneshwari S, Devaraja S, Kemparaju K, Girish KS (2012) Attenuation of adjuvant-induced arthritis by dietary sesamol via modulation of inflammatory mediators, extracellular matrix degrading enzymes and antioxidant status. Eur J Nutr 52(7):1787–1799. https://doi.org/10.1007/S00394-012-0482-6

Heshmati A, Dolatian M, Mojab F, Shakeri N, Nikkhah S, Mahmoodi Z (2016) The effect of peppermint (*Mentha piperita*) capsules on the severity of primary dysmenorrhea. J Herb Med 6(3):137–141. https://doi.org/10.1016/J.HERMED.2016.05.001

Heyninck K, Lahtela-Kakkonen M, Van Der Veken P, Haegeman G, Berghe WV (2014) Withaferin A inhibits NF-kappaB activation by targeting cysteine 179 in IKKβ. Biochem Pharmacol 91(4):501–509. https://doi.org/10.1016/J.BCP.2014.08.004

Higgins JP, Green S, Collaboration C (2008) Cochrane handbook for systematic reviews of interventions: Wiley online library

Ho JHC, Hong CY (2011) Salvianolic acids: small compounds with multiple mechanisms for cardiovascular protection. J Biomed Sci. https://doi.org/10.1186/1423-0127-18-30

Hochberg MC, Altman RD, April KT, Benkhalti M, Guyatt G, McGowan J, Towheed T, Welch V, Wells G, Tugwell P (2012) America College of Rheumatology 2012 recommendations for the use of nonpharmacologic and pharmacologic therapies in osteoarthritis of the hand, hip, and knee. Arthritis Care Res 64(4):465–474. https://doi.org/10.1002/ACR.21596

Hootman JM, Helmick CG, Barbour KE, Theis KA, Boring MA (2016) Updated projected prevalence of self-reported doctor-diagnosed arthritis and arthritis-attributable activity limitation among US adults, 2015–2040. Arthritis Rheumatol 68(7):1582–1587. https://doi.org/10.1002/ART.39692

Hoscheid J, Cardoso MLC (2015) Sucupira as a potential plant for arthritis treatment and other diseases. Arthritis 2015. https://downloads.hindawi.com/archive/2015/379459.pdf

Hou C-W, Lin Y-T, Chen Y-L, Wang Y-H, Chou J-L, Ping L-Y, Jeng K-C (2013) Neuroprotective effects of carnosic acid on neuronal cells under ischemic and hypoxic stress. Nutr Neurosci 15(6):257–263. https://doi.org/10.1179/1476830512Y.0000000021

Hsu DZ, Chen SJ, Chu PY, Liu MY (2013) Therapeutic effects of sesame oil on monosodium urate crystal-induced acute inflammatory response in rats. Springerplus 2(1):1–10. https://doi.org/10.1186/2193-1801-2-659

Hsu DZ, Chu PY, Jou IM (2016) Daily sesame oil supplement attenuates joint pain by inhibiting muscular oxidative stress in osteoarthritis rat model. J Nutr Biochem 29:36–40. https://doi.org/10.1016/J.JNUTBIO.2015.10.007

Hu C-X, Hu K-Y, Wang J-F (2020) Potential role of the compound Eucommia bone tonic granules in patients with osteoarthritis and osteonecrosis: a retrospective study. World J Clin Cases 8(1):53–53. https://doi.org/10.12998/WJCC.V8.I1.46

Huang THW, Tran VH, Duke RK, Tan S, Chrubasik S, Roufogalis BD, Duke CC (2006) Harpagoside suppresses lipopolysaccharide-induced iNOS and COX-2 expression through inhibition of NF-$κ$B activation. J Ethnopharmacol 104(1–2):149–155. https://doi.org/10.1016/J.JEP.2005.08.055

Huang RY, Chu YL, Jiang ZB, Chen XM, Zhang X, Zeng X (2014a) Glycyrrhizin suppresses lung adenocarcinoma cell growth through inhibition of thromboxane synthase. Cell Physiol Biochem Int J Exp Cell Physiol Biochem Pharmacol 33(2):375–388. https://doi.org/10.1159/000356677

Huang S-H, Lee C-H, Wang H-M, Chang Y-W, Lin C-Y, Chen C-Y, Chen Y-H (2014b) 6-dehydrogingerdione restrains lipopolysaccharide-induced inflammatory responses in RAW 264.7 macrophages. J Agric Food Chem 62 (37):9171–9179. https://doi.org/10.1021/JF501665V

Hucho T, Levine JD (2007) Signaling pathways in sensitization: toward a nociceptor cell biology. Neuron 55(3):365–376. https://doi.org/10.1016/J.NEURON.2007.07.008

Hyrich KL, Watson KD, Silman AJ, Symmons DPM, Register BSRB (2006) Predictors of response to anti-TNF-$α$ therapy among patients with rheumatoid arthritis: results from the British society for rheumatology biologics register. Rheumatology 45(12):1558–1565. https://doi.org/10.1093/RHEUMATOLOGY/KEL149

Ilmawati RR, Amin AZ, Amin M (2017a) Alliin as a natural bioactive from single bulb garlic (*Allium sativum*) for nitric oxide (NO) increasing in atherosclerotic process based on insilico screening. Biol Med Nat Product Chem 6(2):59–62. https://doi.org/10.14421/BIOMEDICH.2017.62.59-62

Inanmdar W, Sultana A, Mubeen U, Rahman K (2016) Clinical efficacy of *Trigonella foenum graecum* (Fenugreek) and dry cupping therapy on intensity of pain in patients with primary dysmenorrhea. Chin J Integr Med. https://doi.org/10.1007/S11655-016-2259-X

Izzo AA, Borrelli F, Capasso R, Di Marzo V, Mechoulam R (2009) Non-psychotropic plant cannabinoids: new therapeutic opportunities from an ancient herb. Trends

Pharmacol Sci 30(10):515–527. https://doi.org/10.1016/J.TIPS.2009.07.006

Jaafarpour M, Hatefi M, Najafi F, Khajavikhan J, Khani A (2015b) The effect of cinnamon on menstrual bleeding and systemic symptoms with primary dysmenorrhea. Iran Red Crescent Med J 17(4):e27032–e27032. https://doi.org/10.5812/IRCMJ.17(4)2015.27032

Jaafarpour M, Hatefi M, Khani A, Khajavikhan J (2015a) Comparative effect of cinnamon and ibuprofen for treatment of primary dysmenorrhea: a randomized double-blind clinical trial. J Clin Diagnostic Res JCDR 9(4):QC07. https://doi.org/10.7860/JCDR/2015/12084.5783

Jahromi B, Pirvulescu I, Candido KD, Knezevic NN (2021) Herbal medicine for pain management: efficacy and drug interactions. Pharmaceutics 13(2):1–43. https://doi.org/10.3390/PHARMACEUTICS13020251

Jain V, Pareek A, Ratan Y, Singh N (2015) Standardized fruit extract of *Momordica charantia* L. protect against vincristine induced neuropathic pain in rats by modulating GABAergic action, antimitotoxic, NOS inhibition, anti-inflammatory and antioxidative activity. S Afr J Bot 97:123–132. https://doi.org/10.1016/J.SAJB.2014.12.010

Jain V, Pareek A, Paliwal N, Ratan Y, Jaggi AS, Singh N (2014) Antinociceptive and antiallodynic effects of *Momordica charantia* L. in tibial and sural nerve transection-induced neuropathic pain in rats. Nutr Neurosci 17(2):88–96. https://doi.org/10.1179/1476830513Y.0000000069

Jalali FSS, Tajik H, Hadian M (2010) Efficacy of topical application of alcoholic extract of yarrow in the healing process of experimental burn wounds in rabbit. Comp Clin Pathol 21(2):177–181. https://doi.org/10.1007/S00580-010-1081-7

Jalalpure SS, Agrawal N, Patil MB, Chimkode R, Tripathi A (2008) Antimicrobial and wound healing activities of leaves of *Alternanthera sessilis* Linn. Int J Green Pharm. https://doi.org/10.22377/IJGP.V2I3.18

Jales STL, Barbosa RDM, Silva GRD, Severino P, Moura TFADL (2021) Natural polysaccharides from *Aloe vera* L. gel (*Aloe barbadensis* Miller): processing techniques and analytical methods. Polysaccharides. https://doi.org/10.1002/9781119711414.CH1

Jamil SS, Nizami Q, Salam M (2007) *Centella asiatica* (Linn.) Urban—a review. Indian J Nat Products Resour 158–170

Jana S, Shekhawat GS (2010) Anethum graveolens: an Indian traditional medicinal herb and spice. Pharmacogn Rev 4(8):179–184. https://doi.org/10.4103/0973-7847.70915

Jenabi E, Fereidoony B (2015) Effect of *Achillea millefolium* on relief of primary dysmenorrhea: a double-blind randomized clinical trial. J Pediatr Adolesc Gynecol 28(5):402–404. https://doi.org/10.1016/J.JPAG.2014.12.008

Jeong JB, Ju SY, Park JH, Lee JR, Yun KW, Kwon ST, Lim JH, Chung GY, Jeong HJ (2009) Antioxidant activity in essential oils of *Cnidium officinale* makino and *Ligusticum chuanxiong* hort and their inhibitory effects on DNA damage and apoptosis induced by ultraviolet B in mammalian cell. Cancer Epidemiol 33(1):41–46. https://doi.org/10.1016/J.CANEP.2009.04.010

Jeong JW, Lee HH, Lee KW, Kim KY, Kim SG, Hong SH, Kim G, Park C, Kim HK, Choi YW, Choi YH (2016a) Mori folium inhibits interleukin-1β-induced expression of matrix metalloproteinases and inflammatory mediators by suppressing the activation of NF-κB and p38 MAPK in SW1353 human chondrocytes. Int J Mol Med 37(2):452–460. https://doi.org/10.3892/IJMM.2015.2443

Jeong YY, Ryu JH, Shin J-H, Kang MJ, Kang JR, Han J, Kang D (2016b) Comparison of anti-oxidant and anti-inflammatory effects between fresh and aged black garlic extracts. Molecules 21(4):430. https://doi.org/10.3390/MOLECULES21040430

Jermini M, Dubois J, Rodondi PY, Zaman K, Buclin T, Csajka C, Orcurto A, Rothuizen EL (2019) Complementary medicine use during cancer treatment and potential herb-drug interactions from a cross-sectional study in an academic centre. Sci Rep 9(1):5078–5078. https://doi.org/10.1038/S41598-019-41532-3

Jha NK (2007) Mimosa pudica: lajjalu. Phytopharm 8:3–8

Ji K, Fang L, Zhao H, Li Q, Shi Y, Xu C, Wang Y, Du L, Wang J, Liu Q (2017) Ginger oleoresin alleviated γ-ray irradiation-induced reactive oxygen species via the Nrf2 protective response in human mesenchymal stem cells. Oxidative Med Cell Longev 2017:1480294

Jiang J-S, He J, Feng Z-M, Zhang P-C (2010) Two new quinochalcones from the florets of *Carthamus tinctorius*. Org Lett 12(6):1196–1199. https://doi.org/10.1021/OL902971W

Jiang X, Qu Q, Li M, Miao S, Li X, Cai W (2014) Horsetail mixture on rheumatoid arthritis and its regulation on TNF-α and IL-10. Pak J Pharm Sci 27(6):2019–2023

Jimenez P, Cabrero P, Basterrechea JE, Tejero J, Cordoba-Diaz D, Cordoba-Diaz M, Girbes T (2014a) Effects of short-term heating on total polyphenols, anthocyanins, antioxidant activity and lectins of different parts of dwarf elder (*Sambucus ebulus* L). Plant Foods Hum Nutr 69(2):168–174. https://doi.org/10.1007/S11130-014-0417-X

Jimenez P, Cabrero P, Basterrechea JE, Tejero J, Cordoba-Diaz D, Cordoba-Diaz M, Girbes T (2014b) Effects of short-term heating on total polyphenols, anthocyanins, antioxidant activity and lectins of different parts of dwarf elder (*Sambucus ebulus* L.). Plant Foods Hum Nutr 69(2):168–174. https://doi.org/10.1007/S11130-014-0417-X

