



E-ISSN: 2707-2835

P-ISSN: 2707-2827

www.pharmacognosyjournal.com

IJPLS 2021; 2(1): 61-66

Received: 20-01-2021

Accepted: 25-03-2021

Rasika J Patil

Department of Quality Assurance Smt. Kishoritai Bhojar College of Pharmacy, Kamptee, Rashtrasant Tukadoji Maharaj University, Nagpur, Maharashtra, India

Samiksha M Nikam

Department of Quality Assurance Smt. Kishoritai Bhojar College of Pharmacy, Kamptee, Rashtrasant Tukadoji Maharaj University, Nagpur, Maharashtra, India

Priya S Milmile

Department of Quality Assurance Smt. Kishoritai Bhojar College of Pharmacy, Kamptee, Rashtrasant Tukadoji Maharaj University, Nagpur, Maharashtra, India

Nishant B Awandekar

Department of Quality Assurance Smt. Kishoritai Bhojar College of Pharmacy, Kamptee, Rashtrasant Tukadoji Maharaj University, Nagpur, Maharashtra, India

Dr. Milind J Umekar

Department of Quality Assurance Smt. Kishoritai Bhojar College of Pharmacy, Kamptee, Rashtrasant Tukadoji Maharaj University, Nagpur, Maharashtra, India

Corresponding Author:

Rasika J Patil

Department of Quality Assurance Smt. Kishoritai Bhojar College of Pharmacy, Kamptee, Rashtrasant Tukadoji Maharaj University, Nagpur, Maharashtra, India

Herbal treatment for migraine

Rasika J Patil, Samiksha M Nikam, Priya S Milmile, Nishant B Awandekar and Dr. Milind J Umekar

DOI: <https://doi.org/10.33545/27072827.2021.v2.i1a.29>

Abstract

Migraine is a debilitating neurovascular disorder with a number of targeted, tolerant and effective treatments. The formulation made in plant-based plants, holds great promise in the identification of new therapeutic goals for migraine. Therefore, safety and performance tests are essential. We are reviewing some of the phytomedicines that may be useful in the treatment of migraine-feverfew (*Tanacetum Parthenium*), butterbur (*Petasites hybridus*), menthol (*Mentha piperita*), coriander (*C. sativum*), Ginkgobiloba (*Gingko macrophylla K. Koch*), Ginger (*Zingiber officinale Rosc.*), Matricaria chamomilla (*Matricaria recutita*), Curcumin (*Curcuma longa*), Lavender (*Lavandula spica*) in terms of their mechanisms and evidence of migraine treatment. The results of this systematic review suggest that many herbal remedies, through their many physiological influences, emerge as options for improving migraine treatment. However, other high-level studies are important to evaluate their effectiveness and safety as a treatment for migraine.

Keywords: Migraine, herbal treatment, feverfew, menthol

Introduction

Migraine is a chronic disease that affects about 20% of people in India ^[1]. Is a disease that affects a large proportion of the world's population, with a higher proportion of women (15%) than men (6%) ^[2]. Migraine is a severe headache that is sometimes accompanied by sensitivity to light, sound and movement of the head ^[3, 4]. It is characterized by a recurring episodic headache that lasts 4-72 hours associated with any two (inconsistent, piercing, stiffening, moderate or severe) or one of the symptoms (nausea and / or vomiting, photophobia and phonophobia) ^[5, 6]. It is a varied and complex disease ^[7, 8]. It contains two major clinical subtypes: migraine with or without aura. Migraine with aura (classic migraine), preceded by an aura that includes some of the most recognizable neurological symptoms including bright lights, scotomas, castles, and neurological disorders, as well as motor, which occur approximately 20-40 minutes before of headache about 19-30% of migraine patients. Migraine without aura has many migraine headaches and is often accompanied by nausea, vomiting, photophobia, and phonophobia, which may be exacerbated by physical activity ^[9]. Two percent of people regularly suffer from migraine ^[10, 11].

