





Nutrition and Phytotherapy: A Winning Combination Against Headache

Lydia Ferrara1*

¹Department of Pharmacy, University of Naples Federico II, Naples, Italy

Corresponding Author: Lydia Ferrara, Department of Pharmacy, University of Naples Federico II, Via Domenico Montesano 49, 80131 Naples, Italy. Tel: +39-3331931172, Email: lyferrar@unina.it

Received August 14, 2018; Accepted December 6, 2018; Online Published March 15, 2019

Abstract

Headache is an endemic, pathological disease that affects all individuals, regardless of age, gender, or social status. The causes of this phenomenon are many, and not all are known. Headaches vary in duration and severity and have a significant incidence in daily life. Pain is the main manifestation that can be associated with lacrimation, nausea, irritability, and dizziness. It is very difficult to find a specific treatment, and the medicaments used often have debilitating side effects that discourage their intake for long periods. Many doctors believe that proper nutrition and a healthy lifestyle as much as possible will offer more possibilities for preventing headaches and relieving painful symptoms. A valid help also comes from phytotherapy. Today the use of natural methods is more and more pleasing to patients, because they can continue the cure for a long time without the fear of undesirable effects. Many plants have been known since ancient times for their effectiveness in the treatment of migraine, and modern analytical methods have scientifically demonstrated the validity of their use and the mechanism of action of the effective active compounds present in them.

Keywords: Headache, Pain, Phytotherapy, Medicinal Plant, Food

Citation: Ferrara L. Nutrition and phytotherapy: a winning combination against headache. Int J Med Rev. 2019;6(1):6-13. doi:10.29252/IJMR-060102.

Introduction

Headache is a pathological form of endemic character that prevents the performance of normal activities, both working and relational. It is difficult to consider both the multiple causes and the various factors competing in this event, due to the lack of objective parameters that allow the clear classification of the various types of headache.¹

Migraine, the scientific term in which headache is indicated, is classified in many categories and sub-categories considering not only the quality, intensity, and cyclicity of pain, but also the way it manifests itself. A primary headache is generally distinguished from hormonal or environmental causes, including migraine, tension headache, and cluster headache; a secondary headache is the main symptom of other disorders, such as allergies, sinusitis, hypertension, osteoarthritis, digestive difficulties; pain that manifests itself following the excessive intake of some substances such as coffee, alcohol, and drugs; pain resulting from a lack of substances such as sugars, or in particular physical conditions, physical exertion, stress, or environmental, excessive cold or altitude.²⁻⁴ The main manifestation is pain that can be localized to the occipital region or diffused to the whole skull, pulsating or strongly intensive, excruciating, monolateral with involvement of the ocular region and the occipital area.⁵ Periodicity also represents a characteristic of the headache in addition to different durations of pain. Often, there are well-defined associated symptoms, such as lacrimation and irritation of the conjunctiva, nasal congestion, eye swelling, or pupil contraction, found especially in cluster headaches. The warning symptoms of pathological onset, like irritability, fatigue, and intolerance to noise, are characteristic of migraine that can degenerate even into blurred vision, alteration of sensitivity, and disorders of consciousness found in the most severe cases of migraine with aura. The presence of attacks is variable depending on whether it is an episodic, chronic, or recurrent headache, and the duration may vary from half an hour to 1 hour, on two or three consecutive days.

Today there is no specific treatment for headaches, and sufferers often resort to empirical methods or self-medication. The agents available for the treatment of headaches are few and often have side effects such as sedation and nausea, which weaken, even if temporarily, so they cannot be used continuously.⁸⁻¹⁰

Food-Headache Relationship

The use of proper nutrition to prevent and alleviate the symptoms of headache is a practice the origins of which are very old. Hippocrates knew well the relationship between the ingestion of some substances and the onset of migraine for which many foods can be the main cause due to the

presence of certain nutrients.^{11,12} It has been ascertained that in a migraine attack, two phases occur, one of intracranial vasoconstriction and one of extracranial vasodilation with the release of some endogenous vasoactive substances such as serotonin, histamine, various prostaglandins and neuropeptides. Predisposed persons must avoid foods that contain these substances or that induce their release in the bloodstream.¹³

Tyrammine, present in fermented or cured cheeses, sausages, wine, beer, seed oils, soy and also many species of fruit, is often one of the substances responsible for headache. Tyramine is an amine derived from decarboxylation of the amino acid tyrosine, which is degraded to an inactive metabolite following the intervention of a monoamine oxidase (MAO).14,15 Intestinal tyramine may be of an exogenous nature following the ingestion of the previouslymentioned foods rich in this substance or endogenous for the transformation of the amino acid tyrosine present in the foods ingested with the intervention of tyrosine microbial decarboxylase. Intestinal tyramine is degraded by the MAO of the intestine and the liver, but in cases of high concentrations, due either to an excessive consumption of the specified foods or to a condition of primary MAO insufficiency which may occur in some individuals, it is not degraded in the correct way. An excessive quantity passes in circulation, manifesting symptoms due to the action that this substance has on the vessels and the nerve endings. In addition to tachycardia and hypertension, a pulsating headache can occur because of its action on the cerebral vessels.

Phenylethylamine present in chocolate and the histamine present in many cheeses, eggs, strawberries, crustaceans, etc are vasoactive amino acids which act directly on the blood vessels and may cause the onset of a headache. 16,17 Phenylthylamine is a substance naturally present in the brain and responsible for the modulation of experiences associated with pleasure and mental awareness. It is released into the brain when the individual experiences feelings of joy and love, so it has been called "the molecule of love." It is known that phenylethylamine, once taken orally, readily crosses the blood-brain barrier and becomes immediately available in the brain where it acts in competition with dopamine on the presynaptic receptors with an increased dopaminergic action. This ability to modulate dopaminergic transmission means that phenylethylamine is able to alleviate depression and attention disorders and improve concentration and mood, but at the same time, it is one of the causes of postprandial migraine.