Joe B, Vijaykumar M, Lokesh BR (2010) Biological properties of curcumin-cellular and molecular mechanisms of action. Crit Rev Food Sci Nutr 44(2):97–111. https://doi.org/10.1080/10408690490424702

Juárez-Vázquez MDC, Carranza-Álvarez C, Alonso-Castro AJ, González-Alcaraz VF, Bravo-Acevedo E, Chamarro-Tinajero FJ, Solano E (2013) Ethnobotany of medicinal plants used in Xalpatlahuac, Guerrero, México. J Ethnopharmacol 148(2):521–527. https://doi.org/10.1016/J.JEP.2013.04.048

Julius D, Basbaum AI (2001) Molecular mechanisms of nociception. Nature 413(6852):203–210. https://doi.org/10.1038/35093019

Jurenka JS (2009) Anti-inflammatory properties of curcumin, a major constituent of Curcuma longa: a review of preclinical and clinical research. Altern Med Rev J Clin Ther 14(2):141–153

Kamatou GPP, Vermaak I, Viljoen AM, Lawrence BM (2013) Menthol: a simple monoterpene with remarkable biological properties. Phytochemistry 96:15–25. https://doi.org/10.1016/J.PHYTOCHEM.2013.08.005

Kanter M (2007) Effects of *Nigella sativa* and its major constituent, thymoquinone on sciatic nerves in experimental diabetic neuropathy. Neurochem Res 33(1):87–96. https://doi.org/10.1007/S11064-007-9419-5

Kashefi F, Khajehei M, Tabatabaeichehr M, Alavinia M, Asili J (2014) Comparison of the effect of ginger and zinc sulfate on primary dysmenorrhea: a placebo-controlled randomized trial. Pain Manag Nurs 15(4):826–833. https://doi.org/10.1016/J.PMN.2013.09.001

Kasper S, Caraci F, Forti B, Drago F, Aguglia E (2010) Efficacy and tolerability of *Hypericum* extract for the treatment of mild to moderate depression. Eur Neuropsychopharmacol 20(11):747–765. https://doi.org/10.1016/J.EURONEURO.2010.07.005

Kassem AA, Labib GS (2016) Flash dissolving sublingual almotriptan malate lyotabs for management of migraine. Int J Pharm Pharm Sci 9(1):125. https://doi.org/10.22159/IJPPS.2017V9I1.15489

Kasture VS, Kasture SB, Chopde CT (2002) Anticonvulsive activity of Butea monosperma flowers in laboratory animals. Pharmacol Biochem Behav 72(4):965–972

Kaur S, Muthuraman A (2019) Ameliorative effect of gallic acid in paclitaxel-induced neuropathic pain in mice. Toxicol Rep 6:505–513

Kaur G, Bali A, Singh N, Jaggi AS (2015) Ameliorative potential of Ocimum sanctum in chronic constriction injury-induced neuropathic pain in rats. An Acad Bras Ciênc 87(1):417–429. https://doi.org/10.1590/0001-3765201520130008

Kaur S, Lakshmanan P (2015) Hibiscus rosa-sinesis leaves polysaccharide as solubility enhancing agent for poorly soluble drug. Pharm Pharmacol Int J. https://doi.org/10.15406/PPIJ.2015.02.00040

Kazemi M (2015a) Phenolic profile, antioxidant capacity and anti-inflammatory activity of *Anethum graveolens* L. essential oil. Nat Product Res 29(6):551–553. https://doi.org/10.1080/14786419.2014.951934

Kazemi M (2015b) Phytochemical composition of *Thymus vulgaris* L. essential oil. J Essent Oil Bear Plants 18 (3):751–753. https://doi.org/10.1080/0972060X.2014.985733

Kemper FH (2011) chromatographic fingerprint analysis of herbal medicines: thin-layer and high performance liquid chromatography of chinese drugs. Int J Phytother Phytopharmacol 18(14):1292–1293

Khajuria A, Gupta A, Suden P, Singh S, Malik F, Singh J, Gupta BD, Suri KA, Srinivas VK, Ella K, Qazi GN (2008) Immunomodulatory activity of biopolymeric fraction BOS 2000 from Boswellia serrata. Phytother Res PTR 22 (3):340–348. https://doi.org/10.1002/PTR.2320

Khalid M, Tufail S, Aslam Z, Butt A (2017) Osteoarthritis: from complications to cure. Int J Clin Rheumatol. https://doi.org/10.4172/1758-4272.1000152

Khan MA, Subramaneyaan M, Arora VK, Banerjee BD, Ahmed RS (2015) Effect of *Withania somnifera* (Ashwagandha) root extract on amelioration of oxidative stress and autoantibodies production in collagen-induced arthritic rats. J Complement Integr Med 12(2):117–125. https://doi.org/10.1515/JCIM-2014-0075

Khan MA, Ahmed RS, Chandra N, Arora VK, Ali A (2019) In vivo, extract from withania somnifera root ameliorates arthritis via regulation of key immune mediators of inflammation in experimental model of arthritis. AntiInflammatory Antiallergy Agents Med Chem 18 (1):55–70. https://doi.org/10.2174/1871523017666181116092934

Khayyal MT, El-Ghazaly MA, Abdallah DM, Okpanyi SN, Kelber O, Weiser D (2005) Mechanisms involved in the anti-inflammatory effect of a standardized willow bark extract. Arzneimittelforschung 55(11):677–687. https://doi.org/10.1055/S-0031-1296917

Khyade MS, Vaikos NP (2011) Phytochemical and antibacterial properties of leaves of *Alstonia scholaris* R. Br. Afr J Biotechnol 8(22):6434–6436. https://doi.org/10.4314/ajb.v8i22.66163

Kizhakkedath R (2013) Clinical evaluation of a formulation containing *Curcuma longa* and *Boswellia serrata* extracts in the management of knee osteoarthritis. Mol Med Rep 8 (5):1542–1548. https://doi.org/10.3892/MMR.2013.1661

Klepser TB, Klepser ME (1999) Unsafe and potentially safe herbal therapies. Am J Health Syst Pharm 56(2):125–138. https://doi.org/10.1093/AJHP/56.2.125

Koh W, Shin JS, Lee J, Lee IH, Lee SK, Ha IH, Chung HJ (2017) Anti-inflammatory effect of cortex eucommiae via modulation of the toll-like receptor 4 pathway in lipopolysaccharide-stimulated RAW 264.7 macrophages. J Ethnopharmacol 209:255–263. https://doi.org/10.1016/J.JEP.2017.08.001

Köhler BM, Günther J, Kaudewitz D, Lorenz H (2019) Current therapeutic options in the treatment of rheumatoid arthritis. J Clin Med 8(7):938–938. https://doi.org/10.3390/JCM8070938

Kolasinski SL, Neogi T, Hochberg MC, Oatis C, Guyatt G, Block J, Callahan L, Copenhaver C, Dodge C, Felson D, Gellar K, Harvey WF, Hawker G, Herzig E, Kwoh CK, Nelson AE, Samuels J, Scanzello C, White D, Reston J (2020) 2019 American college of rheumatology/arthritis foundation guideline for the management of osteoarthritis of the hand, hip, and knee. Arthritis Rheumatol 72 (2):220–233. https://doi.org/10.1002/ART.41142

Kopustinskiene DM, Bernatonyte U, Maslii Y, Herbina N, Bernatoniene J (2022) Natural herbal non-opioid topical pain relievers-comparison with traditional therapy. Pharmaceutics 14(12):2648. https://doi.org/10.3390/PHARMACEUTICS14122648

Kowalski R, Sugier D, Sugier P, Ko\lodziej B (2015) Evaluation of the chemical composition of essential oils with respect to the maturity of flower heads of *Arnica montana* L. and *Arnica chamissonis* Less. Cultivated for industry. Ind Crops Prod 76:857–865

Kremer M, Salvat E, Muller A, Yalcin I, Barrot M (2016) Antidepressants and gabapentinoids in neuropathic pain: mechanistic insights. Neuroscience 338:183–206. https://doi.org/10.1016/J.NEUROSCIENCE.2016.06.057

Krishnasamy K, Sivanandy P, Rosman AN, DiyanaShapheri A, TengChew T, Jia N, Lau X, Zi M, Yeong Y, Ong M, Muniirah B, HaaniMeetooa U, Ng E, Govindarajan A, Shanmugasundaram A (2020) Comparison of efficacy and safety of newer drugs approved for the treatment of migraine disorder: a review. Artic Int J Pharm Pharm Sci. https://doi.org/10.22159/ijpps.2020v12i7.37440

Kshirsagar AD, Panchal PV, Harle UN, Nanda RK, Shaikh HM (2014) Anti-inflammatory and antiarthritic activity of anthraquinone derivatives in rodents. Int J Inflamm. https://doi.org/10.1155/2014/690596

Kulkarni YA, Agarwal S, Garud MS (2015) Effect of Jyotishmati (*Celastrus paniculatus*) seeds in animal models of pain and inflammation. J Ayurveda Integr Med 6(2):88–88. https://doi.org/10.4103/0975-9476.146540

Kumari OS, Rao NB, Reddy VK (2015) Phyto-chemical analysis and antimicrobial activity of Hibiscus rosa-sinensis. World J Pharm Pharm Sci 4(5):766–771

Lahiri M, Morgan C, Symmons DPM, Bruce IN (2012) Modifiable risk factors for RA: Prevention, better than cure? Rheumatology 51(3):499–512. https://doi.org/10.1093/RHEUMATOLOGY/KER299

Lane NE, Shidara K, Wise BL (2017) Osteoarthritis year in review 2016: clinical. Osteoarthr Cartil 25(2):209–215. https://doi.org/10.1016/J.JOCA.2016.09.025

Lantz RC, Chen GJ, Sarihan M, Sólyom AM, Jolad SD, Timmermann BN (2007) The effect of extracts from ginger rhizome on inflammatory mediator production. Phytomedicine 14(2–3):123–128. https://doi.org/10.1016/J.PHYMED.2006.03.003

Last AR, Hulbert K (2009) Chronic low back pain: evaluation and management. Am Fam Phys 79(12):1067–1074

Lazarus GS, Cooper DM, Knighton DR, Margolis DJ, Percoraro RE, Rodeheaver G, Robson MC (1994) Definitions and guidelines for assessment of wounds and evaluation of healing. Wound Repair Regen 2(3):165–170. https://doi.org/10.1046/J.1524-475X.1994.20305.X

Lecour S, Suleman N, Deuchar GA, Somers S, Lacerda L, Huisamen B, Opie LH (2005) Pharmacological preconditioning with tumor necrosis factor-α activates signal transducer and activator of transcription-3 at reperfusion without involving classic prosurvival kinases (Akt and extracellular signal-regulated kinase). Circulation 112 (25):3911–3918. https://doi.org/10.1161/CIRCULATIONAHA.105.581058

Lee HY, Park SH, Lee M, Kim H-J, Ryu SY, Kim ND, Hwang BY, Hong JT, Han S-B, Kim Y (2012) 1-Dehydro-[10]-gingerdione from ginger inhibits IKK$β$ activity for NF-$κ$B activation and suppresses NF-$κ$B-regulated expression of inflammatory genes. Br J Pharmacol 167 (1):128–140. https://doi.org/10.1111/J.1476-5381.2012.01980.X

Lem HW, Lee AC (2017) The effectiveness of ginger compress on non-specific low back pain. J Fundam Appl Sci 9 (6S):1173–1186

Lesjak M, Beara I, Simin N, Pintać D, Majkić T, Bekvalac K, Orčić D, Mimica-Dukić N (2018) Antioxidant and anti-inflammatory activities of quercetin and its derivatives. J Funct Foods 40:68–75. https://doi.org/10.1016/J.JFF.2017.10.047

Lewis MAO (2003) Burket's oral medicine. Diagnosis and treatment, 10th edn. J Orthod 30(4):346. https://doi.org/10.1093/ORTHO/30.4.346

Li S, Yu Y, Yue Y, Zhang Z, Su K (2013) Microbial infection and rheumatoid arthritis. J Clin Cell Immunol 4(6):174. https://doi.org/10.4172/2155-9899.1000174