Pathophysiology

The pathophysiology of migraine is complex and has many implications for how effective herbal treatment is. Primarily the brain stem, hypothalamus, thalamus, and cerebral cortex are critical areas of the brain that reverse migraine pain. The migraine headache process begins in large part in the blood vessels of the meninges, especially the internal arteries, and the meninges themselves. In fact, the only way to find out is to try to get a migraine. While vasodilation of these vessels was believed to be the first event of a migraine headache, it is now clear that this rarely occurs, but rather neurogenic inflammation involving trigeminal nerves and blocking 5-HT_{1B} / 1D receptors are the main sources of the problem. Additional information from the skin and muscles of the head is also transmitted through the trigeminal nerve to the central nervous system and contributes to the development and progression of migraine. Many vasoactive neuropeptides are important regulators of neurogenic inflammation, platelet activation / aggregation, and mast-cell degranulation seen in migraine, including serotonin, a calcitonin-related peptide (CGRP), pituitary adenylate cyclase-

activating peptide (PACAP), histamine, substance P, neurokinin A, bradykinin, and prostaglandins [12].

Available treatments and their adverse effects

All patients with migraine require intensive treatment for each attack, while others require prophylactic pharmacotherapy. There are two types of anti-migraine medications: indirect therapies, such as analgesics and non-inflammatory drugs (NSAIDs), and specific therapies, such as ergotamine and 5-HT_{1B} / D agonists (triptans) [13]. In migraine prevention treatments, b-blockers and anti-epileptic medications are some of the most widely used and well-studied methods of nonspecific prophylactics. However, these prophylactic drugs benefit treatment by only about 25%, and all have very serious side effects [14]. Among these critical therapies, triptans are considered to be the most effective [13]. Triptan medication, one of the most effective treatments for acute migraines, <50% of patients have no pain within two hours of taking it, and approximately 30% have a recurrent headache within 24 hours [15, 16]. Therefore, there is a great deal of alternative therapies and alternative therapies for migraine [12]. However, recurrence, side effects of triptans, and heart safety are major drawbacks of these therapies [13]. Therefore, better treatments for migraine are needed.

Use of herbals as alternative treatment for migraine

There is a growing body of evidence supporting the effectiveness of various 'complementary' therapies and other medications in the management of migraine. Promising tools for treating migraine patients are herbal products [17]. Medicinal plants play a major role in human health care. Traditional medicine refers to a wide range of ancient natural health practices such as Ayurveda, Siddha and Unani. The use of herbal remedies is slowly increasing in the western world, with about 40 percent of people reporting herbal remedies in the past year [18]. Many herbal remedies and formulas are effective for those who suffer from migraine, both as an effective treatment and prevention, especially when combined with the diagnosis and elimination of migraine causes [12]. Nature has been a source of healing properties for a long time and an astonishing number of modern medicines have come from natural sources, many of which are based on their use in traditional medicine.

Herbal products are described as, by their medicinal properties, they may or may not have a beneficial effect on the treatment of migraine patients [17].

Feverfew

Feverfew is currently used for migraine headache prophylaxis and to treat arthritis [19]. This (*Tanacetum parthenium* L.) of the family Asteraceae (daisy) is a perennial daisy plant found mainly in gardens and roadsides in the Balkan mountains of Europe and can now be found in Australia, China, Japan, North and South America, and North America.

The mechanism of action of feverfew remains unknown, [20] although researchers have raised many possibilities: inhibition of serotonin release, inhibition of prostaglandin synthesis, inhibition of platelet aggregation and inhibition, inhibition of polymorphonuclear leukocyte degranulation, prevention of phagocytosis human population, inhibition of mast-cell histamine release, cytotoxic activity against

human tumors, antimicrobial activity, and antithrombotic activity [20, 21]. Feverfew can inhibit the release of serotonin from platelets in a similar way to methysergide maleate, an ergot alkaloid [22]. The irreversible inhibition of syntaglandin synthesis is thought to occur in a different way than that of salicylates, possibly by inhibiting cyclooxygenase and phospholipase A₂. Alpha-methylene butyrolactones found in feverfew, especially parthenolid and epoxyartemorin, have been shown to inevitably inhibit thromboxane B₂ and leukotriene B₄ in human leukocytes [23]. Inhibition of thromboxane B₂ and leukotriene B₄ indicates that phospholipase, possibly phospholipase A₂, is inhibited. Some researchers have reported that inhibition of phagocytosis of human neutrophils could reduce tissue damage by oxygen radicals.