A link between serotonin and migraine attacks has been shown, and during these attacks, a significant reduction is observed in plasma levels of serotonin, a substance known to play an important role as a neuromediator. It participates, in fact, in the regulation of numerous activities in the central nervous system, such as pain threshold control, sleep induction, regulation of pituitary endocrine activity, neuronal excitability, thermoregulation, appetite, sexual behavior, and aggression. Its presence in the brain is determined by the transformation of tryptophan, an amino acid present in many foods such as meat, dairy products, dates, and hazelnuts. In

nerve cells, tryptophan, which is an essential amino acid, undergoes a degradation process first to triptamine, then to 5-hydroxytryptophan, and finally to serotonin. In the cardiovascular system, serotonin acts on the contraction of the arteries, contributing to the control of blood pressure; likewise, in the skeletal muscles, serotonin dilates vessels and improves vascularization.¹⁹

The daily consumption of too much coffee can cause headache attacks. The caffeine contained not only in coffee, but also in other drinks tends to stimulate the nervous system and, therefore, to favor the mechanism that leads to the appearance of a headache. The ingestion of cold foods also favors the immediate appearance of a headache attack, even if with a short duration, because of excessive stimulation of the nerve endings in the palate. To avoid this phenomenon, it is important to drink unfrozen drinks and consume ice creams and slushes slowly.^{20,21}

Alcoholic beverages, irrespective of their alcohol content, should be consumed in moderation, because they cause vasodilation and contain as fermentation products biogenic amines, tyramine, and histamine, responsible for headache attacks.^{22,23} In wine, white wine in particular, sulfur dioxide is another cause of headache. Its use is still considered essential, because it allows vintners, without causing them to resort to the use of sophisticated and expensive technical means, to keep under control the microbial and oxidative state of the must-wine, avoiding the unwanted microbial and oxidative processes that can radically alter the organoleptic characteristics of the finished product. Sulfur dioxide plays several important roles: it inhibits the activity of some enzymes, increases the solvent power of must-wine with regard to the coloring matter, protects the color of mustwine, causes antioxidant action on alcohols due to its high tendency to produce sulphate ions, direct clarifying action in the production of silent musts by acting directly on the growth rate of the yeast population and on slowing down the fermentation process.24

Those who are predisposed and particularly sensitive to sodium chloride, the main component in cooking salt, can suffer headaches when eating particularly tasty dishes.²⁵ Headache is often caused by substances not naturally present in food but added to it voluntarily, during technological processes, to improve preservation, or to enhance the organoleptic properties and are known as food additives.²⁶

Sausages, especially salami, should be consumed only occasionally because of the presence of nitrites, substances with vasodilating action. Monosodium glutamate, a flavor enhancer and additive approved by the European Community, can cause a type of headache called "Chinese syndrome", because it is a typical ingredient in Chinese cuisine. Even fasting can trigger a headache; the intake of a low quantity of sugars can cause a hypoglycemic crisis, the so-called "sugar decrease," which has a dilating effect on the blood vessels of the brain.²⁷ To avoid this annoyance which generally appears mid-morning and to ensure an energy reserve, it is advisable not to neglect breakfast, which must be complete, combined with coffee, tea or milk, biscuits, rusks, and jam or fruit juices.²⁸

Phytotherapy and Headache

In folk medicine there are numerous treatments for headache consisting of the local application of herbs or preparations such as infusions, herbal teas, and decoctions used to wet the forehead and other painful parts or for oral intake.²⁹

The administration of medicinal plants for the treatment of headaches dates back to many centuries before Christ, and phytotherapy was practiced electively by the Chinese and the Persians who classified headaches as: (1) simple and non-recurrent; (2) bilateral applicant; or (3) unilateral applicant. For each of these forms, medicinal herbs were prescribed for their analgesic activity, many of which have had their therapeutic action evaluated using modern analytical techniques.

Plant choice for use in the treatment of headaches is very important, because it must meet certain requirements and be effective against various symptoms. For symptomatic treatment, the drug must show a high affinity and specificity for the type 1 serotonin receptor and antagonistic action against the type 3 receptor to eliminate the feeling of nausea; prophylactic treatment, on the other hand, must show antagonist specificity on the type 2 serotonin receptor. Other important requirements are increased endorphin levels, lack of activity on the cholinergic or adrenergic receptor, lack of undesirable side effects such as sedation and gastrointestinal disorders, easy availability on the market, and low cost.³⁰

Opium was one of the first remedies used against pain. It was well known in antiquity and used for anesthesia during surgical procedures, for post-operative pain, and for chronic pain. The topical application and the oral ingestion of opium were prescribed to treat violent, recurrent, and intractable headaches. In his medical manual, Giovanni Plateario, a doctor from the Salerno school, mentions in particular two preparations based on opium: diacodium, a solution based on poppy capsules left to macerate in wine and sugar, and olibanum, tablets containing opium and incense. During past centuries, opium and its derivatives have been the most widely used analgesics for strong pain. The application of different opioids is now considered an effective treatment for intractable daily headaches, for episodic treatments of acute headaches, or for tension headaches as well as for the treatment of rare, moderate, and violent headaches that do not respond to traditional treatments.31,32