Li J, Li Z, Zhao J, Wang W, Zhao X, Xu B, Li L, Zhang L, Ren J, Khan IA, Li S (2017a) A novel tropoloisoquinoline alkaloid, neotatarine, from *Acorus calamus* L. Chem Biodivers 14(10):e1700201. https://doi.org/10.1002/cbdv.201700201

Li Y, He S, Tang J, Ding N, Chu X, Cheng L, Ding X, Liang T, Feng S, Rahman SU, Wang X, Wu J (2017b) Andrographolide inhibits inflammatory cytokines secretion in LPS-stimulated RAW2647 cells through suppression of NF-$κ$B/MAPK signaling pathway. Evid-Based Complement Altern Med. https://doi.org/10.1155/2017/8248142

Liao ZT, Pan YF, Huang JL, Huang F, Chi WJ, Zhang KX, Lin ZM, Wu YQ, He WZ, Wu J, Xie XJ, Huang JX, Wei QJ, Li TW, Wu Z, Yu BY, Gu JR (2009) An epidemiological survey of low back pain and axial spondyloarthritis in a Chinese Han population. Scand J Rheumatol 38(6):455–459. https://doi.org/10.3109/03009740902978085

Liguori L, Califano R, Albanese D, Raimo F, Crescitelli A, Di Matteo M (2017) Chemical composition and antioxidant properties of five white onion (*Allium cepa* L.) landraces. J Food Qual. https://doi.org/10.1155/2017/6873651

Lin YL, Wang GJ, Huang CL, Lee YC, Liao WC, Lai WL, Lin YJ, Huang NK (2009) Ligusticum chuanxiong as a potential neuroprotectant for preventing serum deprivation-induced apoptosis in rat pheochromocytoma cells: functional roles of mitogen-activated protein kinases. J Ethnopharmacol 122(3):417–423. https://doi.org/10.1016/J.JEP.2009.02.011

Linden MPM, Woude D, Ioan-Facsinay A, Levarht EWN, Stoeken-Rijsbergen G, Huizinga TWJ, Toes REM, Mil AHMH (2009) Value of anti–modified citrullinated vimentin and third-generation anti–cyclic citrullinated peptide compared with second-generation anti–cyclic citrullinated peptide and rheumatoid factor in predicting disease outcome in undifferentiated arthritis and rh. Arthritis Rheum 60(8):2232–2241. https://doi.org/10.1002/ART.24716

Lipton RB, Göbel H, Einhäupl KM, Wilks K, Mauskop A (2004) Petasites hybridus root (butterbur) is an effective preventive treatment for migraine. Neurology 63 (12):2240–2244. https://doi.org/10.1212/01.WNL.0000147290.68260.11

Lu H, Jiang J, Xie G, Liu W, Yan G (2013) Effects of an aqueous extract of Eucommia on articular cartilage in a rat model of osteoarthritis of the knee. Exp Ther Med 6 (3):684–688. https://doi.org/10.3892/ETM.2013.1223

Luo J, Song W, Yang G, Xu H, Chen K (2015) Compound danshen (*Salvia miltiorrhiza*) dripping pill for coronary heart disease: an overview of systematic reviews. Am J Chin Med 43(1):25–43. https://doi.org/10.1142/S0192415X15500020

Ma Y, Wu H (2012) Chemical constituents of *Sambucus* L. Chin J Org Chem 32(11):2063. https://doi.org/10.6023/cjoc201204025

Ma CH, Wu CH, Jou IM, Tu YK, Hung CH, Chou WC, Chang YC, Hsieh PL, Tsai KL (2019) PKR promotes oxidative stress and apoptosis of human articular chondrocytes by causing mitochondrial dysfunction through p38 MAPK activation—PKR activation causes apoptosis in human chondrocytes. Antioxidants 8(9):370–370. https://doi.org/10.3390/ANTIOX8090370

Madden VJ, O'sullivan P, Fisher J, Malambule B (2013) 'Our training left us unprepared'—two physiotherapists reflections after working with women with low back pain in a rural Zulu community in South Africa. J Commun Health Sci 8(2):1–18

Maghbooli M, Golipour F, Esfandabadi AM, Yousefi M (2014) Comparison between the efficacy of ginger and sumatriptan in the ablative treatment of the common migraine. Phytother Res 28(3):412–415. https://doi.org/10.1002/PTR.4996

Mahdavi M, Taherian M, Maghsoudi H, Taherian R (2018) Potential role of herbal medicine in alleviating pain and inflammation in *Osteoarthritis*: a review. J Cell Mol Anesth 3(1):35–44. https://doi.org/10.22037/JCMA.V3I1.19119

Marcucci E, Bartoloni E, Alunno A, Leone MC, Cafaro G, Luccioli F, Valentini V, Valentini E, Paglia GMCL, Bonifacio AF, Gerli R (2018) Extra-articular rheumatoid arthritis. Reumatismo 70(4):212–224. https://doi.org/10.4081/reumatismo.2018.1106

Martin PR (2010) Behavioral management of migraine headache triggers: learning to cope with triggers. Curr Pain Headache Rep 14(3):221–227. https://doi.org/10.1007/S11916-010-0112-Z

Martyn JAJ, Mao J, Bittner EA (2019) Opioid tolerance in critical illness. N Engl J Med 380(4):365–378. https://doi.org/10.1056/NEJMRA1800222

Masoumi SZ, Asl HR, Poorolajal J, Panah MH, Oliaei SR (2016) Evaluation of mint efficacy regarding dysmenorrhea in comparison with mefenamic acid: a double blinded randomized crossover study. Iran J Nurs Midwifery Res 21(4):363–367. https://doi.org/10.4103/1735-9066.185574

Mateen S, Zafar A, Moin S, Khan AQ, Zubair S (2016) Understanding the role of cytokines in the pathogenesis of rheumatoid arthritis. Clin Chim Acta 455:161–171. https://doi.org/10.1016/J.CCA.2016.02.010

Mathieu D (ed) (2006) Handbook on hyperbaric medicine, vol 27. Springer, New York, p 812

McAlindon TE, Bannuru RR, Sullivan MC, Arden NK, Berenbaum F, Bierma-Zeinstra SM, Hawker GA, Henrotin Y, Hunter DJ, Kawaguchi H, Kwoh K, Lohmander S, Rannou F, Roos EM, Underwood M (2014) OARSI guidelines for the non-surgical management of knee osteoarthritis. Osteoarthritis Cartilage 22(3):363–388. https://doi.org/10.1016/J.JOCA.2014.01.003

McCurdy CR, Sufka KJ, Smith GH, Warnick JE, Nieto MJ (2006) Antinociceptive profile of salvinorin A, a structurally unique kappa opioid receptor agonist. Pharmacol Biochem Behav 83(1):109–113. https://doi.org/10.1016/J.PBB.2005.12.011

McKenna D, Jones K, Hughes K (2001) Efficacy, safety, and use of ginkgo biloba in clinical and preclinical applications. Altern Ther Health Med 7(5):70–90

Mehmood A, Miana GA, Khan AU (2018) Anti-inflammatory actions of *Berberis lycium* (Whole plant) in acute and chronic models of inflammation in mice. J Anim Plant Sci 28(3):754–760

Meng Q, Niu Y, Niu X, Roubin RH, Hanrahan JR (2009) Ethnobotany, phytochemistry and pharmacology of the genus *Caragana* used in traditional Chinese medicine. J Ethnopharmacol 124(3):350–368. https://doi.org/10.1016/J.JEP.2009.04.048

Menke NB, Ward KR, Witten TM, Bonchev DG, Diegelmann RF (2007) Impaired wound healing. Clin Dermatol 25 (1):19–25. https://doi.org/10.1016/J.CLINDERMATOL.2006.12.005

Middaugh SJ, Pawlick K (2002) Biofeedback and behavioral treatment of persistent pain in the older adult: a review and a study. Appl Psychophysiol Biofeedback 27:185–202. https://doi.org/10.1023/A:1016208128254

Millichap JG, Yee MM (2003) The diet factor in pediatric and adolescent migraine. Pediatr Neurol 28(1):9–15. https://doi.org/10.1016/S0887-8994(02)00466-6

Mintah SO, Asafo-Agyei T, Archer M-A, Junior PA-A, Boamah D, Kumadoh D, Appiah A, Ocloo A, Boakye YD, Agyare C (2019) Medicinal plants for treatment of prevalent diseases. In: Pharmacognosy—medicinal plants. IntechOpen, London. https://doi.org/10.5772/INTECHOPEN.82049

Mirabi P, Dolatian M, Mojab F, Majd HA (2011) Effects of valerian on the severity and systemic manifestations of dysmenorrhea. Int J Gynecol Obstet 115(3):285–288. https://doi.org/10.1016/J.IJGO.2011.06.022

Mirabi P, Alamolhoda SH, Esmaeilzadeh S, Mojab F (2014) Effect of medicinal herbs on primary dysmenorrhoea- a systematic review. Iran J Pharm Res 13(3):757–767

Mirabi P, Alamolhoda S, Yazdkhasti M, Mojab F (2018) The effects of lemon balm on menstrual bleeding and the systemic manifestation of dysmenorrhea. Iran J Pharm Res IJPR 17(Suppl2):214

Miraj S, Alesaeidi S (2016) A systematic review study of therapeutic effects of *Matricaria recuitta* chamomile (chamomile). Electron Phys 8(9):3024–3031. https://doi.org/10.19082/3024

Miraj S et al (2016) *Melissa officinalis* L: a review study with an antioxidant prospective. J Evid-Based Integr Med 22 (3):385–394. https://doi.org/10.1177/2156587216663433

Mittal N, Ginwal H, Varshney V (2009) Pharmaceutical and biotechnological potential of *Acorus calamus* Linn.: an indigenous highly valued medicinal plant species. Pharmacogn Rev 3(5):93–103

Mncwangi N, Chen W, Vermaak I, Viljoen AM, Gericke N (2012) Devil's Claw—a review of the ethnobotany, phytochemistry and biological activity of *Harpagophytum procumbens*. J Ethnopharmacol 143(3):755–771

Mobasheri A, Batt M (2016) An update on the pathophysiology of osteoarthritis. Ann Phys Rehabil Med 59(5–6):333–339. https://doi.org/10.1016/J.REHAB.2016.07.004

Mockel M, Searle J, Muller R, Slagman A, Storchmann H, Oestereich P, Wyrwich W, Ale-Abaei A, Vollert JO, Koch M, Somasundaram R (2013) Chief complaints in medical emergencies: Do they relate to underlying disease and outcome? The charité emergency medicine study (CHARITEM). Eur J Emerg Med 20(2):103–108. https://doi.org/10.1097/MEJ.0B013E328351E609

Moelants EAV, Mortier A, Damme JV, Proost P (2013) Regulation of TNF-α with a focus on rheumatoid arthritis. Immunol Cell Biol 91(6):393–401. https://doi.org/10.1038/ICB.2013.15

Moghaddasi Mohammad S, Kashanisup HH (2012) Pot marigold (*Calendula officinalis*) medicinal usage and

cultivation. Sci Res Essays 7(14):1468–1472. https://doi.org/10.5897/SRE11.630

Moll R, Derry S, Moore RA, McQuay HJ (2011) Single dose oral mefenamic acid for acute postoperative pain in adults. Cochrane Database Syst Rev. https://doi.org/10.1002/14651858.CD007553.PUB2

Monteith TS, Goadsby PJ (2010) Acute migraine therapy: new drugs and new approaches. Curr Treat Options Neurol 13(1):1–14. https://doi.org/10.1007/S11940-010-0105-6

Moqbel SAA, He Y, Xu L, Ma C, Ran J, Xu K, Wu L (2020) Rat chondrocyte inflammation and osteoarthritis are ameliorated by Madecassoside. Oxid Med Cell Longev. https://doi.org/10.1155/2020/7540197

Mora JC, Przkora R, Cruz-Almeida Y (2018) Knee osteoarthritis: Pathophysiology and current treatment modalities. J Pain Res 11:2196–2196. https://doi.org/10.2147/JPR.S154002