Butterbur

Petasites species comes from a ring around the Northern Hemisphere and belongs to the Asteraceae family. Butterbur, a plant native to Europe, is derived from the rhizomes and stems of the perennial butterbur bush (*P. hybridus*). In traditional medicine, butterbur extract has been used to treat disease, asthma, stomach ailments, respiratory diseases, and cancer. Commercial butterbur extracts can be extracted from the root, rhizome (underground stem), or plant leaves.

The mechanism of action of the Petasites is not fully understood, it may be active in calcium channel control and inhibition of peptide leukotriene biosynthesis, thereby affecting the inflammatory eruption associated with migraine [24]. The chemically active substances of butterbur are sesquiterpenes such as petasin and isopetasin. They have a strong anti-inflammatory effect by inhibiting leukotriene synthesis and COX-2-mediated prostaglandin E₂ release [25]. While the butterbur plant also contains pyrrolizidine alkaloids, which are hepatotoxic, carcinogenic, lung toxic and prothrombotic; these are derived from available commercially available preparations, such as Petadolex Petaforce, Petadolor H, Tesalin, and Tussilago) [26, 27]. However, patients should be advised to use only certified butterbur products labeled "PA-free". The efficacy of Petasites hybridus in migraine prevention has been tested in several studies [28, 29].

Menthol

Menthol is a naturally occurring compound found in mint plants such as peppermint and spearmint. It promotes a cooling sensation when applied to the skin and mucosal skin and works on nerve fibers and smooth muscle fibers.

Menthol has several side effects that can positively affect migraine pathology. It has analgesic effects by making the kappa opioid receptor; acts on TRPM8 receptors to produce a cooling sensation and inhibits energy-sensitive sodium channels (inhibiting sensory reduction); as a spasmolytic agent, it may contribute to the tendency of precranial tissue and by correcting myofascial input, reduce cognitive impairment such as migraine intolerance; can prevent the transmission of nociceptive sensations from pain-producing vessels, through the branches of the trigeminal nerve, to higher brain centers; and with its anti-inflammatory effects, by suppressing prostaglandin E₂, leukotriene B₄, and interleukin-1 β , it may act as a pain reliever [30, 31, 32, 33, 34].

Coriander

Coriander (*C. sativum*), a member of the family Apiaceae (Umbelliferae), Fruit (seeds) forms an important component of curry powder and is traditionally used to treat intestinal disorders such as loss of appetite, dyspepsia, bloating, diarrhea, pain, and vomiting. Fruits (seeds and pericarp) are the most widely used coriander plant and the most important nutrients are essential oils and oils [35].

Coriander and its constituents as a promising treatment for migraines as shown in animal studies that coriander has analgesic and anti-inflammatory activity and can delay both neurogenic pain and inflammation [36, 37]. Linalol Corriander is considered safe and well tolerated, based on animal toxicology studies [38, 39]. However, it can lower blood glucose levels and have hypotensive effects so caution is needed in qualified individuals [40, 41].

Ginkgo biloba

Ginkgo leaves are found in the ginkgo biloba tree, and the Ginkgoaceae Ginkgo family is a distinct tree that has no close relatives [42]. Ginkgolide B, extracted from herbs from the leaves of the *Ginkgo biloba* tree, is a natural reaction to glutamate action in the CNS [43].

In addition, it is a powerful anti-inflammatory agent (PAF). PAF is a potent inflammatory and nociceptive agent released during the inflammatory process [44]. Indeed, PAF, released from platelets and leukocytes, during the first phase of a migraine attack, can strengthen the trigeminal-vascular endothelium and cause pain [45, 46]. Therefore, ginkgolide B can be considered as a promising medical aid in the treatment of migraine with aura *Ginkgo biloba*.

Ginger

Ginger (*Zingiber officinale* Rosc.), belonging to a tropical and sub-tropical family – Zingiberaceae, originating in South-East Asia and introduced to many parts of the globe, has been cultivated for thousands of years as a spice and for medicinal purposes [47].