The analgesic effect of Cannabis sativa was well known in antiquity. Cannabis was prescribed to relieve the painful symptomatology of very persistent headache due to its action both in the central and peripheral nervous systems. Parenteral and intranasal injections were recommended to avoid the side effects caused by oral treatment of migraine and for nausea, vomiting, and gastroparesis related to headache. The powerful analgesic effect of cannabis as a drug suggests that its components, tetrahydrocannabinoids, control the interaction of pain with specific receptors. Cannabinoids, in fact, produce analgesia through the activation of a brain circuit comparable to that mediated by opioids. Some researchers have shown that the human body produces the endocannabinoid anandamide, which is able to bind to the same receptors as natural cannabinoids.³³ The CB1 and CB2 receptors have

been identified, and both are found in the central nervous system, many organs, and peripheral tissues. Depending on the cell type, the dose, and the state of the organism, the activation of these receptors involves a multitude of effects, some unpleasant and others of particular importance, such as the effective reduction of pain syndromes particularly resistant to usual pharmacological treatments. Research has facilitated the production of drugs that stimulate one or the other cannabinoid receptor and produce an analgesic effect on intensive and chronic headaches.³⁴⁻³⁶

The administration of Mirrh, *Commiphora myrrha*, in patients with unilateral headaches was considered effective for calming pain. To verify the analgesic effect of myrrh, the reactivity to pain after administration of a saline suspension of myrrh was tested in rats. The animals were placed on a hot metal plate, and it was observed that myrrh increased reaction latency in rats.

The results of a recent study indicate that myrrh has analgesic activity against some of the most widespread and painful symptoms, especially headaches, muscle pain, joint pain, and low back pain. Compared with the best known painkillers, it showed similar effects, although it required a longer course of treatment (about 20 days); however, none of the volunteers reported undesirable side effects or toxicity on the liver and kidneys with doses up to 11.5 mg/kg of body weight per day for 8-12 weeks of treatment.³⁷

Analgesic properties have been attributed to the presence in myrrh resin of bioactive sesquiterpenes with furanodiene structures: furanoeudesma-1,3-diene, lindestrene, and curzerene, which are responsible for the aroma and high analgesic activity of myrrh.

Subsequent studies have shown that furanoeudesma-1-diene, the most abundant component in myrrh, is responsible for the analgesic effect, the activity of which was blocked by naloxone, indicating an interaction with the opioid mechanisms of the brain.³⁸⁻⁴⁰

Garlic, Allium sativum, which is currently recognized as particularly effective in the treatment of blood pressure, was considered a useful analgesic even for the treatment of headache. In fact, it contains several active substances that show antioxidant action and the inhibition of platelet aggregation and thromboxane A2 production. Garlic owes its healing properties to the presence of different sulfur compounds, including alliine which, when fresh garlic is crushed, is converted into allicin by the enzyme alliinase action. This substance has antioxidant properties and promotes a lowering of blood pressure, cholesterol levels, and glycemic levels. It acts by slowing down the oxidation of LDL proteins with a consequent reduction in the formation of atherosclerotic plaques and inhibition of adhesion and platelet aggregation, due to direct action, both obstructing the biosynthetic pathway leading to the formation of inflammatory substances such as prostaglandins and thromboxanes. 41-43

The medicinal use of Feverfew, *Tanacetum partenium* L., has existed since ancient times. In fact, remains of this plant have been found during excavations in the Neolithic villages of the Caucasus, and in the Mediterranean area, observations on the properties of Partenio can be found in numerous texts

by Greek and Latin authors, such as Plinio in his Naturalis Historia and Dioscoride in De Materia Medica.

In 17th-century England, this plant was recognized as having good efficacy for all head pains, anticipating the results of recent studies dating back to the seventies, which have demonstrated the efficacy of feverfew against migraine. In ancient times this plant was known and used above all to alleviate menstrual pain. Modern studies have shown that the active ingredients are flavonoids and sesquiterpenes, including parthenolide, monoterpenes, spirochetalenol ethers, polyphenols, and tannins. The most important active ingredients are lactonic sesquiterpenes, whose biological effects concern the reduction of the excitability of smooth muscles, i.e. vasoconstriction in the presence of inflammation mediators; inhibition of prostaglandin synthesis; reduction of exocytosis, superior to non-steroidal anti-inflammatory drugs; and interactions with the synthesis and reception pathways of serotonin. The aerial parts of the plant are used for the preparation of extracts, which can be taken in tablets, capsules, infusions, or tinctures at a recommended dose equivalent to at least 250 mg parthenolide per day orally. The beneficial effects are usually apparent within only two weeks. Clinical studies of the use of feverfew mainly relate to therapeutic activity in migraine. An important study on migraine prevention showed a reduction in the frequency of attacks and their intensity.44-47 Recent research has shown a remarkable activity toward migraine, in particular those defined as vasomotor, in which there is an alternation of stimuli on blood vessels that determines vasoconstriction and subsequent vasodilation. All this causes a deformation in the walls of the same vessels, which then press on the neighboring nerve endings, triggering pain which can become more and more excruciating due to the concomitant production of mediators that enhance the painful signal. As regards the mechanism of action, an inhibition of prostaglandin synthesis that appears to be mediated by an inhibitory effect on phospholipase has been demonstrated. The anti-inflammatory action of parthenolide would also contribute an inhibitory effect on both the enzyme 5-lipo-oxygenase and the cyclooxygenase and nitroxide synthase. Moreover, it has recently been shown that the administration of feverfew extract in experimental animals produces analgesic effects. Murphy et al obtained positive results on pain highlighting how feverfew helps to improve the migraine syndrome, even if it does not heal it, as the benefit ends with the end of treatment.⁴⁸ To achieve lasting relief with this plant, a constant intake is required, thus, it is recommended that migraine sufferers use it as a preventive remedy for a fairly long period of time. However, precautions are necessary, because sufficient studies to ascertain the long-term safety of the plant are lacking.⁴⁹