Moreno-Salazar SF, Robles-Zepeda RE, Johnson DE (2008) Plant folk medicines for gastrointestinal disorders among the main tribes of Sonora, Mexico. Fitoterapia 79(2):132–141. https://doi.org/10.1016/J.FITOTE.2007.07.009

Moslemi L, Bekhradi R, Galini-Moghaddam T, Tabari M (2012) Comparative effect of fennel extract on the intensity of primary dysmenorrhea. Afr J Pharm Pharmacol 6(29):1770–1773. https://doi.org/10.5897/AJPP12.356

Mrugacz G, Grygoruk C, Sieczyński P, Grusza M, Bołkun I, Pietrewicz P (2013) Etiopathogenesis of dysmenorrhea. Med Wieku Rozwoj 17(1):85–89

Muhammad AA, Arulselvan P, Cheah PS, Abas F, Fakurazi S (2016) Evaluation of wound healing properties of bioactive aqueous fraction from *Moringa oleifera* Lam on experimentally induced diabetic animal model. Drug Des Dev Ther 10:1715–1730. https://doi.org/10.2147/DDDT.S96968

Mur E, Hartig F, Eibl G, Schirmer M (2002) Randomized double blind trial of an extract from the pentacyclic alkaloid-chemotype of uncaria tomentosa for the treatment of rheumatoid arthritis. J Rheumatol 29(4):678–681

Murphy NJ, Eyles JP, Hunter DJ (2016) Hip osteoarthritis: etiopathogenesis and implications for management. Adv Ther 33(11):1921–1921. https://doi.org/10.1007/S12325-016-0409-3

Muthuraman A, Diwan V, Jaggi AS, Singh N, Singh D (2008) Ameliorative effects of *Ocimum sanctum* in sciatic nerve transection-induced neuropathy in rats. J Ethnopharmacol 120(1):56–62. https://doi.org/10.1016/J.JEP.2008.07.049

Muthuraman A, Singh N, Jaggi AS (2010) Effect of hydroalcoholic extract of *Acorus calamus* on tibial and sural nerve transection-induced painful neuropathy in rats. J Nat Med 65(2):282–292. https://doi.org/10.1007/S11418-010-0486-6

Muthuraman A, Singh N (2012) Neuroprotective effect of saponin rich extract of *Acorus calamus* L. in rat model of chronic constriction injury (CCI) of sciatic nerve-induced neuropathic pain. J Ethnopharmacol 142(3):723–731. https://doi.org/10.1016/J.JEP.2012.05.049

Nabavi SF, Lorenzo AD, Izadi M, Sobarzo-Sánchez E, Daglia M, Nabavi SM (2015) Antibacterial effects of cinnamon: from farm to food. Cosmet Pharm Ind Nutr 7(9):7729–7748. https://doi.org/10.3390/NU7095359

Naderi Z, Mozaffari-Khosravi H, Dehghan A, Nadjarzadeh A, Huseini HF (2016) Effect of ginger powder supplementation on nitric oxide and C-reactive protein in elderly knee osteoarthritis patients: a 12-week double-blind randomized placebo-controlled clinical trial. J Tradit Complement Med 6(3):199–203. https://doi.org/10.1016/J.JTCME.2014.12.007

Nahrstedt A, Schmidt M, Jäggi R, Metz J, Khayyal MT (2007) Willow bark extract: the contribution of polyphenols to the overall effect. Wien Med Wochenschr 157(13):348–351. https://doi.org/10.1007/S10354-007-0437-3

Narwade S, Bangar G, Sudrik A (2023) A review on herbal medicinal plants used in diabetic treatment. J Pharmacogn Phytochem 12(1):597–603

Natour J, Cazotti LDA, Ribeiro LH, Baptista AS, Jones A (2014) Pilates improves pain, function and quality of life in patients with chronic low back pain: a randomized controlled trial. Clin Rehabil 29(1):59–68. https://doi.org/10.1177/0269215514538981

Navarro M, Arnaez E, Moreira I, Hurtado A, Monge D, Monagas M (2019) Polyphenolic composition and antioxidant activity of *Uncaria tomentosa* commercial bark products. Antioxidants 8(9):339–339. https://doi.org/10.3390/ANTIOX8090339

Nayak BS, Pereira LP, Maharaj D (2007) Wound healing activity of *Carica papaya* L. in experimentally induced diabetic rats. Int J Exp Biol 739–743

Nayak, B. S., Raju, S. S., Eversley, M., & Ramsubhag, A. (2009). Evaluation of wound healing activity of Lantana camara L. – a Preclinical study. *Phytotherapy Research*, *23*(2), 241–245. https://doi.org/10.1002/PTR.2599

Neekhra S, Awasthi H, Singh DP (2021) Beneficial effects of sambucus nigra in chronic stress-induced neurobehavioral and biochemical perturbation in rodents. Pharmacogn J 13(1):155–161. https://doi.org/10.5530/PJ.2021.13.22

Nguyen GC, Croitoru K, Silverberg MS, Steinhart AH, Weizman AV (2016) Use of complementary and alternative medicine for inflammatory bowel disease is associated with worse adherence to conventional therapy: the COMPLIANT study. Inflamm Bowel Dis 22(6):1412–1417. https://doi.org/10.1097/MIB.0000000000000773

Nonose N, Pereira JA, Machado PRM, Rodrigues MR, Sato DT, Martinez CAR (2014) Oral administration of curcumin (i) can attenuate the neutrophil inflammatory response in zymosan-induced arthritis in rats. Acta Cir Bras 29(11):727–734. https://doi.org/10.1590/S0102-86502014001800006

Noroozian M, Raeesi S, Hashemi R, Khedmat L, Vahabi Z (2018) Pain: the neglect issue in old people's life. Open Access Maced J Med Sc 6(9):1778. https://doi.org/10.3889/OAMJMS.2018.335

Nour AH, Yap SS, Nour AH, Nour AH (2017) Extraction and chemical compositions of ginger (*Zingiber officinale roscoe*) essential oils as cockroaches repellent. Aust J Basic Appl Sci 11(3):1–8

Nucci-Martins C, Martins DF, Nascimento LF, Venzke D, Oliveira AS, Frederico MJS, Silva FRMB, Brighente IMC, Pizzolatti MG, Santos ARS (2015) Ameliorative potential of standardized fruit extract of *Pterodon pubescens* Benth on neuropathic pain in mice: evidence for

the mechanisms of action. J Ethnopharmacol 175:273–286. https://doi.org/10.1016/J.JEP.2015.09.005

Obolskiy D, Pischel I, Feistel B, Glotov N, Heinrich M (2011) *Artemisia dracunculus* L. (Tarragon): a critical review of its traditional use, chemical composition, pharmacology, and safety. J Agric Food Chem 59(21):11367–11384. https://doi.org/10.1021/jf202277w

Obrosova IG, Watcho P, Stavniichuk R, Ribnicky DM, Raskin I (2010) High-fat diet-induced neuropathy of prediabetes and obesity: effect of PMI-5011, an ethanolic extract of *Artemisia dracunculus* L. Mediat Inflamm. https://doi.org/10.1155/2010/268547

Olesen J (2018) Headache classification committee of the international headache society (IHS) the international classification of headache disorders. Cephalalgia 38(1):1–211

Or TCT, Yang CLH, Law AHY, Li JCB, Lau ASY (2011) Isolation and identification of anti-inflammatory constituents from *Ligusticum chuanxiong* and their underlying mechanisms of action on microglia. Neuropharmacology 60(6):823–831. https://doi.org/10.1016/J.NEUROPHARM.2010.12.002

Orav A, Raal A, Arak E (2010) Content and composition of the essential oil of *Chamomilla recutita* (L.) rauschert from some European countries. Nat Product Res 24(1):48–55. https://doi.org/10.1080/14786410802560690

Oso B, Abey N, Oyeleke O, Olowookere B (2018) Comparative study of the in vitro antioxidant properties of methanolic extracts of chromolaena odorata and ageratum conyzoides used in wound healing. Int Ann Sci 6(1):8–12. https://doi.org/10.21467/ias.6.1.8-12

Ovalle-Magallanes B, Déciga-Campos M, Mata R (2017) Antihyperalgesic activity of a mexicanolide isolated from Swietenia humilis extract in nicotinamide-streptozotocin hyperglycemic mice. Biomed Pharmacother 92:324–330. https://doi.org/10.1016/J.BIOPHA.2017.05.073

Owens C, Conaghan PG (2016) Improving joint pain and function in osteoarthritis. Practitioner 260(1799):17–20

Pablo-Pérez SS, Parada-Cruz B, Barbier OC, Meléndez-Camargo ME (2018) The ethanolic extract of *Eysenhardtia polystachya* (Ort.) Sarg. Bark and its fractions delay the progression of rheumatoid arthritis and show antinociceptive activity in murine models. Iran J Pharm Res IJPR 17(1):248–248

Panahi Y, Alishiri GH, Parvin S, Sahebkar A (2016) Mitigation of systemic oxidative stress by curcuminoids in osteoarthritis: results of a randomized controlled trial. J Dietary Suppl 13(2):209–220. https://doi.org/10.3109/19390211.2015.1008611

Parada-Turska J, Rzeski W, Zgrajka W, Majdan M, Kandefer-Szerszeń M, Turski W (2006) Kynurenic acid, an endogenous constituent of rheumatoid arthritis synovial fluid, inhibits proliferation of synoviocytes in vitro. Rheumatol Int 26(5):422–426. https://doi.org/10.1007/s00296-005-0057-4

Pareek A, Suthar M, Rathore GS, Bansal V (2011) Feverfew (*Tanacetum parthenium* L.): a systematic review. Pharmacogn Rev 5(9):103–110. https://doi.org/10.4103/0973-7847.79105

Park SH, Kim SK, Shin IH, Kim HG, Choe JY (2009) Effects of AIF on knee osteoarthritis patients: double-blind, randomized placebo-controlled study. Korean J Physiol Pharmacol 13(1):33–37. https://doi.org/10.4196/KJPP.2009.13.1.33

Paul J, Khan S, Mahammed S, Asdaq B (2010) Wound healing evaluation of chloroform and methanolic extracts of mimosa pudica roots in rats. Int J Biol Med Res 1(4):223–227

Pawar RS, Toppo FA, Mandloi AS, Shaikh S (2015) Exploring the role of curcumin containing ethanolic extract obtained from *Curcuma longa* (rhizomes) against retardation of wound healing process by aspirin. Indian J Pharmacol 47(2):160–166. https://doi.org/10.4103/0253-7613.153422

Peirs C, Seal RP (2016) Neural circuits for pain: recent advances and current views. Science 354(6312):578–584. https://doi.org/10.1126/SCIENCE.AAF8933

Peng W, Wang L, Qiu X, Jiang Y, Han T, Pan L, Jia X, Qin L, Zheng C (2016) Therapeutic effects of *Caragana pruinosa* Kom. roots extract on type II collagen-induced arthritis in rats. J Ethnopharmacol 191:1–8. https://doi.org/10.1016/J.JEP.2016.06.028

Percival NJ (2002) Classification of wounds and their management. Surg Infect (larchmt) 20(5):114–117. https://doi.org/10.1383/SURG.20.5.114.14626

Pereira DF, Zanon RB, Dos Santos M, Boligon AA, Athayde ML (2013) Antioxidant activities and triterpenoids isolated from *Alternanthera brasiliana* (L.) Kuntze leaves. Nat Product Res 27(18):1660–1663. https://doi.org/10.1080/14786419.2012.750313

Pinheiro MMG, Radulović NS, Miltojević AB, Boylan F, Dias Fernandes P (2014) Antinociceptive esters of N-methylanthranilic acid: mechanism of action in heat-mediated pain. Eur J Pharmacol 727(1):106–114. https://doi.org/10.1016/J.EJPHAR.2013.12.042

Pinheiro MMG, Miltojević AB, Radulović NS, Abdul-Wahab IR, Boylan F, Fernandes PD (2015) Anti-inflammatory activity of *Choisya ternata* kunth essential oil, ternanthranin, and its two synthetic analogs (Methyl and Propyl N-Methylanthranilates). PLoS ONE 10(3):e0121063–e0121063. https://doi.org/10.1371/JOURNAL.PONE.0121063