Ginger have been proposed to justify the analgesic action of ginger, including the inhibition of arachidonic acid metabolism via the cyclooxygenase (COX) pathways, similar to the non-steroidal anti-inflammatory drugs [48]. Ginger also acts to block lipoxygenase (LOX), another enzyme associated with the arachidonic acid pathway [49]. The concomitant inhibition of COX and LOX may increase anti-inflammatory action and reduce its side effects [50]. Furthermore, shogaols seem to modulate neuroinflammatory response through the down-regulation of inflammatory markers on microglial cells [51], while gingerols may act as agonists of the capsaicin-activated vanilloid receptors [52]. To date, only a few uncontrolled studies and one case report have shown the analgesic effect of ginger in migraine [53, 54, 55].

Chamomile

Matricaria chamomilla (same name: *Matricaria recutita*), better known as chamomile (also spelled camomile), German chamomile (Skip to top: ab "German chamomile"), Hungarian chamomile (kamilla), chamomile wild, chamomile blue, or fragrant mayweed [56, 57] is an annual plant of the compound family Asteraceae.

Nitric Oxide is a critical molecule that causes migraine headaches. Prevention or reduction of its integration may be helpful in treating migraine attacks and pain [58]. No one

plays a vital role in rehabilitating moderate sensitivity. Subsequently, NO synthase (NOS) inhibition is a target in the treatment of migraine [59]. Chamomile hydrophilic compounds (polyphenolic compounds [Flavonoides] including apigenin as a major compound) inhibit the expression of NOS in active macrophages and can lead to inhibition of NO secretion and synthesis [60]. Such an effect can be seen in the essential oils of chamomile including chamazulene [61] and in addition, it can reduce inflammation in the workplace and reduce migraine pain. Chamomile is traditionally used for inflammation, pain, neuralgia, etc. [62]. The carrier for this preparation, sesame oil including fatty acids and sesamine, was traditionally used alone as a headache remedy [63, 63]. Sesame oil has shown anti-inflammatory effects in its external use to prevent chemical-induced phlebitis [65]. Combined with other therapeutic drugs, it has also had an analgesic effect similar to salicylate ointment in patients with osteoarthritis of the knee [66]. Sesamine as an important active compound of sesame oil also has anti-inflammatory activity [67]. In hindsight, it is expected that sesame oil is not only a carrier but also helpful in reducing pain during migraine attacks.

Curcumin

Curcumin is the first yellow dye separated from turmeric (*Curcuma longa*). The main curcuminoid found in the turmeric rhizome and is one of the most well-known plant polyphenols [68].

Several methods have been suggested to show the protective effect of curcumin on neurological problems. Curcumin has anti-inflammatory properties [69] and can alter the expression of cytokines, chemokines, and many apoptotic factors. The molecule is listed as a cytokine anti-inflammatory drug that can slow down the activation of several transcription factors such as NF- κ B (nuclear factor kappa-light-chain-enhancer of activated B cells), signal transducer and activator for writing, and and AP-1 (activator protein 1) [70]. Interestingly, curcumin has been listed as a potential NF- κ B inhibitor [71]. Notably, curcumin can maintain mitochondrial function, its potency, and ultimately cell function and synaptic function [72].

Lavender

Lavender is an evergreen flowering plant [73] from the Lamiales family in the western Mediterranean [74], growing up to 10 feet (3 m) in height and with purple lilac flowers [73]. Lavender is a plant used in traditional medicine of the Lamiaceae family. Lavender has a long list of applications [75] and a long history of medical use [76].

Numerous studies have been conducted to determine the mechanism of lavender activity in neuronal tissues. Lavender inhibits the inflammatory response of lipopolysaccharide in the human monocyte THP-1 cell effect, which may be associated with HSP70 expression. The weakest antioxidant and cholinergic inhibition was reported with lavender [77, 78] and linalool [79, 80]. Linalool inhibits the release of acetylcholine and alters ion channel activation in neuromuscular integration [81].

Conclusion

Herbal medicine, through their many physical influences, presents it as a possible way to improve the treatment of migraine. As an independent treatment, the strongest evidence for prophylactic treatment of migraine in humans

is the limited extraction of Butterbur roots, which have been found in feverfew operations included. Preliminary evidence from the study suggests that curcumin may be an effective treatment for migraine, although greater efficacy is found in combination with omega-3 fatty acids or CoQ10. As a powerful treatment for migraine, positive findings have been found in the topical and intranasal delivery of menthol / peppermint oil. Treatment with Butterbur, coriander, Ginkgo Bailoba, Ginger lavender, and chamomile has been well researched in these ingredients. All in all, despite the promise, further research into the safety and effectiveness of alternative therapies for migraine treatment is needed before certain conclusions can be made.