To widen the field of action of feverfew, it is recommended that it be associated with other plants that have antiinflammatory activity, such as the root of *Harpagophytum procumbens* DC, the activity of which on all forms of joint inflammation has been ascertained. This plant is traditionally known as the Devil's Claw for the four hard, ribbon-shaped appendages that characterize its ovoid fruits which caused serious injuries on the body of animals resulting in extreme

pain and forcing the animal to do an "angry" dance. It was used for its digestive, analgesic, and antipyretic effects among the peoples of Africa.⁵⁰ Modern research has shown beneficial effects of this plant for the treatment of rheumatic, arthritic, and low back pain. The main chemical constituents present in the root of the plant and responsible for its therapeutic activity are the iridoids arpagoside, arpagide, and procumbide. Compared with many other anti-inflammatory plants that have active ingredients that have been known and used since antiquity, the Devil's Claw has been used in Europe only since 1958 when German researchers were the first to publish botanical pharmacology works on the active ingredients of its root. Studies have confirmed its antiinflammatory and pain-relieving properties known for a long time by the African populations of Namibia, the homeland of the plant which, deservedly, has won the name "plant cortisone". It is particularly effective against muscle-tension headache, arthritis, pains during childbirth, algomenorrhea, and sciatica. Its anti-inflammatory effect depends very much on the mode of administration and on the nature of the inflammation if acute or chronic. The mechanisms of action are not well known, but the action is certainly not FANS, since it does not inhibit the activity of COX and does not alter prostaglandin levels.

The analgesic and anti-inflammatory properties of the Devil's Claw have been confirmed by numerous studies conducted in vitro on rodents and on humans.⁵¹⁻⁵³ Recently, an extract from Harpagophytum procumbens was shown to possess antioxidant activity. This could be another mechanism through which the Devil's Claw exerts its anti-inflammatory and analgesic action by virtue of the fact that in the case of acute and chronic inflammatory pathologies it has been demonstrated that there is liberation of reactive oxygen species.⁵⁴

The presence of polyphenols with antioxidant activity explains why the Persian doctor Rhazes recommended that patients suffering from chronic and recurrent headaches eat an apple or a quince before meals to prevent the onset of the disease. It has been shown that the antioxidant mechanisms and the reactivity of the oxygen and nitro group present an important action in the different types of headaches. Diets supplemented with foods that have a high capacity to absorb oxygen radicals, such as apples, appear to reduce α and β TNF (tumor necrosis factor) levels in neuronal tissues. In his book "Man lā yaḥḍuru ṭabīb; medical advice for the general public," Rhazes, a Persian doctor described in 36 chapters the composition of foods and drugs that could easily be found at pharmacies, markets, in well-equipped kitchens, or in military camps, so that each person could follow the instructions and prepare the appropriate recipes with good results. The diseases treated in the book are the most widespread among the population: migraine, colds, coughs, depression, and diseases of the eye, ear, and stomach, for which doctors are not always seen.55

Among the many herbs traditionally used in other populations, some deserve special attention for their activity and effectiveness confirmed by experiments in modern times. In medieval Persia, nasal administration of willow oil

was recommended to relieve pain in patients with recurrent headaches. In the first half of the nineteenth century, salicin, the active ingredient of willow bark, was isolated, and subsequently, salicylic acid was obtained. Today, synthetically obtained salicylic acid is an important analgesic, anti-inflammatory, and antipyretic compound. Acetylsalicylic acid is commonly used as an analgesic and prophylactic in different types of headaches, because it reduces the frequency, duration, and intensity of migraine attacks and both episodic and tension-type headaches. Furthermore, acetylsalicylic acid has also been indicated in the early stages of chronic paroxysmal migraine. ⁵⁶⁻⁵⁸

Rose oil has long been considered beneficial in the treatment of both unilateral and recurrent headache and bilateral headaches. Chemical analyses have shown that rose oil contains eugenol as its main component, to which the anti-inflammatory action is attributed, following the inhibition of the synthesis of prostaglandins and leukotrienes. Eugenol inhibited the activity of the cyclooxygenase and of lipoxygenase in an experimental model in vitro, showing high antioxidant activity. In tests on rats, eugenol inhibited the nociceptive response induced by formalin; an antinociceptive effect could be mediated by the capsaicin receptor located on the sensor terminals present on the spine.⁵⁹

Eugenol is naturally present in the essential oil of various plants of the families of Lamiacee, Laureacee, Mirtacee, and Miristicaceae; traditional medicine uses this compound as an anti-inflammatory and antioxidant. Many studies have confirmed the presence of these properties.^{60,61}

Lavandula angustifolia Mill is rich in essential oil and is especially indicated for headaches caused by fatigue and stress in the forms of both an extract and an essential oil for its sedative and antispastic properties.⁶² It exerts a rebalancing action on the central nervous system, being simultaneously tonic and sedative. It calms anxiety, agitation, and nervousness; relieves headaches and disorders caused by stress; and helps reconcile sleep. Lavandula contains eugenol as a main component. Other components are linalool, linalyl acetate, limonene, cineol, camphor, alpha terpineol, tannins, ursolic acid, and rosmarinic acid. Known since ancient times for its slightly hypnotic qualities, it also has antimicrobial and bactericidal activity and is slightly astringent. It is used as an antispasmodic and a sedative for light forms of insomnia, headache, migraine, and nervousness. It also presents a slightly hypotensive action.63