Pljevljakušić D, Rančić D, Ristić M, Vujisić L, Radanović D, Dajić-Stevanović Z (2012) Rhizome and root yield of the cultivated *Arnica montana* L., chemical composition and histochemical localization of essential oil. Ind Crops Prod 39:177–189

Prakash V, Jaiswal N, Srivastava M (2017) A review on medicinal properties of *Centella asiatica*. Asian J Pharm Clin Res 10(10):69–74. https://doi.org/10.22159/AJPCR.2017.V10I10.20760

Pranay W, Priya S, Aparna S (2023) A detailed review of various herbal treatment options for potentially curing or ameliorating pain in diabetic neuropathy. Curr Tradit Med 9(2):1–18

Prasad S, Tyagi AK, Aggarwal BB (2014) Recent developments in delivery, bioavailability, absorption and metabolism of curcumin: the golden pigment from golden spice. Cancer Res Treat 46(1):2–18. https://doi.org/10.4143/CRT.2014.46.1.2

Prasad S, Aggarwal BB (2011) Turmeric, the golden spice. Herb Med Biomol Clin Aspects Second Ed 263–288

Prieto JM (2014) Update on the efficacy and safety of Petadolex®, a butterbur extract for migraine prophylaxis. Bot Targets Ther 4:1–9. https://doi.org/10.2147/BTAT.S54023

Qnais EY, Abu-Dieyeh M, Abdulla FA, Abdalla SS (2010) The antinociceptive and anti-inflammatory effects of Salvia officinalis leaf aqueous and butanol extracts. Pharm Biol 48(10):1149–1156. https://doi.org/10.3109/13880200903530763

Qu J, Mélot C, Appelboom T (2017) Synofit premium in refractory low back pain: a retrospective observational study. Open J Rheumatol Autoimmune Diseases 07 (02):120–127. https://doi.org/10.4236/OJRA.2017.72011

Radfar S, Shahoie R, Noori B, Jalilian F, Nasab LH (2018) Comparative study on the effect of *Matricaria chamomile* and *Achillea millefolium* capsules on primary dysmenorrhea intensity of dormitory students of Kurdistan University of Medical Sciences, 2018. J Pharm Res Int 25 (3):1–7. https://doi.org/10.9734/JPRI/2018/V25I330101

Rahnama P, Montazeri A, Huseini HF, Kianbakht S, Naseri M (2012) Effect of *Zingiber officinale* R. rhizomes (ginger) on pain relief in primary dysmenorrhea: a placebo randomized trial. BMC Complement Altern Med 12(1):1–7. https://doi.org/10.1186/1472-6882-12-92

Raja AE, Vijayalakshmi M, Devalarao G (2009) *Acorus calamus* Linn.: chemistry and biology. Res J Pharm Technol 2(2):256–261

Rajapakse T, Pringsheim T (2016) Nutraceuticals in migraine: a summary of existing guidelines for use. Headache J Head Face Pain 56(4):808–816. https://doi.org/10.1111/HEAD.12789

Ramadan G, Al-Kahtani MA, El-Sayed WM (2010) Anti-inflammatory and anti-oxidant properties of *Curcuma longa* (Turmeric) versus *Zingiber officinale* (Ginger) rhizomes in rat adjuvant-induced arthritis. Inflammation 34(4):291–301. https://doi.org/10.1007/S10753-010-9278-0

Ramakanth GSH, Uday Kumar C, Kishan PV, Usharani P (2016) A randomized, double blind placebo controlled study of efficacy and tolerability of Withaina somnifera extracts in knee joint pain. J Ayurveda Integr Med 7 (3):151–157. https://doi.org/10.1016/J.JAIM.2016.05.003

Ramalingam M, Yong-Ki P (2010) Free radical scavenging activities of cnidium officinale makino and ligusticum chuanxiong Hort. Methanolic Extr Pharmacogn Mag 6 (24):323–330. https://doi.org/10.4103/0973-1296.71794

Rangkadilok N, Pholphana N, Mahidol C, Wongyai W, Saengsooksree K, Nookabkaew S, Satayavivad J (2010) Variation of sesamin, sesamolin and tocopherols in sesame (*Sesamum indicum* L.) seeds and oil products in Thailand. Food Chem 122(3):724–730

Rather MA, Dar BA, Sofi SN, Bhat BA, Qurishi MA (2016) Foeniculum vulgare: a comprehensive review of its traditional use, phytochemistry, pharmacology, and safety. Arab J Chem 9:S1574–S1583. https://doi.org/10.1016/J.ARABJC.2012.04.011

Ray D, Mukherjee S, Falchi M, Bertelli A, Carlo Braga P, Das KD (2010) Amelioration of myocardial ischemic reperfusion injury with *Calendula officinalis*. Curr Pharm Biotechnol 11(8):849–854

Re TA, Mooney D, Antignac E, Dufour E, Bark I, Srinivasan V, Nohynek G (2009) Application of the threshold of toxicological concern approach for the safety evaluation of calendula flower (*Calendula officinalis*) petals and extracts used in cosmetic and personal care products. Food Chem Toxicol 47(6):1246–1254. https://doi.org/10.1016/J.FCT.2009.02.016

Recinella L, Chiavaroli A, di Giacomo V, Antolini MD, Acquaviva A, Leone S, Brunetti L, Menghini L, Ak G, Zengin G, Simone SCD, Ferrante C, Orlando G (2020) Anti-Inflammatory and neuromodulatory effects induced by tanacetum parthenium water extract: results from in silico, in vitro and ex vivo studies. Molecules 26(1):22–22. https://doi.org/10.3390/MOLECULES26010022

Rehman H, Begum W, Anjum F, Tabasum H, Zahid S (2015) Effect of rhubarb (Rheum emodi) in primary dysmenorrhoea: a single-blind randomized controlled trial. J Complement Integr Med 12(1):61–69. https://doi.org/10.1515/JCIM-2014-0004

Rios J, Passe MM (2004) Evidenced-based use of botanicals, minerals, and vitamins in the prophylactic treatment of migraines. J Am Acad Nurse Pract 16(6):251–256. https://doi.org/10.1111/J.1745-7599.2004.TB00447.X

Robles-Zepeda RE, Valenzuela-Antelo O, Garibay-Escobar A, Velázquez-Contreras C, Navarro-Navarro M, Contreras LR, Corral OL, Lozano-Taylor J (2011) Use of complementary and alternative medicine in a region of Northwest Mexico. J Altern Complement Med 17(9):787–788. https://doi.org/10.1089/ACM.2011.0234

Rocha-González HI, Blaisdell-López E, Granados-Soto V, Navarrete A (2010) Antinociceptive effect of 7-hydroxy-3,4-dihydrocadalin isolated from Heterotheca inuloides: role of peripheral 5-HT1 serotonergic receptors. Eur J Pharmacol 649(1–3):154–160. https://doi.org/10.1016/J.EJPHAR.2010.09.022

Rocha-González HI, Ramírez-Aguilar M, Granados-Soto V, Reyes-García JG, Torres-López JE, Huerta-Cruz JC, Navarrete A (2014) Antineuropathic effect of 7-hydroxy-3,4-dihydrocadalin in streptozotocin-induced diabetic rodents. BMC Complement Altern Med 14(1):1–12. https://doi.org/10.1186/1472-6882-14-129

Rodrigues MRA, Kanazawa LKS, Neves TLMHD, Silva CFD, Horst H, Pizzolatti MG, Santos ARS, Baggio CH, Werner MFDP (2012) Antinociceptive and anti-inflammatory potential of extract and isolated compounds from the leaves of Salvia officinalis in mice. J Ethnopharmacol 139 (2):519–526. https://doi.org/10.1016/J.JEP.2011.11.042

Rodríguez-Chávez JL, Rufino-González Y, Ponce-Macotela M, Delgado G (2015) In vitro activity of 'Mexican Arnica' heterotheca inuloides cass natural products and some derivatives against *Giardia intestinalis*. Parasitology 142 (4):576–584. https://doi.org/10.1017/S0031182014001619

Russo EB (2008) Cannabinoids in the management of difficult to treat pain. Ther Clin Risk Manag 4(1):245–259. https://doi.org/10.2147/TCRM.S1928

Russo E, Guy GW (2006) A tale of two cannabinoids: the therapeutic rationale for combining tetrahydrocannabinol and cannabidiol. Med Hypotheses 66(2):234–246. https://doi.org/10.1016/J.MEHY.2005.08.026

Russo EB, Jiang H-E, Li X, Sutton A, Carboni A, del Bianco F, Mandolino G, Potter DJ, Zhao Y-X, Bera S, Zhang Y-B, Lü E-G, Ferguson DK, Hueber F, Zhao L-C, Liu C-J,

Wang Y-F, Li C-S (2008) Phytochemical and genetic analyses of ancient cannabis from Central Asia. J Exp Bot 59(15):4171–4182. https://doi.org/10.1093/JXB/ERN260

Saddiqe Z, Naeem I, Maimoona A (2010) A review of the antibacterial activity of *Hypericum perforatum* L. J Ethnopharmacol 131(3):511–521

Saeidnia S, Gohari AR, Mokhber-Dezfuli N, Kiuchi F (2011) A review on phytochemistry and medicinal properties of the genus *Achillea*. DARU J Fac Pharm Tehran Univ Med Sci 19(3):186–186

Safakhah HA, Taghavi T, Rashidy-Pour A, Vafaei AA, Sokhanvar M, Mohebbi N, Rezaei-Tavirani M (2016) Effects of saffron (*Crocus sativus* L.) stigma extract and its active constituent crocin on neuropathic pain responses in a rat model of chronic constriction injury. Iran J Pharm Res IJPR 15(1):261–261

Sagar NA, Pareek S, Gonzalez-Aguilar GA (2020) Quantification of flavonoids, total phenols and antioxidant properties of onion skin: a comparative study of fifteen Indian cultivars. J Food Sci Technol 57(7):2423–2432. https://doi.org/10.1007/S13197-020-04277-W

Saikia I, Hazarika M, Tamuly C (2015) Synthesis, characterization of bio-derived ZnO nanoparticles and its catalytic activity. Mater Lett 161:29–32. https://doi.org/10.1016/J.MATLET.2015.08.068

Salehi B, Albayrak S, Antolak H, Kręgiel D, Pawlikowska E, Sharifi-Rad M, Uprety Y, Fokou PVT, Yousef Z, Zakaria ZA, Varoni EM, Sharopov F, Martins N, Iriti M, Sharifi-Rad J (2018) Aloe genus plants: from farm to food applications and phytopharmacotherapy. Int J Mol Sci 19(9):2843–2843. https://doi.org/10.3390/IJMS19092843

Salmalian H, Saghebi R, Moghadamnia AA, Bijani A, Faramarzi M, Amiri FN, Bakouei F, Behmanesh F, Bekhradi R (2014) Comparative effect of thymus vulgaris and ibuprofen on primary dysmenorrhea: a triple-blind clinical study. Caspian J Intern Med 5(2):88–88

Sanadgol N, Zahedani SS, Sharifzadeh M, Khalseh R, Barbari GR, Abdollahi M (2017) Recent updates in imperative natural compounds for healthy brain and nerve function: a systematic review of implications for multiple sclerosis. Curr Drug Targets 18(13):1499–1517. https://doi.org/10.2174/1389450118666161108124414

Sánchez-Reus MI, Gómez del Rio MA, Iglesias I, Elorza M, Slowing K, Benedí J (2007) Standardized Hypericum perforatum reduces oxidative stress and increases gene expression of antioxidant enzymes on rotenone-exposed rats. Neuropharmacology 52(2):606–616. https://doi.org/10.1016/J.NEUROPHARM.2006.09.003

Sangsoy K, Mongkolporn O, Imsabai W, Luengwilai K (2017) Papaya carotenoids increased in Oxisols soils. Agric Nat Resour 51(4):253–261. https://doi.org/10.1016/J.ANRES.2017.10.003