References

- Gupta VK. Migraine-related vertigo: The challenge of the basic sciences. *Clinical neurology and neurosurgery* 2005;1(108):109-10.
- Lipton RB, Stewart WF. The epidemiology of migraine. *European neurology* 1994;34(2):6-11.
- Goadsby PJ. Recent advances in understanding migraine mechanisms, molecules and therapeutics. *Trends in molecular medicine* 2007;13(1):39-44.
- Goadsby PJ. The vascular theory of migraine—a great story wrecked by the facts. *Brain* 2009;132(1):6-7.
- Olsen J. Headache Classification Subcommittee of the International Headache Society. *The International Classification of Headache Disorders: 2nd edition. Cephalalgia* 2004;24:9-160.
- Wang D, Yuan X, Liu T *et al.* Neuroprotective activity of lavender oil on transient focal cerebral ischemia in mice, *Molecules* 2012;17(8):9803-9817.
- Buse DC, Greisman JD, Baigi K, Lipton RB. Migraine progression: a systematic review. *Headache: The Journal of Head and Face Pain* 2019;59(3):306-38.
- Gazerani P. Migraine and diet. *Nutrients* 2020;12(6):1658.
- Samsam M. Central nervous system acting drugs in treatment of migraine headache. *Central Nervous System Agents in Medicinal Chemistry (Formerly Current Medicinal Chemistry-Central Nervous System Agents)* 2012;12(3):158-72.
- Takaku S, Osono E, Kuribayashi H, Takaku C, Hiramata N, Takahashi H. A case of migraine without aura that was successfully treated with an herbal medicine. *The Journal of Alternative and Complementary Medicine* 2013;19(12):970-2.
- Olesen J, Ashina M. Emerging migraine treatments and drug targets. *Trends in pharmacological sciences* 2011;32(6):352-9.
- Yarnell E. Herbal medicine and migraine. *Alternative and Complementary Therapies* 2017;23(5):192-201.
- Magis D, Schoenen J. Treatment of migraine: update on new therapies. *Current opinion in neurology* 2011;24(3):203-10.
- Task force, Evers S, Afra J, Frese A, Goadsby PJ, Linde M, May A *et al.* EFNS guideline on the drug treatment of migraine—report of an EFNS task force. *European Journal of Neurology* 2006;13(6):560-72.
- Ferrari MD, Roon KI, Lipton RB, Goadsby PJ. Oral triptans (serotonin 5-HT_{1B/1D} agonists) in acute migraine treatment: a meta-analysis of 53 trials. *The Lancet* 2001;358(9294):1668-75.
- Goadsby PJ, Sprenger T. Current practice and future directions in the prevention and acute management of migraine. *The Lancet Neurology* 2010;9(3):285-98.
- D'Andrea G, Cevoli S, Cologno D. Herbal therapy in migraine. *Neurological Sciences* 2014;35(1):135-40.
- Arulmozhi DK, Veeranjanyulu A, Bodhankar SL. The herbal approach for the treatment of migraine.
- Force LH. Massachusetts College of Pharmacy and Health Sciences, and the Dana Farber Cancer Institute.
- Hobbs C. Feverfew. *Herbalgram* 1989;20:26-35.
- Hayes NA, Foreman JC. The activity of compounds extracted from feverfew on histamine release from rat mast cells. *Journal of pharmacy and pharmacology* 1987;39(6):466-70.
- Heptinstall S, Williamson L, White A, Mitchell JR. Extracts of feverfew inhibit granule secretion in blood platelets and polymorphonuclear leucocytes. *The Lancet* 1985;325(8437):1071-4.
- Sumner H, Salan U, Knight DW, Hoult JR. Inhibition of 5-lipoxygenase and cyclo-oxygenase in leukocytes by feverfew: Involvement of sesquiterpene lactones and other components. *Biochemical pharmacology* 1992;43(11):2313-20.
- Eaton J. Butterbur, herbal help for migraine. *Nat Pharm* 1998;2(1):23-4.
- Taylor FR. Nutraceuticals and headache: the biological basis. *Headache: the journal of head and face pain* 2011;51(3):484-501.
- Giles M, Ulbricht C, Singh Khalsa KP, Kirkwood CD, Park C, Basch E. Butterbur: an evidence-based systematic review by the natural standard research collaboration. *Journal of herbal pharmacotherapy* 2005;5(3):119-43.
- Sun-Edelstein C, Mauskop A. Alternative headache treatments: nutraceuticals, behavioral and physical treatments. *Headache: The Journal of Head and Face Pain* 2011;51(3):469-83.
- Grossmann M, Schmidramsl H. An extract of *Petasites hybridus* is effective in the prophylaxis of migraine. *International journal of clinical pharmacology and therapeutics* 2000;38(9):430-5.
- Lipton RB, Göbel H, Einhüpl KM, Wilks K, Mauskop A. *Petasites hybridus* root (butterbur) is an effective preventive treatment for migraine. *Neurology* 2004;63(12):2240-4.
- Borhani Haghighi A, Motazedian S, Rezaii R. Therapeutic potentials of menthol in migraine headache: Possible mechanisms of action. *Medical Hypotheses* 2007;69(2):455.
- Galeotti N, Mannelli LD, Mazzanti G, Bartolini A, Ghelardini C. Menthol: a natural analgesic compound. *Neuroscience letters* 2002;322(3):145-8.
- Göbel H, Schmidt G, Soyka D. Effect of peppermint and eucalyptus oil preparations on neurophysiological and experimental algometric headache parameters. *Cephalalgia* 1994;14(3):228-34.
- Morenilla-Palao C, Luis E, Fernández-Peña C, Quintero E, Weaver JL, Bayliss DA *et al.* Ion channel profile of TRPM8 cold receptors reveals a role of TASK-3 potassium channels in thermo sensation. *Cell reports* 2014;8(5):1571-82.
- Pergolizzi Jr JV, Taylor Jr R, LeQuang JA, Raffa RB, NEMA Research Group. The role and mechanism of action of menthol in topical analgesic products. *Journal*