An ancient remedy for headache that is widely used in India is ginger, *Zingiber officinalis* Roscoe. It is a spicy flavored root widely used in oriental cuisine and traditionally used in Indian medicine to treat nausea, vomiting, and headaches. Its action is carried out on the central nervous system, with anticonvulsive and analgesic activity. The dry extract titrated of ginger is useful as a preventive and curative in patients with recurrent headache crisis. Its anti-inflammatory action seems to be due to the inhibition of enzymes that stimulate the production of inflammatory substances, with a mechanism of action similar to that of non-steroidal anti-inflammatory drugs. The rhizome contains various active ingredients: essential oil mainly composed of zingiberene, gingeroli and

shogaoli, principles responsible for its pungent taste, resins, and mucilage. The action of ginger occurs mainly at the circulatory level. In fact, during a migraine crisis, the first phase of vasoconstriction is followed by vasodilation. During this period, the beneficial effect of ginger appears as a vascular stimulant, because it helps blood circulation by inhibiting the enzyme cyclooxygenase which intervenes in the formation of clots, thus avoiding the danger of embolism. The active ingredients of other spices, capsaicin, piperine, quercetin, curcumin, crocetine, cinnamaldehyde, and allyl sulphide, have been studied and it has been determined that they inhibit the platelet aggregation induced by different agonists, such as ADP, collagen, arachidonic acid, and platelet thromboxane formation. The use of these in the preventive treatment of headaches is very limited because of the high cost of spices and the lack of research.66-69

Topical application of the *Artemisia absinthium* leaf infusion has been recommended for migraine treatment. The antinociceptive effect of different Artemisia subtypes was detected in rats and mice. *Artemisia* essential oil has analgesic, antipyretic, and anti-inflammatory properties when administered intraperitoneally. The antipyretic activity was attributed to 24z-ethylcholesta-7.22-dien-3beta-ol a sterol identified in the essential oil. To 5,6,3,5'-tetramethoxy 7,4'-hydroxyflavone, a flavone identified in the hydroalcoholic extract of *A. absinthium*, is attributed the anti-inflammatory activity in vitro following the inhibition of the oxygenase cycle 2 (COX- 2), of prostaglandin PGE-2 and nitric oxide, as evidenced by experiments on RAW cell lines 264.7 stimulated with lipopolysaccharides.⁷⁰⁻⁷³

Boswellia, Boswellia serrata Roxb, is another effective treatment for different types of headaches. The non-phenolic fraction obtained from its gum has shown analgesic and sedative effects due to the presence of boswellic acids with particular pharmacological activity, both on animals and on humans. It is able to inhibit the enzyme 5-lipoxygenase which is involved in the processes of chronic inflammation typical of immunological and allergic reactions. The enzyme in particular is responsible for the synthesis of leukotrienes (important chemical mediators of joint inflammation) and is also implicated in other chronic inflammatory diseases such as headaches, ulcerative colitis, and bronchial asthma. Unlike common Nonsteroidal anti-inflammatory drugs, boswellic acids do not interfere with the synthesis of prostaglandins and have not shown ulcerogenic effects. The anti-inflammatory action of Boswellia was also evaluated with clinical methods, and the variation in erythrocyte sedimentation rate has been determined. It was possible to ascertain that the treatment was safe and well tolerated, even in long-term therapy.^{74,75}

Some native Australian plants used in traditional medicine have been studied to identify the bioactive compounds responsible for the action against headaches. A dichloromethane extract from the *Cymbopogon ambiguus* plant, known as the Australian citronella, has shown inhibitory activity in platelet aggregation induced by ADP (adenosine diphosphate and in the release of serotonin). Several phenylpropenoids have been identified in the extract, including eugenol and helicinine for which the inhibitory

action has been confirmed as evidence of the therapeutic effectiveness of this plant in the treatment of headaches and inflammatory conditions. The leaves of this plant have a strong lemon scent when they are crushed and can be used to prepare infusions and in inhalation therapies. Research has shown that tea is suitable for relieving headaches, migraine, and inflammation, confirming the custom of aborigines who used it for headache treatment chest infections, and muscle cramps.76

Conclusions

There are many foods that can cause a headache crisis, because they contain particular substances that alter the intracranial blood circulation and, with the effect of vasodilatation followed or preceded by vasoconstriction, cause pain. To avoid food headaches, the only remedy is to pay close attention to the food, trying to recognize and avoid foods and beverages that contain the substances responsible for this effect. For the nutritionist it is very important to know the chemical composition of food and pay attention to food additives which are often the triggering factor. A healthy and correct diet with the appropriate choice of food both in quantity and quality turns out to be an effective form of headache prevention. To combat the onset of headaches, some foods that exert a vasodilator action are recommended. They reduce the spasm of the vessels, a phenomenon that occurs at the beginning of a primary headache crisis, such as rice and wheat germ, liver, fatty fish like salmon and mackerel, oil seeds, fresh and dry yeast which contain high concentrations of vitamin PP. Equally recommended are foods rich in vitamin E, such as olive oil, dried fruit, broccoli, and cabbage that can be useful in neutralizing the free radicals responsible for some forms of headache. It is important to follow a healthy and balanced diet containing meat and fresh vegetables containing magnesium, which is effective in preventing headache. Other recommended foods are milk, yogurt, white bread, sugar, honey, fish, and cereals. Some spices are also recommended, including chili that contains capsaicin, a substance capable of regulating blood circulation and reducing the production of substances that transmit pain.

Current research in the field of phytotherapy is also a great help by proposing the use of plants used in the past that have anti-inflammatory and analgesic action and are able to counteract the mechanisms considered at the base of the main forms of headaches. Organic compounds such as flavonoids, terpenoids, and phenylpropanoids seem to be able to block, in vivo, the chemical mediators involved in the onset of headaches as well as the production of enzymes that promote the biosynthesis of prostaglandins, mediators of inflammation.

Conflict of Interest Disclosures

The author declares she has no conflicts of interest.

References

- Silberstein SD. Chronic daily headache. J Am Osteopath Assoc. 2005;105(4 Suppl 2):23s-29s.
- Ziegler DK, Hassanein RS. Specific headache phenomena: their frequency and coincidence. Headache. 1990;30(3):152-156.