Santana LF, Inada AC, Santo BLSDE, Filiú WFO, Pott A, Alves FM, Guimarães RDCA, Freitas KDC, Hiane PA (2019) Nutraceutical potential of carica papaya in metabolic syndrome. Nutrients 11(7):1608–1608. https://doi.org/10.3390/NU11071608

Sasaki K, El Omri A, Kondo S, Han J, Isoda H (2013) Rosmarinus officinalis polyphenols produce anti-depressant like effect through monoaminergic and cholinergic functions modulation. Behav Brain Res 238(1):86–94. https://doi.org/10.1016/J.BBR.2012.10.010

Schadich E, Hlaváč J, Volná T, Varanasi L, Hajdúch M, Džubák P (2016) Effects of ginger phenylpropanoids and quercetin on Nrf2-ARE pathway in human BJ fibroblasts and HaCaT keratinocytes. BioMed Res Int 2016. https://www.hindawi.com/journals/bmri/2016/2173275/abs/

Sciences VE-AJ of P & 2010, undefined. (n.d.) Safflower (*Carthamus tinctorius* L.) the underutilized and neglected crop: a review. Cabdirect.Org

Scurrah A, Shiner CT, Stevens JA, Faux SG (2018) Regional nerve blockade for early analgesic management of elderly patients with hip fracture – a narrative review. Anaesthesia 73(6):769–783. https://doi.org/10.1111/ANAE.14178

Semwal RB, Semwal DK, Combrinck S, Viljoen AM (2015) Gingerols and shogaols: important nutraceutical principles from ginger. Phytochemistry 117:554–568. https://doi.org/10.1016/J.PHYTOCHEM.2015.07.012

Sendl A (1995) *Allium sativum* and *Allium ursinum*: part 1 chemistry, analysis, history, botany. Phytomedicine 1(4):323–339. https://doi.org/10.1016/S0944-7113(11)80011-5

Sengupta K, Krishnaraju AV, Vishal AA, Mishra A, Trimurtulu G, Sarma KV, Raychaudhuri SK, Raychaudhuri SP (2010) Comparative efficacy and tolerability of 5-Loxin® and Aflapin® against osteoarthritis of the knee: a double blind, randomized, placebo controlled clinical study. Int J Med Sci 7(6):377–377. https://doi.org/10.7150/IJMS.7.366

Serpell M, Ratcliffe S, Hovorka J, Schofield M, Taylor L, Lauder H, Ehler E (2014) A double-blind, randomized, placebo-controlled, parallel group study of THC/CBD spray in peripheral neuropathic pain treatment. Eur J Pain 18(7):999–1012. https://doi.org/10.1002/j.1532-2149.2013.00445.x

Sewall GK, Robertson KM, Connor NP, Heisey DM, Hartig GK (2003) Effect of topical mitomycin on skin wound contraction. Arch Facial Plast Surg 5(1):59–62. https://doi.org/10.1001/ARCHFACI.5.1.59

Shafeie N, Naini AT, Jahromi HK (2015) Comparison of different concentrations of calendula officinalis gel on cutaneous wound healing. Biomed Pharmacol J 8(2):979–992. https://doi.org/10.13005/BPJ/850

Shara M, Stohs SJ (2015) Efficacy and safety of white willow bark (*Salix alba*) extracts. Phytother Res 29(8):1112–1116. https://doi.org/10.1002/PTR.5377

Sharma ML, Bani S, Singh GB (1989) Anti-arthritic activity of boswellic acids in bovine serum albumin (BSA)-induced arthritis. Int J Immunopharmacol 11(6):647–652. https://doi.org/10.1016/0192-0561(89)90150-1

Sharma P, Kharkwal AC, Kharkwal H, Abdin MZ, Varma A (2014a) A review on pharmacological properties of Aloe vera. Int J Pharm Sci Rev Res 29(2):31–37

Sharma S, Gupta R, Thakur SC (2014b) Attenuation of collagen induced arthritis by centella asiatica methanol fraction via modulation of cytokines and oxidative stress. Biomed Environ Sci 27(12):926–938. https://doi.org/10.3967/BES2014.133

Sharma S, Arif M, Nirala RK, Gupta R, Thakur SC (2016) Cumulative therapeutic effects of phytochemicals in

Arnica montana flower extract alleviated collagen-induced arthritis: inhibition of both pro-inflammatory mediators and oxidative stress. J Sci Food Agric 96 (5):1500–1510. https://doi.org/10.1002/JSFA.7252

Sharma H, Chauhan P, Singh S (2018) Evaluation of the anti-arthritic activity of *Cinnamomum cassia* bark extract in experimental models. Integr Med Res 7(4):366–373. https://doi.org/10.1016/j.imr.2018.08.002

Shashank D, Rajendra SV, Mistry A (2017) An overview of phytoconstituents and pharmacological activities of celastrus paniculatus willd. J Pharm Res 16(4):307–313

Shaw D, Graeme L, Pierre D, Elizabeth W, Kelvin C (2012) Pharmacovigilance of herbal medicine. Good Pract Tradit Chin Med Res -Genom Era 140(3):513–518. https://doi.org/10.1016/j.jep.2012.01.051

Shimizu T, Takahata M, Kameda Y, Endo T, Hamano H, Hiratsuka S, Ota M, Iwasaki N (2015) Sialic acid-binding immunoglobulin-like lectin 15 (Siglec-15) mediates periarticular bone loss, but not joint destruction, in murine antigen-induced arthritis. Bone 79:65–70. https://doi.org/10.1016/J.BONE.2015.05.029

Shu D, He J, Chen J (2009) Neuroprotective effects and mechanisms of Chuanxiong Chatiao pulvis against MPTP-induced dopaminergic neurotoxicity in mice model of Parkinson's disease. China J Chin Mater Med 34 (19):2494–2497

Siddiqui MZ (2011) Boswellia serrata, a potential antiinflammatory agent: an overview. Indian J Pharm Sci 73(3):255–261. https://doi.org/10.4103/0250-474X.93507

Simon LS (2012) Relieving pain in America: a blueprint for transforming prevention, care, education, and research. J Pain Palliat Care Pharmacother 26(2):197–198. https://doi.org/10.3109/15360288.2012.678473

Simón-Arceo K, González-Trujano ME, Coffeen U, Fernández-Mas R, Mercado F, Almanza A, Contreras B, Jaimes O, Pellicer F (2017) Neuropathic and inflammatory antinociceptive effects and electrocortical changes produced by Salvia divinorum in rats. J Ethnopharmacol 206:115–124. https://doi.org/10.1016/J.JEP.2017.05.016

Singh D, Aggarwal A, Maurya R, Naik S (2007) Withania somnifera inhibits NF-κB and AP-1 transcription factors in human peripheral blood and synovial fluid mononuclear cells. Phytother Res 21(10):905–913. https://doi.org/10.1002/PTR.2180

Singh N, Bhalla M, de Jager P, Gilca M (2011) An overview on ashwagandha: a rasayana (Rejuvenator) of ayurveda. Afr J Tradit Complement Altern Med 8(5 Suppl):213–213. https://doi.org/10.4314/AJTCAM.V8I5S.9

Singh SP, Kumar S, Mathan SV, Tomar MS, Singh RK, Verma PK, Kumar A, Kumar S, Singh RP, Acharya A (2020) Therapeutic application of Carica papaya leaf extract in the management of human diseases. DARU J Pharm Sci 28(2):735–744. https://doi.org/10.1007/S40199-020-00348-7

Singh H, Arora R, Arora S, Singh B (2017) Ameliorative potential of *Alstonia scholaris* (Linn.) R. Br. Against chronic constriction injury-induced neuropathic pain in rats. BMC Complement Altern Med. https://doi.org/10.1186/S12906-017-1577-7

Soliman MM, Hyrich KL, Lunt M, Watson KD, Symmons DPM, Ashcroft DM, Register BSRB (2012) Effectiveness of rituximab in patients with rheumatoid arthritis: observational study from the British society for rheumatology biologics register. J Rheumatol 39(2):240–246. https://doi.org/10.3899/JRHEUM.110610

Solomon DH, Husni ME, Wolski KE, Wisniewski LM, Borer JS, Graham DY, Libby P, Lincoff AM, Lüscher TF, Menon V, Yeomans ND, Wang Q, Bao W, Berger MF, Nissen SE (2018) Differences in safety of nonsteroidal antiinflammatory drugs in patients with osteoarthritis and patients with rheumatoid arthritis: a randomized clinical trial. Arthritis Rheumatol 70(4):537–546. https://doi.org/10.1002/ART.40400

Somboonwong J, Kankaisre M, Tantisira B, Tantisira MH (2012) Wound healing activities of different extracts of Centella asiatica in incision and burn wound models: an experimental animal study. BMC Complement Altern Med 12(1):1–7. https://doi.org/10.1186/1472-6882-12-103

Sommer C (2016) Exploring pain pathophysiology in patients. Science 354(6312):588–592. https://doi.org/10.1126/SCIENCE.AAF8935

Sommer C, Kress M (2004) Recent findings on how proinflammatory cytokines cause pain: peripheral mechanisms in inflammatory and neuropathic hyperalgesia. Neurosci Lett 361(1–3):184–187. https://doi.org/10.1016/J.NEULET.2003.12.007

Song M, Huai B, Shi Z, Li W, Xi Y, Liu Z, Zhang J, Zhou J, Qiao Y, Liu D (2023) The efficacy and safety of Chinese herbal medicine in the treatment of painful diabetic neuropathy: a systematic review and meta-analysis. Front Pharmacol 14:1072991. https://doi.org/10.3389/FPHAR.2023.1072991

Sordi R, Castro SN, Lera AT, Irene MN, de Farinazzo MM, Sette C, de Cubero DIG, de Baccarin ALC, del Giglio A (2019) Randomized, double-blind, placebo-controlled phase II clinical trial on the use of uncaria tomentosa (Cat's Claw) for aromatase inhibitor-induced arthralgia: a pilot study. J Nat Remedies 19(1):24–31. https://doi.org/10.18311/JNR/2019/22867

Sotnikova R, Ponist S, Navarova J, Mihalova D, Tomekova V, Strosova M, Bauerova K (2009) Effects of sesame oil in the model of adjuvant arthritis. Neuroendocrinol Lett 30 (1):22

Souza JSN, Machado LL, Pessoa ODL, Braz-Filho R, Overk CR, Yao P, Cordell GA, Lemos TLG (2005) Pyrrolizidine alkaloids from Heliotropium indicum. J Braz Chem Soc 16(6B):1410–1414. https://doi.org/10.1590/S0103-50532005000800019

Sparks JA, Karlson EW (2016) The roles of cigarette smoking and the lung in the transitions between phases of preclinical rheumatoid arthritis. Curr Rheumatol Rep 18 (3):1–17. https://doi.org/10.1007/S11926-016-0563-2

Spindola HM, Servat L, Rodrigues RAF, Sousa IMO, Carvalho JE, Foglio MA (2011) Geranylgeraniol and 6α,7β-dihydroxyvouacapan-17β-oate methyl ester isolated from Pterodon pubescens Benth.: further investigation on the antinociceptive mechanisms of action. Eur J Pharmacol 656(1):45–51. https://doi.org/10.1016/j.ejphar.2011.01.025

Sritoomma N, Moyle W, Cooke M, O'Dwyer S (2014) The effectiveness of Swedish massage with aromatic ginger oil

in treating chronic low back pain in older adults: a randomized controlled trial. Complement Ther Med 22 (1):26–33. https://doi.org/10.1016/J.CTIM.2013.11.002

Srivastava JK, Shankar E, Gupta S (2010) Chamomile: a herbal medicine of the past with a bright future (Review). Mol Med Rep 3(6):895–901. https://doi.org/10.3892/MMR.2010.377

Stevens CJ, Murphy C, Roberts R, Lucas L, Silva F, Fuller DQ (2016) Between China and South Asia: a middle asian corridor of crop dispersal and agricultural innovation in the bronze age. Holocene 26(10):1541–1555. https://doi.org/10.1177/0959683616650268

Stovner LJ, Hagen K, Jensen R, Katsarava Z, Lipton R, Scher A, Steiner T, Zwart JA (2007) The global burden of headache: a documentation of headache prevalence and disability worldwide. Cephalalgia Int J Headache 27 (3):193–210. https://doi.org/10.1111/J.1468-2982.2007.01288.X