- of clinical pharmacy and therapeutics 2018;43(3):313-9.
35. Sahib NG, Anwar F, Gilani AH, Hamid AA, Saari N, Alkharfy KM. Coriander (*Coriandrum sativum* L.): A potential source of high-value components for functional foods and nutraceuticals-A review. *Phytotherapy Research* 2013;27(10):1439-56.
 36. Laribi B, Kouki K, M'Hamdi M, Bettaieb T. Coriander (*Coriandrum sativum* L.) and its bioactive constituents. *Fitoterapia* 2015;103:9-26.
 37. Taherian AA, Vafaei AA, Ameri J. Opiate system mediate the antinociceptive effects of *Coriandrum sativum* in mice. *Iranian journal of pharmaceutical research: IJPR* 2012;11(2):679.
 38. Nitha B, Janardhanan KK. Aqueous-ethanolic extract of morel mushroom mycelium *Morchella esculenta*, protects cisplatin and gentamicin induced nephrotoxicity in mice. *Food and Chemical Toxicology* 2008;46(9):3193-9.
 39. Wei JN, Liu ZH, Zhao YP, Zhao LL, Xue TK, Lan QK. Phytochemical and bioactive profile of *Coriandrum sativum* L. *Food Chemistry* 2019;286:260-267.
 40. Aissaoui A, Zizi S, Israili ZH, Lyoussi B. Hypoglycemic and hypolipidemic effects of *Coriandrum sativum* L. in Meriones shawi rats. *Journal of Ethno pharmacology* 2011;137(1):652-61.
 41. Hussain F, Jahan N, Rahman KU, Sultana B, Jamil S. Identification of hypotensive biofunctional compounds of *Coriandrum sativum* and evaluation of their angiotensin-converting enzyme (ACE) inhibition potential. *Oxidative medicine and cellular longevity* 2018.
 42. Salvador RL. Herbal medicine—Ginkgo. *CPI/PC* 1995;52:39-41.
 43. Williams B, Watanabe CM, Schultz PG, Rimbach G, Krucker T. Age-related effects of Ginkgo biloba extract on synaptic plasticity and excitability. *Neurobiology of aging* 2004;25(7):955-62.
 44. Akisü M, Kültürsay N, Coker I, Hüseyinov A. Platelet-activating factor is an important mediator in hypoxic ischemic brain injury in the new born rat. *Neonatology* 1998;74(6):439-44.
 45. D'andrea G, Hasselmark L, Alecci M, Cananzi A, Perini F, Welch KM. Platelet secretion from dense and alpha-granules *in vitro* in migraine with or without aura. *Journal of Neurology, Neurosurgery & Psychiatry* 1994;57(5):557-61.
 46. Sarchielli P, Alberti A, Coppola F, Baldi A, Gallai B, Floridi A *et al.* Platelet-activating factor (PAF) in internal jugular venous blood of migraine without aura patients assessed during migraine attacks. *Cephalalgia* 2004;24(8):623-30.
 47. Park EJ, Pezzuto JM. Botanicals in cancer chemoprevention. *Cancer and Metastasis Reviews* 2002;21(3):231-55.
 48. Grzanna R, Lindmark L, Frondoza CG. Ginger—an herbal medicinal product with broad anti-inflammatory actions. *Journal of medicinal food* 2005;8(2):125-32.
 49. Kiuchi F, Iwakami S, Shibuya M, Hanaoka F, Sankawa U. Inhibition of prostaglandin and leukotriene biosynthesis by gingerols and diarylheptanoids. *Chemical and Pharmaceutical Bulletin* 1992;40(2):387-91.