- doi:10.1111/j.1526-4610.1990.hed3003152.x.
- Olesen J, Lipton RB. Headache classification update 2004. Curr Opin Neurol. 2004;17(3):275-282. doi:10.1097/00019052-200406000-00007.
- Abu Bakar N, Tanprawate S, Lambru G, Torkamani M, Jahanshahi M, Matharu M. Quality of life in primary headache disorders: A review. Cephalalgia. 2016;36(1):67-91. doi:10.1177/0333102415580099.
- Karl HW, Trescot AM. Nerve Entrapment Headaches at the Temple: Zygomaticotemporal and/or Auriculotemporal Nerve? Pain Physician. 2019;22(1):E15-e36.
- Robbins MS, Lipton RB. The epidemiology of primary headache disorders. Semin Neurol. 2010;30(2):107-119. doi:10.1055/s-0030-1249220.
- Mathew PG, Garza I. Headache. Semin Neurol. 2011;31(1):5-17. doi:10.1055/s-0031-1271313.
- Lupi C, Benemei S, Guerzoni S, Pellesi L, Negro A. Pharmacokinetics and pharmacodynamics of new acute treatments for migraine. Expert Opin Drug Metab Toxicol. 2019;15(3):189-198. doi:10.108 0/17425255.2019.1578749.
- Tfelt-Hansen PC, Pihl T, Hougaard A, Mitsikostas DD. Drugs targeting 5-hydroxytryptamine receptors in acute treatments of migraine attacks. A review of new drugs and new administration forms of established drugs. Expert Opin Investig Drugs. 2014;23(3):375-385. doi:10.1517/13543784.2014.861817.
- 10. Capi M, de Andres F, Lionetto L, et al. Lasmiditan for the treatment of migraine. Expert Opin Investig Drugs. 2017;26(2):227-234. doi:1 0.1080/13543784.2017.1280457.
- 11. Savi L, Rainero I, Valfre W, Gentile S, Lo Giudice R, Pinessi L. Food and headache attacks. A comparison of patients with migraine and tension-type headache. Panminerva Med. 2002;44(1):27-31.
- 12. Holzhammer J, Wober C. Alimentary trigger factors that provoke migraine and tension-type headache. Schmerz. 2006;20(2):151-159. doi:10.1007/s00482-005-0390-2.
- 13. Jansen SC, van Dusseldorp M, Bottema KC, Dubois AE. Intolerance to dietary biogenic amines: a review. Ann Allergy Asthma Immunol. 2003;91(3):233-240; quiz 241-232, 296. doi:10.1016/ s1081-1206(10)63523-5.
- 14. Luthy J, Schlatter C. Biogenic amines in food: effects of histamine, tyramine and phenylethylamine in the human. Z Lebensm Unters Forsch. 1983;177(6):439-443. doi:10.1007/bf01409672.
- 15. D'Andrea G, Terrazzino S, Fortin D, Cocco P, Balbi T, Leon A. Elusive amines and primary headaches: historical background and prospectives. Neurol Sci. 2003;24 Suppl 2:S65-67. doi:10.1007/ s100720300044.
- 16. Martin VT, Vij B. Diet and headache: part 1. Headache. 2016;56(9):1543-1552. doi:10.1111/head.12953.
- 17. Martin VT, Vij B. Diet and headache: Part 2. Headache. 2016;56(9):1553-1562. doi:10.1111/head.12952.
- 18. le Grand SM, Supornsilpchai W, Saengjaroentham C, Srikiatkhachorn A. Serotonin depletion leads to cortical hyperexcitability and trigeminal nociceptive facilitation via the nitric oxide pathway. Headache. 2011;51(7):1152-1160. doi:10.1111/j.1526-4610.2011.01931.x.
- 19. Supornsilpchai W, Sanguanrangsirikul S, Maneesri S, Srikiatkhachorn A. Serotonin depletion, cortical spreading depression, and trigeminal nociception. Headache. 2006;46(1):34-39. doi:10.1111/j.1526-4610.2006.00310.x.
- 20. Scher Al, Stewart WF, Lipton RB. Caffeine as a risk factor for chronic daily headache: a population-based study. Neurology. 2004;63(11):2022-2027. doi:10.1212/WNL.65.1.180.
- 21. Bird N, MacGregor EA, Wilkinson MI. Ice cream headache--site, duration, and relationship to migraine. Headache. 1992;32(1):35-38. doi:10.1111/j.1526-4610.1992.hed3201035.x.
- 22. Panconesi A. Alcohol and migraine: trigger factor, consumption, mechanisms. A review. J Headache Pain. 2008;9(1):19-27. doi:10.1007/s10194-008-0006-1.
- 23. Peatfield RC. Relationships between food, wine, and beer-