Strodtbeck F (2001) Physiology of wound healing. Newborn Infant Nurs Rev 1(1):43–52. https://doi.org/10.1053/NBIN.2001.23176

Sugier D, Sugier P, Kowalski R, Kolodziej B, Olesińska K (2017) Foliar boron fertilization as factor affecting the essential oil content and yield of oil components from flower heads of *Arnica montana* L. and *Arnica chamissonis* Less. Cultivated for industry. Ind Crops Products 109:587–597

Sumantran VN, Joshi AK, Boddul S, Koppikar SJ, Warude D, Patwardhan B, Chopra A, Chandwaskar R, Wagh UV (2011) Antiarthritic activity of a standardized, multiherbal, ayurvedic formulation containing boswellia serrata: in vitro studies on knee cartilage from osteoarthritis patients. Phytother Res 25(9):1375–1380. https://doi.org/10.1002/PTR.3365

Sun X, He C, Yang X, Guo L, Li X (2015) Isoflavones and pterocarpans from *Caragana changduensis*. Biochem Syst Ecol 61:516–519. https://doi.org/10.1016/J.BSE.2015.07.018

Sun-Edelstein C, Mauskop A (2011) Alternative headache treatments: nutraceuticals, behavioral and physical treatments. Headache J Head Face Pain 51(3):469–483. https://doi.org/10.1111/J.1526-4610.2011.01846.X

Surin WR, Ananthaswamy K (2011) Recent advances on the pharmacological profile of Butea monosperma. GERF Bull Biosci 2(1):33–40

Tachjian A, Maria V, Jahangir A (2010) Use of herbal products and potential interactions in patients with cardiovascular diseases. J Am Coll Cardiol 55(6):515–525. https://doi.org/10.1016/J.JACC.2009.07.074

Takeoka GR, Dao L, Harden L, Pantoja A, Kuhl JC (2013) Antioxidant activity, phenolic and anthocyanin contents of various rhubarb (*Rheum* spp.) varieties. Int J Food Sci Technol 48(1):172–178. https://doi.org/10.1111/J.1365-2621.2012.03174.X

Tavakkoli A, Ahmadi A, Razavi BM, Hosseinzadeh H (2017) Black seed (*Nigella sativa*) and its constituent thymoquinone as an antidote or a protective agent against natural or chemical toxicities. Iran J Pharm Res IJPR 16 (Suppl):2–2

Taylor FR (2011) Nutraceuticals and headache: the biological basis. Headache J Head Face Pain 51(3):484–501. https://doi.org/10.1111/J.1526-4610.2011.01847.X

Tewari S, Salman M, Thadani S, Singh S, Ahmad A (2015) A study of pregabalin, tramadol, their combination and *Nigella sativa* in neuropathic pain in rats. Int J Pharm Sci Res 6(10):4406

Thakur R, Jain N, Pathak R, Sandhu SS (2011) Practices in wound healing studies of plants. Evid-Based Complement Altern Med. https://doi.org/10.1155/2011/438056

Thiagarajan VRK, Shanmugam P, Krishnan UM, Muthuraman A, Singh N (2012a) Ameliorative potential of Butea monosperma on chronic constriction injury of sciatic nerve induced neuropathic pain in rats. Anais Acad Bras Cienc 84(4):1091–1104. https://doi.org/10.1590/S0001-37652012005000063

Thiagarajan VRK, Shanmugam P, Krishnan UM, Muthuraman A, Singh N (2012b) Antinociceptive effect of *Butea monosperma* on vincristine-induced neuropathic pain model in rats. Toxicol Ind Health 29(1):3–13. https://doi.org/10.1177/0748233711432573

Thole JM, Kraft TFB, Sueiro LA, Kang Y-H, Gills JJ, Cuendet M, Pezzuto JM, Seigler DS, Lila MA (2007) A comparative evaluation of the anticancer properties of european and american elderberry fruits. J Med Food 9(4):498–504. https://doi.org/10.1089/JMF.2006.9.498

Tian J, Zhao Y, Liu Y, Liu Y, Chen K, Lyu S (2017a) Roles and mechanisms of herbal medicine for diabetic cardiomyopathy: current status and perspective. Oxid Med Cell Longev. https://doi.org/10.1155/2017/8214541

Tian J, Zhao Y, Liu Y, Liu Y, Chen K, Lyu S (2017b) Roles and mechanisms of herbal medicine for diabetic cardiomyopathy: current status and perspective. Oxid Med Cell Long. https://doi.org/10.1155/2017/8214541

Tlacomulco-Flores LL, Déciga-Campos M, González-Trujano ME, Carballo-Villalobos AI, Pellicer F (2020) Antinociceptive effects of *Salvia divinorum* and bioactive salvinorins in experimental pain models in mice. J Ethnopharmacol 248:112276–112276. https://doi.org/10.1016/J.JEP.2019.112276

Topoľská D, Valachová K, Rapta P, Šilhár S, Panghyová E, Horváth A, Šoltés L (2015) Antioxidative properties of *Sambacus nigra* extracts. Chem Pap 69(9):1202–1210. https://doi.org/10.1515/CHEMPAP-2015-0138

Tricco AC, Lillie E, Zarin W, O'Brien KK, Colquhoun H, Levac D, Moher D, Peters MDJ, Horsley T, Weeks L, Hempel S, Akl EA, Chang C, McGowan J, Stewart L, Hartling L, Aldcroft A, Wilson MG, Garritty C, Straus SE (2018) PRISMA extension for scoping reviews (prisma-scr): checklist and explanation. Ann Intern Med 169 (7):467–473. https://doi.org/10.7326/M18-0850

Tulsulkar J, Shah ZA (2013) Ginkgo biloba prevents transient global ischemia-induced delayed hippocampal neuronal death through antioxidant and anti-inflammatory mechanism. Neurochem Int 62(2):189–197. https://doi.org/10.1016/J.NEUINT.2012.11.017

Ueda H (2008) Peripheral mechanisms of neuropathic pain – involvement of lysophosphatidic acid receptor-mediated demyelination. Mol Pain 4(1):1–13. https://doi.org/10.1186/1744-8069-4-11

Ulbricht C, Basch E, Cheung L, Goldberg H, Hammerness P, Isaac R, Khalsa KPS, Romm A, Rychlik I, Varghese M, Weissner W, Windsor RC, Wortley J (2014) An evidence-based systematic review of elderberry and elderflower (*Sambucus nigra*) by the natural standard research collaboration. J Diet Suppl 11(1):80–120. https://doi.org/10.3109/19390211.2013.859852

Ullah R, Ahmad S, Atiq A, Hussain H, Rehman N, Elsalam NMA, Adnan M (2015) Quantification and antibacterial activity of flavonoids in coffee samples. Afr J Tradit Complement Altern Med 12(4):84–86. https://doi.org/10.4314/ajtcam.v12i4.13

Umar S, Zargan J, Umar K, Ahmad S, Katiyar CK, Khan HA (2012) Modulation of the oxidative stress and inflammatory cytokine response by thymoquinone in the collagen induced arthritis in Wistar rats. Chem Biol Interact 197 (1):40–46. https://doi.org/10.1016/J.CBI.2012.03.003

Umar S, Umar K, Sarwar AHMG, Khan A, Ahmad N, Ahmad S, Katiyar CK, Husain SA, Khan HA (2014) Boswellia serrata extract attenuates inflammatory mediators and oxidative stress in collagen induced arthritis. Phytomedicine 21(6):847–856. https://doi.org/10.1016/J.PHYMED.2014.02.001

Upadhyay RK (2017) Nutritional and therapeutic potential of allium vegetables. J Nutr Ther 6(1):18–37. https://doi.org/10.6000/1929-5634.2017.06.01.3

Uttra AM, Alamgeer SM, Shabbir A, Jahan S, Bukhari IA, Assiri AM (2019) Ribes orientale: a novel therapeutic approach targeting rheumatoid arthritis with reference to pro-inflammatory cytokines, inflammatory enzymes and anti-inflammatory cytokines. J Ethnopharmacol 237:92–107. https://doi.org/10.1016/J.JEP.2019.03.019

Vaillancourt F, Silva P, Shi Q, Fahmi H, Fernandes JC, Benderdour M (2011) Elucidation of molecular mechanisms underlying the protective effects of thymoquinone against rheumatoid arthritis. J Cell Biochem 112(1):107–117. https://doi.org/10.1002/JCB.22884

Valerio M, Awad AB (2011) β-Sitosterol down-regulates some pro-inflammatory signal transduction pathways by increasing the activity of tyrosine phosphatase SHP-1 in J774A.1 murine macrophages. Int Immunopharmacol 11 (8):1012–1017. https://doi.org/10.1016/J.INTIMP.2011.02.018

Van Breemen RB, Tao Y, Li W (2011) Cyclooxygenase-2 inhibitors in ginger (*Zingiber officinale*). Fitoterapia 82 (1):38–43. https://doi.org/10.1016/J.FITOTE.2010.09.004

Van Hecke O, Austin SK, Khan RA, Smith BH, Torrance N (2014) Neuropathic pain in the general population: a systematic review of epidemiological studies. Pain 155 (4):654–662. https://doi.org/10.1016/J.PAIN.2013.11.013

Venkatachalam T, Kumar VK, Selvi PK, Maske AO, Kumar NS (2011) Physicochemical and preliminary phytochemical studies on the *Lantana camara* (L.) fruits. Int J Pharm Pharm Sci 3(1):52–54

Vos T, Flaxman AD, Naghavi M, Lozano R, Michaud C, Ezzati M, Shibuya K, Salomon JA, Abdalla S, Aboyans V, Abraham J, Ackerman I, Aggarwal R, Ahn SY, Ali MK, Almazroa MA, Alvarado M, Anderson HR, Anderson LM, Murray CJL (2012) Years lived with disability (YLDs) for 1160 sequelae of 289 diseases and injuries 1990–2010: a systematic analysis for the global burden of disease study 2010. Lancet 380(9859):2163–2196. https://doi.org/10.1016/S0140-6736(12)61729-2

Voukeng IK, Beng VP, Kuete V (2016) Antibacterial activity of six medicinal Cameroonian plants against Gram-positive and Gram-negative multidrug resistant phenotypes. BMC Complement Altern Med. https://doi.org/10.1186/S12906-016-1371-Y

Waggas AM, Balawi EA (2008) Neurophysiological study on possible protective effect of rosemary (Rosmarinus officinalis) leaves extract in male albino rats treated with acrylamide. Am-Eurasian J Sci Res 3(2):163–171

Wang T, Liu B, Zhang W, Wilson B, Hong JS (2004) Andrographolide reduces inflammation-mediated dopaminergic neurodegeneration in mesencephalic neuron-glia cultures by inhibiting microglial activation. J Pharmacol Exp Ther 308(3):975–983. https://doi.org/10.1124/JPET.103.059683

Wang H, Zhang C, Wu Y, Ai Y, Lee DY-W, Dai R (2014) Comparative pharmacokinetic study of two boswellic acids in normal and arthritic rat plasma after oral administration of Boswellia serrata extract or Huo Luo Xiao Ling Dan by LC-MS. Biomed Chromatogr 28 (10):1402–1408. https://doi.org/10.1002/BMC.3182

Wang ZY, Shi SY, Li SJ, Chen F, Chen H, Lin HZ, Lin JM (2015) Efficacy and safety of duloxetine on osteoarthritis knee pain: a meta-analysis of randomized controlled trials. Pain Med 16(7):1373–1385. https://doi.org/10.1111/PME.12800

Webster R, Norman P, Goodacre S, Thompson AR, McEachan RRC (2014) Illness representations, psychological distress and non-cardiac chest pain in patients attending an emergency department. Psychol Health 29(11):1265–1282. https://doi.org/10.1080/08870446.2014.923885

Wegener T, Lüpke NP (2003) Treatment of patients with arthrosis of hip or knee with an aqueous extract of Devil's Claw (*Harpagophytum procumbens* DC.). Phytother Res 17(10):1165–1172. https://doi.org/10.1002/PTR.1322