 50. Martel-Pelletier J, Lajeunesse D, Reboul P, Pelletier JP. Therapeutic role of dual inhibitors of 5-LOX and COX, selective and non-selective non-steroidal anti-inflammatory drugs. *Annals of the rheumatic diseases* 2003;62(6):501-9.
 51. Ha SK, Moon E, Ju MS, Kim DH, Ryu JH, Oh MS *et al.* 6-Shogaol, a ginger product, modulates neuroinflammation: a new approach to neuroprotection. *Neuropharmacology* 2012;63(2):211-23.
 52. Dedov VN, Tran VH, Duke CC, Connor M, Christie MJ, Mandadi S *et al.* Gingerols: a novel class of vanilloid receptor (VR1) agonists. *British journal of pharmacology* 2002;137(6):793-8.
 53. Cady RK, Schreiber CP, Beach ME, Hart CC. Gelstat Migraine ((R)) (sublingually administered feverfew and ginger compound) for acute treatment of migraine when administered during the mild pain phase. *Medical science monitor* 2005;11(9):PI65-9.
 54. Mustafa T, Srivastava KC. Ginger (*Zingiber officinale*) in migraine headache. *Journal of Ethno pharmacology* 1990;29(3):267-73.
 55. Maghbooli M, Golipour F, Moghimi Esfandabadi A, Yousefi M. Comparison between the efficacy of ginger and sumatriptan in the ablative treatment of the common migraine. *Phytotherapy research* 2014;28(3):412-5.
 56. Pitman CR. *Wild Flowers of Britain and Northern Europe*, by Richard Fitter, Alastair Fitter and Marjorie Blamey. Collins£ 1.60. Oryx 1975;13(1):93-4.
 57. Stace C. *New flora of the British Isles*. Cambridge University Press 2010.
 58. Olesen J. The role of nitric oxide (NO) in migraine, tension-type headache and cluster headache. *Pharmacology & therapeutics* 2008;120(2):157-71.
 59. Barbanti P, Egeo G, Aurilia C, Fofi L, Della-Morte D. Drugs targeting nitric oxide synthase for migraine treatment. *Expert opinion on investigational drugs* 2014;23(8):1141-8.
 60. Bhaskaran N, Shukla S, Srivastava JK, Gupta S. Chamomile: an anti-inflammatory agent inhibits inducible nitric oxide synthase expression by blocking RelA/p65 activity. *International journal of molecular medicine* 2010;26(6):935-40.
 61. Ansari M, Rafiee K, Emamgholipour S, Fallah MS. Migraine: Molecular basis and herbal medicine. *Advanced Topics in Neurological Disorders*. London: In Tech Open 2012, 187-214.
 62. Srivastava JK, Shankar E, Gupta S. Chamomile: a herbal medicine of the past with a bright future. *Molecular medicine reports* 2010;3(6):895-901.
 63. Morris JB. Food, industrial, nutraceutical, and pharmaceutical uses of sesame genetic resources. *Trends in new crops and new uses* 2002;1(1):153-6.
 64. Phitak T, Pothacharoen P, Settakorn J, Poopimol W, Caterson B, Kongtawelert P. Chondroprotective and anti-inflammatory effects of sesamin. *Phytochemistry* 2012;80:77-88.
 65. Nekuzad N, Torab TA, Mojab F, Alavi-Majd H, Azadeh P, Ehtejab G. Effect of external use of sesame oil in the prevention of chemotherapy-induced phlebitis. *Iranian journal of pharmaceutical research: IJPR* 2012;11(4):1065.
 66. Zahmatkash M, Vafaeenasab MR. Comparing analgesic effects of a topical herbal mixed medicine with