- precipitated migrainous headaches. Headache. 1995;35(6):355-357. doi:10.1111/j.1526-4610.1995.hed3506355.x.
- 24. Finocchi C, Sivori G. Food as trigger and aggravating factor of migraine. Neurol Sci. 2012;33 Suppl 1:S77-80. doi:10.1007/s10072-012-1046-5.
- Campbell DA, Hay KM, Tonks EM. An investigation of the salt and water balance in migraine. Br Med J. 1951;2(4745):1424-1429. doi:10.1136/bmj.2.4745.1424.
- 26. Orr SL. Diet and nutraceutical interventions for headache management: A review of the evidence. Cephalalgia. 2016;36(12):1112-1133. doi:10.1177/0333102415590239.
- Torelli P, Manzoni GC. Fasting headache. Curr Pain Headache Rep. 2010;14(4):284-291. doi:10.1007/s11916-010-0119-5.
- Walter S. Lifestyle behaviors and illness-related factors as predictors of recurrent headache in U.S. adolescents. J Neurosci Nurs. 2014;46(6):337-350. doi:10.1097/jnn.00000000000000095.
- De Weerdt CJ, Bootsma HP, Hendriks H. Herbal medicines in migraine prevention Randomized double-blind placebocontrolled crossover trial of a feverfew preparation. Phytomedicine. 1996;3(3):225-230. doi:10.1016/s0944-7113(96)80057-2.
- Ferrari MD, Saxena PR. On serotonin and migraine: a clinical and pharmacological review. Cephalalgia. 1993;13(3):151-165. doi:10.1046/j.1468-2982.1993.1303151.x.
- Plateariuo JG. Practica brevis: un manuale di medicina pratica del XII secolo. Tuscania: Penne & Papyri; 2015.
- Presley CC, Lindsley CW. DARK Classics in Chemical Neuroscience:
 Opium, a Historical Perspective. ACS Chem Neurosci.
 2018;9(10):2503-2518. doi:10.1021/acschemneuro.8b00459.
- Devane WA, Hanus L, Breuer A, et al. Isolation and structure of a brain constituent that binds to the cannabinoid receptor. Science. 1992;258(5090):1946-1949. doi:10.1126/science.1470919.
- 34. Lochte BC, Beletsky A, Samuel NK, Grant I. The use of cannabis for headache disorders. Cannabis Cannabinoid Res. 2017;2(1):61-71. doi:10.1089/can.2016.0033.
- Kim PS, Fishman MA. Cannabis for pain and headaches: primer. Curr Pain Headache Rep. 2017;21(4):19. doi:10.1007/s11916-017-0619-7.
- 36. Baron EP. Comprehensive review of medicinal marijuana, cannabinoids, and therapeutic implications in medicine and headache: what a long strange trip it's been. Headache. 2015;55(6):885-916. doi:10.1111/head.12570.
- Germano A, Occhipinti A, Barbero F, Maffei ME. A pilot study on bioactive constituents and analgesic effects of MyrLiq®, a Commiphora myrrha extract with a high furanodiene content. Biomed Res Int. 2017;2017:3804356. doi:10.1155/2017/3804356.
- 38. Morteza-Semnani K, Saeedi M. Constituents of the essential oil of *Commiphora myrrha* (Nees) Engl. var. molmol. J Essent Oil Res. 2003;15(1):50-51. doi:10.1080/10412905.2003.9712264.
- Hanus LO, Rezanka T, Dembitsky VM, Moussaieff A. Myrrhcommiphora chemistry. Biomed Pap Med Fac Univ Palacky Olomouc Czech Repub. 2005;149(1):3-27. doi:10.5507/ bp.2005.001.
- Shen T, Li GH, Wang XN, Lou HX. The genus *Commiphora*: a review of its traditional uses, phytochemistry and pharmacology. J Ethnopharmacol. 2012;142(2):319-330. doi:10.1016/j.jep.2012.05.025.
- 41. Foushee DB, Ruffin J, Banerjee U. Garlic as a natural agent for the treatment of hypertension: a preliminary report. Cytobios. 1982;34(135-36):145-152.
- Reuter HD. Allium sativum and Allium ursinum: Part 2 pharmacology and medicinal application. Phytomedicine. 1995;2(1):73-91. doi:10.1016/s0944-7113(11)80052-8.
- 43. Majewski M. *Allium sativum:* facts and myths regarding human health. Rocz Panstw Zakl Hig. 2014;65(1):1-8.
- Johnson ES, Kadam NP, Hylands DM, Hylands PJ. Efficacy of feverfew as prophylactic treatment of migraine. Br Med J (Clin Res Ed). 1985;291(6495):569-573. doi:10.1136/bmj.291.6495.569.
- 45. Heptinstall S, Groenewegen WA, Spangenberg P, Loesche W.