Weiner DK, Ernst E (2004) Complementary and alternative approaches to the treatment of persistent musculoskeletal pain. Clin J Pain 20(4):244–255. https://doi.org/10.1097/00002508-200407000-00006

Weremczuk-Jeżyna I, Wysokińska H, Kalemba D (2011) Constituents of the essential oil from hairy roots and plant roots of *Arnica montana* L. J Essent Oil Res 23(1):91–97. https://doi.org/10.1080/10412905.2011.9700432

Williams ACDC, Craig KD (2016) Updating the definition of pain. Pain 157(11):2420–2423. https://doi.org/10.1097/J.PAIN.0000000000000613

Williams VL, Victor JE, Crouch NR (2013) Red Listed medicinal plants of South Africa: status, trends, and assessment challenges. S Afr J Bot 86:23–35. https://doi.org/10.1016/J.SAJB.2013.01.006

Winter RW, Korzenik JR (2017) The practical pros and cons of complementary and alternative medicine in practice: integrating complementary and alternative medicine into clinical care. Gastroenterol Clin North Am 46(4):907–916. https://doi.org/10.1016/J.GTC.2017.08.013

Wölfle U, Seelinger G, Schempp CM (2013) Topical application of St. John's wort (*Hypericum perforatum*). Planta Med 80(0203):109–120. https://doi.org/10.1055/S-0033-1351019

Woolf CJ (2010) What is this thing called pain? J Clin Investig 120(11):3742–3744. https://doi.org/10.1172/JCI45178

Wu W, Wang Y (2012) Pharmacological actions and therapeutic applications of *Salvia miltiorrhiza* depside salt and its active components. Acta Pharmacol Sin 33(9):1119–1130. https://doi.org/10.1038/aps.2012.126

Xing W, Guo W, Zou CH, Fu TT, Li XY, Zhu M, Qi JH, Song J, Dong CH, Li Z, Xiao Y, Yuan PS, Huang H, Xu X (2015) Acemannan accelerates cell proliferation and skin wound healing through AKT/mTOR signaling pathway. J Dermatol Sci 79(2):101–109. https://doi.org/10.1016/J.JDERMSCI.2015.03.016

Xiong Y, Li M, Sun P, Liang W, Hornbeck RG, Che X, Rao C, Zhao Y, Guo L, Huang Y, Yang H, Li P, Kroes BH, Cui X, Franz G, Wang M (2022) Market access for Chinese herbal medicinal products in Europe-A ten-year review of relevant products, policies, and challenges. Phytomed Int J Phytother Phytopharmacol. https://doi.org/10.1016/J.PHYMED.2022.154237

Yadollah-Damavandi S, Chavoshi-Nejad M, Jangholi E, Nekouyian N, Hosseini S, Seifaee A, Rafiee S, Karimi H, Ashkani-Esfahani S, Parsa Y, Mohsenikia M (2015) Topical hypericum perforatum improves tissue regeneration in full-thickness excisional wounds in diabetic rat model. Evid-Based Complement Altern Med. https://doi.org/10.1155/2015/245328

Yagi A, Yu BP (2018) Prophylactic aloe components on autoimmune diseases: Barbaloin, aloe-emodin, emodin, and fermented butyrate. J Gastroenterol Hepatol Res 7 (2):2535–2541

Yan J, Chen Y, He C, Yang Z, Lü C, Chen X (2012) Andrographolide induces cell cycle arrest and apoptosis in human rheumatoid arthritis fibroblast-like synoviocytes. Cell Biol Toxicol 28:47–56

Yang M, Liu A, Guan S, Sun J, Xu M, Guo D (2006) Characterization of tanshinones in the roots of Salvia miltiorrhiza (Dan-shen) by high-performance liquid chromatography with electrospray ionization tandem mass spectrometry. Rapid Commun Mass Spectrom 20 (8):1266–1280. https://doi.org/10.1002/RCM.2447

Yang CLH, Or TCT, Ho MHK, Lau ASY (2012) Scientific basis of botanical medicine as alternative remedies for rheumatoid arthritis. Clin Rev Allergy Immunol 44 (3):284–300. https://doi.org/10.1007/S12016-012-8329-8

Yin W, Wang TS, Yin FZ, Cai BC (2003) Analgesic and anti-inflammatory properties of brucine and brucine N-oxide extracted from seeds of Strychnos nux-vomica. J Ethnopharmacol 88(2–3):205–214. https://doi.org/10.1016/S0378-8741(03)00224-1

Younesy S, Amiraliakbari S, Esmaeili S, Alavimajd H, Nouraei S (2014) Effects of fenugreek seed on the severity and systemic symptoms of dysmenorrhea. J Reprod Infertility 15(1):48–48

Young IC, Chuang ST, Hsu CH, Sun YJ, Liu HC, Chen YS, Lin FH (2017) Protective effects of aucubin on osteoarthritic chondrocyte model induced by hydrogen peroxide and mechanical stimulus. BMC Complement Altern Med. https://doi.org/10.1186/S12906-017-1581-Y

Younis T, Khan MR, Sajid M, Majid M, Zahra Z, Shah NA (2016) Fraxinus xanthoxyloides leaves reduced the level of inflammatory mediators during in vitro and in vivo studies. BMC Complement Altern Med 16(1):1–16. https://doi.org/10.1186/S12906-016-1189-7

Yu MH, Choi JH, Chae IG, Im HG, Yang SA, More K, Lee IS, Lee J (2013) Suppression of LPS-induced inflammatory activities by *Rosmarinus officinalis* L. Food Chem 136 (2):1047–1054. https://doi.org/10.1016/J.FOODCHEM.2012.08.085

Yuan Y, Lin X, Xu DS, Feng Y, Wang YH (2010) Studies on the in vivo transmigration of chuanxiong bioactive parts for the treatment of migraine. Chin Pharma J 45:694–697

Yuan Fang Z, Lin R, Xiang Yuan B, De Yang G, Liu Y, Zhang H (2008) Tanshinone IIA downregulates the CD40 expression and decreases MMP-2 activity on atherosclerosis induced by high fatty diet in rabbit. J Ethnopharmacol 115(2):217–222. https://doi.org/10.1016/J.JEP.2007.09.025

Yudoh K, Terauchi K, Yui N, Kobayashi H, Fujiya H, Niki H, Musha H (2017) Impact of NAD-dependent deacetylase Sirtuin-1 in the osteophyte formation and the degradation of articular cartilage in osteoarthritis (OA). Osteoarthr Cartil 25:S152–S153. https://doi.org/10.1016/J.JOCA.2017.02.252

Yuliani S, Partadiredja G et al (2018) The neuroprotective effects of an ethanolic turmeric (*Curcuma longa* L.) extract against trimethyltin-induced oxidative stress in rats. Nutr Neurosci 22(11):797–804. https://doi.org/10.1080/1028415X.2018.1447267

Zaka M, Sehgal SA, Shafique S, Abbasi BH (2017) Comparative in silico analyses of *Cannabis sativa*, *Prunella vulgaris* and *Withania somnifera* compounds elucidating the medicinal properties against rheumatoid arthritis. J Mol Graph Model 74:296–304. https://doi.org/10.1016/J.JMGM.2017.04.013

Zanjani TM, Ameli H, Labibi F, Sedaghat K, Sabetkasaei M (2014) The attenuation of pain behavior and serum COX-2 concentration by curcumin in a rat model of neuropathic pain. Korean J Pain 27(3):252–252. https://doi.org/10.3344/KJP.2014.27.3.246

Zargaran A, Borhani-Haghighi A, Faridi P, Daneshamouz S, Kordafshari G, Mohagheghzadeh A (2014) Potential effect and mechanism of action of topical chamomile (*Matricaria chammomila* L.) oil on migraine headache: a medical hypothesis. Med Hypotheses 83(5):566–569. https://doi.org/10.1016/J.MEHY.2014.08.023

Zargaran A, Borhani-Haghighi A, Salehi-Marzijarani M, Faridi P, Daneshamouz S, Azadi A, Sadeghpour H, Sakhteman A, Mohagheghzadeh A (2018) Evaluation of the effect of topical chamomile (*Matricaria chamomilla* L.) oleogel as pain relief in migraine without aura: a randomized, double-blind, placebo-controlled, crossover study. Neurol Sci 39(8):1345–1353. https://doi.org/10.1007/S10072-018-3415-1

Zeng Y, Li Y, Yang J, Pu X, Du J, Yang X, Yang T, Yang S (2017a) Therapeutic role of functional components in alliums for preventive chronic disease in human being. Evid-Based Complement Altern Med. https://doi.org/10.1155/2017/9402849

Zeraati F, Shobeiri F, Nazari M, Araghchian M, Bekhradi R (2014) Comparative evaluation of the efficacy of herbal drugs (fennelin and vitagnus) and mefenamic acid in the

treatment of primary dysmenorrhea. Iran J Nurs Midwifery Res 19(6):584–584

Zgrajka W, Turska M, Rajtar G et al (2013) Kynurenic acid content in anti-rheumatic herbs. Yadda. Icm. Edu. Pl 20 (4):800–802

Zhang Q, Peng W, Wei S, Wei D, Li R, Liu J, Peng L, Yang S, Gao Y, Wu C, Pu X (2019) Guizhi-Shaoyao-Zhimu decoction possesses anti-arthritic effects on type II collagen-induced arthritis in rats via suppression of inflammatory reactions, inhibition of invasion & migration and induction of apoptosis in synovial fibroblasts. Biomed Pharmacother 118:109367–109367. https://doi.org/10.1016/J.BIOPHA.2019.109367

Zhao GR, Zhang HM, Ye TX, Xiang ZJ, Yuan YJ, Guo ZX, Zhao LB (2008) Characterization of the radical scavenging and antioxidant activities of danshensu and salvianolic acid B. Food Chem Toxicol 46(1):73–81. https://doi.org/10.1016/J.FCT.2007.06.034

Zhao LX, Jiang BC, Wu XB, Cao DL, Gao YJ (2014) Ligustilide attenuates inflammatory pain via inhibition of NFκB-mediated chemokines production in spinal astrocytes. Eur J Neurosci 39(8):1391–1402. https://doi.org/10.1111/EJN.12502

Zhao X, Xu Y, Zhao Q, Chen C, Liu A, Huang Z (2012) Curcumin exerts antinociceptive effects in a mouse model of neuropathic pain: descending monoamine system and opioid receptors are differentially involved. Neuropharmacology 62(2):843–854. https://doi.org/10.1016/j.neuropharm.2011.08.050

Zhou G, Pang H, Tang Y, Yao X, Mo X, Zhu S, Guo S, Qian D, Qian Y, Su S, Zhang L, Jin C, Qin Y, Duan J (2013) Hydrophilic interaction ultra-performance liquid chromatography coupled with triple-quadrupole tandem mass spectrometry for highly rapid and sensitive analysis of underivatized amino acids in functional foods. Amino Acids 44(5):1293–1305. https://doi.org/10.1007/s00726-013-1463-7

Zhou G, Li R, Xia T, Ma C, Shen J (2019) Utilizing network pharmacology to explore the underlying mechanism of *Cinnamomum cassia* Presl in treating osteoarthritis. Int J Clin Exp Med 12(12):13359–13369

Zhu MD, Zhao LX, Wang XT, Gao YJ, Zhang ZJ (2014a) Ligustilide inhibits microglia-mediated proinflammatory cytokines production and inflammatory pain. Brain Res Bull 109:54–60. https://doi.org/10.1016/J.BRAINRESBULL.2014.10.002

Zou S, Kumar U (2018) Cannabinoid receptors and the endocannabinoid system: signaling and function in the central nervous system. Int J Mol Sci 19(3):833–833. https://doi.org/10.3390/IJMS19030833

Zou S, Wang C, Cui Z, Guo P, Meng Q, Shi X, Gao Y, Yang G, Han Z (2016) β-Elemene induces apoptosis of human rheumatoid arthritis fibroblast-like synoviocytes via reactive oxygen species-dependent activation of p38 mitogen-activated protein kinase. Pharmacol Rep 68 (1):7–11. https://doi.org/10.1016/J.PHAREP.2015.06.004