- salicylate in patients with knee osteoarthritis. Pakistan journal of biological sciences: PJBS. 2011;14(13):715-9.
67. Asanuma M, Nishibayashi-Asanuma S, Miyazaki I, Kohno M, Ogawa N. Neuroprotective effects of non-steroidal anti-inflammatory drugs by direct scavenging of nitric oxide radicals. Journal of neurochemistry 2001;76(6):1895-904.
68. Aggarwal BB, Kumar A, Bharti AC. Anticancer potential of curcumin: preclinical and clinical studies. Anticancer research 2003;23(1/A):363-98.
69. Ji HF, Shen L. The multiple pharmaceutical potential of curcumin in Parkinson's disease. CNS & Neurological Disorders-Drug Targets (Formerly Current Drug Targets-CNS & Neurological Disorders) 2014;13(2):369-73.
70. Ullah F, Liang A, Rangel A, Gyengesi E, Niedermayer G, Münch G. High bioavailability curcumin: an anti-inflammatory and neurosupportive bioactive nutrient for neurodegenerative diseases characterized by chronic neuroinflammation. Archives of Toxicology 2017;91(4):1623-34.
71. Seo EJ, Fischer N, Efferth T. Phytochemicals as inhibitors of NF- κ B for treatment of Alzheimer's disease. Pharmacological research 2018;129:262-73.
72. Reddy PH, Manczak M, Yin X, Grady MC, Mitchell A, Kandimalla R *et al.* Protective effects of a natural product, curcumin, against amyloid β induced mitochondrial and synaptic toxicities in Alzheimer's disease. Journal of Investigative Medicine 2016;64(8):1220-34.
73. Schiller C, Schiller D. The aromatherapy encyclopedia: a concise guide to over 385 plant oils. Basic Health Publications, Inc 2008.
74. Olapour A, Behaen K, Akhondzadeh R, Soltani F, al Sadat Razavi F, Bekhradi R. The effect of inhalation of aromatherapy blend containing lavender essential oil on cesarean postoperative pain. Anesthesiology and pain medicine 2013;3(1):203.
75. Enteen S. Essential Oils for Pain Relief. Massage Today 2005;5(2):15-7.
76. Koulivand PH, Khaleghi Ghadiri M, Gorji A. Lavender and the nervous system. Evidence-based complementary and alternative medicine 2013.
77. Wang D, Yuan X, Liu T, Liu L, Hu Y, Wang Z *et al.* Neuroprotective activity of lavender oil on transient focal cerebral ischemia in mice. Molecules 2012;17(8):9803-17.
78. Salah SM, Jäger AK. Screening of traditionally used Lebanese herbs for neurological activities. Journal of ethnopharmacology 2005;97(1):145-9.
79. Perry NS, Houghton PJ, Theobald A, Jenner P, Perry EK. *In-vitro* inhibition of human erythrocyte acetyl cholinesterase by *Salvia lavandulaefolia* essential oil and constituent terpenes. Journal of pharmacy and pharmacology 2000;52(7):895-902.
80. Savelev S, Okello E, Perry NS, Wilkins RM, Perry EK. Synergistic and antagonistic interactions of anticholinesterase terpenoids in *Salvia lavandulaefolia* essential oil. Pharmacology Biochemistry and Behavior 2003;75(3):661-8.
81. Re L, Barocci S, Sonnino S, Mencarelli A, Vivani C, Paolucci G *et al.* Linalool modifies the nicotinic receptor-ion channel kinetics at the mouse neuromuscular junction. Pharmacological Research 2000;42(2):177-81.