- Extracts of feverfew may inhibit platelet behaviour via neutralization of sulphydryl groups. J Pharm Pharmacol. 1987;39(6):459-465. doi:10.1111/j.2042-7158.1987.tb03420.x.
- Heptinstall S, Awang DV, Dawson BA, Kindack D, Knight DW, May J. Parthenolide content and bioactivity of feverfew (*Tanacetum parthenium* (L.) Schultz-Bip.). Estimation of commercial and authenticated feverfew products. J Pharm Pharmacol. 1992;44(5):391-395. doi:10.1111/j.2042-7158.1992.tb03631.x.
- 47. Vogler BK, Pittler MH, Ernst E. Feverfew as a preventive treatment for migraine: a systematic review. Cephalalgia. 1998;18(10):704-708. doi:10.1111/j.1468-2982.1998.1810704.x.
- 48. Murphy JJ, Heptinstall S, Mitchell JR. Randomised double-blind placebo-controlled trial of feverfew in migraine prevention. Lancet. 1988;2(8604):189-192. doi:10.1016/S0140-6736(88)92289-1.
- 49. Pittler MH, Vogler BK, Ernst E. Feverfew for preventing migraine. Cochrane Database Syst Rev. 2000(3):Cd002286. doi:10.1002/14651858.cd002286.
- Grant L, McBean DE, Fyfe L, Warnock AM. A review of the biological and potential therapeutic actions of *Harpagophytum* procumbens. Phytother Res. 2007;21(3):199-209. doi:10.1002/ ptr.2029.
- 51. Barnes J, Anderson LA, Phillipson JD. Herbal medicines. 3rd ed. Pharmaceutical Press; 2007:207-214.
- 52. Brien S, Lewith GT, McGregor G. Devil's Claw (*Harpagophytum procumbens*) as a treatment for osteoarthritis: a review of efficacy and safety. J Altern Complement Med. 2006;12(10):981-993. doi:10.1089/acm.2006.12.981.
- 53. Setty AR, Sigal LH. Herbal medications commonly used in the practice of rheumatology: mechanisms of action, efficacy, and side effects. Semin Arthritis Rheum. 2005;34(6):773-784. doi:10.1016/j.semarthrit.2005.01.011.
- Grant L, McBean DE, Fyfe L, Warnock AM. The inhibition of free radical generation by preparations of *Harpagophytum procumbens* in vitro. Phytother Res. 2009;23(1):104-110. doi:10.1002/ptr.2570.
- 55. Rāzī ABMZ, Dinnawī MA. Man of La yaḥduruhu al-Tabib aw qabl tabībuk wusūl al-Tabib. Bayrūt: Dār al-Kutub al-Ilmiyah; al-Ṭab'ah 1: 1999.
- Derry S, Wiffen PJ, Moore RA. Aspirin for acute treatment of episodic tension-type headache in adults. Cochrane Database Syst Rev. 2017;1:Cd011888. doi:10.1002/14651858.CD011888. pub2.
- 57. Lampl C, Voelker M, Steiner TJ. Aspirin is first-line treatment for migraine and episodic tension-type headache regardless of headache intensity. Headache. 2012;52(1):48-56. doi:10.1111/j.1526-4610.2011.01974.x.
- 58. Gaciong Z. The real dimension of analgesic activity of aspirin. Thromb Res. 2003;110(5-6):361-364. doi:10.1016/j. thromres.2003.08.009.
- Fonseca DV, Salgado PR, Aragao Neto Hde C, et al. Orthoeugenol exhibits anti-nociceptive and anti-inflammatory activities. Int Immunopharmacol. 2016;38:402-408. doi:10.1016/j. intimp.2016.06.005.
- Fujisawa S, Murakami Y. Eugenol and Its Role in Chronic Diseases.
 Adv Exp Med Biol. 2016;929:45-66. doi:10.1007/978-3-319-41342-6_3.
- 61. Dal Bo W, Luiz AP, Martins DF, Mazzardo-Martins L, Santos AR. Eugenol reduces acute pain in mice by modulating the glutamatergic and tumor necrosis factor alpha (TNF-alpha) pathways. Fundam Clin Pharmacol. 2013;27(5):517-525. doi:10.1111/j.1472-8206.2012.01052.x.
- 62. Sarmento-Neto JF, do Nascimento LG, Felipe CF, de Sousa DP. Analgesic potential of essential oils. Molecules. 2015;21(1):E20. doi:10.3390/molecules21010020.
- 63. Hajhashemi V, Ghannadi A, Sharif B. Anti-inflammatory and analgesic properties of the leaf extracts and essential oil of *Lavandula angustifolia* Mill. J Ethnopharmacol. 2003;89(1):67-71. doi:10.1016/S0378-8741(03)00234-4.
- 64. Srivastava KC, Mustafa T. Ginger (Zingiber officinale) and rheumatic

- disorders. Med Hypotheses. 1989;29(1):25-28. doi:10.1016/0306-9877(89)90162-X.
- Mustafa T, Srivastava KC. Ginger (Zingiber officinale) in 65. migraine headache. J Ethnopharmacol. 1990;29(3):267-273. doi:10.1016/0378-8741(90)90037-T.
- Raghavendra RH, Naidu KA. Spice active principles as the inhibitors of human platelet aggregation and thromboxane biosynthesis. Prostaglandins Leukot Essent Fatty Acids. 2009;81(1):73-78. doi:10.1016/j.plefa.2009.04.009.
- 67. Hosseinzadeh H, Younesi HM. Antinociceptive and antiinflammatory effects of Crocus sativus L. stigma and petal extracts in mice. BMC Pharmacol. 2002;2:7. doi:10.1186/1471-2210-2-7.
- Srivastava KC. Antiplatelet principles from a food spice clove (Syzygium aromaticum L) [corrected]. Prostaglandins Leukot Essent Fatty Acids. 1993;48(5):363-372. doi:10.1016/0952-3278(93)90116-E.
- 69. Suneetha WJ, Krishnakantha TP. Antiplatelet activity of coriander and curry leaf spices. Pharm Biol. 2005;43(3):230-233. doi:10.1080/13880200590928807.
- Ikram M, Shafi N, Mir I, Do MN, Nguyen P, Le Quesne PW. 24zeta-Ethylcholesta-7,22-Dien-3beta-ol: A Possibly Antipyretic Constituent of Artemisia absinthium. Planta Med. 1987;53(4):389. doi:10.1055/s-2006-962748.

- 71. Khattak SG, Gilani SN, Ikram M. Antipyretic studies on some indigenous Pakistani medicinal plants. J Ethnopharmacol. 1985;14(1):45-51. doi:10.1016/0378-8741(85)90027-3.
- 72. Lee HG, Kim H, Oh WK, et al. Tetramethoxy hydroxyflavone p7F downregulates inflammatory mediators via the inhibition of nuclear factor kappaB. Ann N Y Acad Sci. 2004;1030:555-568. doi:10.1196/annals.1329.065.
- 73. Lopes-Lutz D, Alviano DS, Alviano CS, Kolodziejczyk PP. Screening of chemical composition, antimicrobial and antioxidant activities of Artemisia essential oils. Phytochemistry. 2008;69(8):1732-1738. doi:10.1016/j.phytochem.2008.02.014.
- 74. Lampl C, Haider B, Schweiger C. Long-term efficacy of Boswellia serrata in four patients with chronic cluster headache. Cephalalgia. 2012;32(9):719-722. doi:10.1177/0333102412451357.
- 75. Ammon HP. Boswellic acids (components of frankincense) as the active principle in treatment of chronic inflammatory diseases. Wien Med Wochenschr. 2002;152(15-16):373-378. doi:10.1046/ j.1563-258X.2002.02056.x.
- 76. Grice ID, Rogers KL, Griffiths LR. Isolation of bioactive compounds that relate to the anti-platelet activity of Cymbopogon ambiguus. Evid Based Complement Alternat Med. 2011;2011:467134. doi:10.1093/ecam/nep213.