UCUENCA

Facultad de Odontología

Especialización en Endodoncia

“Global use of ethnomedicinal plants to treat toothache”

Trabajo de titulación previo a la obtención del título de Especialista en Endodoncia.

Modalidad: Artículo científico

Autoras:

Gabriela Elizabeth Saavedra Cornejo

CI: 0104155429

Correo electrónico: gabysaav2009@hotmail.com

Nathaly Fernanda Parra Solano

CI: 0105729206

Correo electrónico: cris27_fer@hotmail.com

Directora:

Ximena Elizabeth Espinosa-Vásquez

CI: 1104021546

Cuenca, Ecuador

16-septiembre-2022

Abstract

Background: Toothache is one of the most common global health problems, and medicinal plants are widely used to relieve the associated pain and inflammation. Several studies have been conducted on the use of plants to treat toothache, but no study has comprehensively assessed the types of plants and the mechanisms of action of the phytochemical compounds involved in their analgesic effect. This review aims to bridge this gap. **Highlights:** This is the first review to collect a large volume of data on the global use of medicinal plants used in the treatment of toothache. It presents the relevant information for dentists, researchers, and academics on using medicinal plants to treat toothache. We found that preclinical studies and state-of-the-art technology hold promise for furthering our knowledge of this important topic. **Conclusion:** In total, 21 species of medicinal plants used to treat toothache were found in America, 29 in Europe, 192 in Africa, 112 in Asia, and 10 in Oceania. The most common species were *Allium sativum*, *Allium cepa*, *Acmella oleracea*, *Jatropha curcas*, *Jatropha gossypiifolia*, and *Syzygium aromaticum*. The most commonly found family of medicinal plants was Asteraceae, followed by Solanaceae, Fabaceae, Lamiaceae, Euphorbiaceae, Rutaceae, and Myrtaceae. The most common phytochemicals found were flavonoids, terpenes, polyphenols, and alkaloids. The reported mechanisms of action involved in toothache analgesia were antioxidant effects, effects mediated by transient receptor potential channels, the γ-aminobutyric acid mechanism, and the cyclooxygenase/lipoxygenase anti-inflammatory mechanism.

Keywords: Toothache. Dental pain. Medicinal plants. Phytochemicals. Flavonoids.

Cláusula de licencia y autorización para publicación en el Repositorio Institucional

Gabriela Elizabeth Saavedra Cornejo en calidad de autor/a y titular de los derechos morales y patrimoniales del trabajo de titulación "Global use of ethnomedicinal plants to treat toothache", de conformidad con el Art. 114 del CÓDIGO ORGÁNICO DE LA ECONOMÍA SOCIAL DE LOS CONOCIMIENTOS, CREATIVIDAD E INNOVACIÓN reconozco a favor de la Universidad de Cuenca una licencia gratuita, intransferible y no exclusiva para el uso no comercial de la obra, con fines estrictamente académicos.

Asimismo, autorizo a la Universidad de Cuenca para que realice la publicación de este trabajo de titulación en el repositorio institucional, de conformidad a lo dispuesto en el Art. 144 de la Ley Orgánica de Educación Superior.

Cuenca, 16 septiembre 2022

Gabriela Elizabeth Saavedra Cornejo

C.I: 0104155429

Cláusula de licencia y autorización para publicación en el Repositorio Institucional

Nathaly Fernanda Parra Solano en calidad de autor/a y titular de los derechos morales y patrimoniales del trabajo de titulación "Global use of ethnomedicinal plants to treat toothache", de conformidad con el Art. 114 del CÓDIGO ORGÁNICO DE LA ECONOMÍA SOCIAL DE LOS CONOCIMIENTOS, CREATIVIDAD E INNOVACIÓN reconozco a favor de la Universidad de Cuenca una licencia gratuita, intransferible y no exclusiva para el uso no comercial de la obra, con fines estrictamente académicos.

Asimismo, autorizo a la Universidad de Cuenca para que realice la publicación de este trabajo de titulación en el repositorio institucional, de conformidad a lo dispuesto en el Art. 144 de la Ley Orgánica de Educación Superior.

Cuenca, 16 septiembre 2022

Nathaly Fernanda Parra Solano

C.I: 0105729206

Cláusula de Propiedad Intelectual

Gabriela Elizabeth Saavedra Cornejo, autor/a del trabajo de titulación "Global use of ethnomedicinal plants to treat toothache", certifico que todas las ideas, opiniones y contenidos expuestos en la presente investigación son de exclusiva responsabilidad de su autor/a.

Cuenca, 16 septiembre-2022

Gabriela Elizabeth Saavedra Cornejo

C.I: 0104155429

Cláusula de Propiedad Intelectual

Nathaly Fernanda Parra Solano, autor/a del trabajo de titulación "Global use of ethnomedicinal plants to treat toothache", certifico que todas las ideas, opiniones y contenidos expuestos en la presente investigación son de exclusiva responsabilidad de su autor/a.

Cuenca, 16 septiembre-2022

Nathaly Fernanda Parra Solano

C.I: 0105729206

1. Introduction

Toothache is an unpleasant sensory and emotional experience [1] originating in a tooth or adjacent structures caused by factors such as caries, periodontal disease, trauma, or dentoalveolar abscess [2]. It is one of the most common health problems worldwide [3]. Toothache has a higher prevalence in lower socioeconomic groups, in whom this disease is not always adequately treated [4], and in developing countries, where access to healthcare is limited. This has led many local communities to resort to using alternatives for toothache relief, such as medicinal plants [3].

Medicinal plants are widely used in dental practices. The World Health Organization has reported that between 65% and 80% of the population in developing countries use them to reduce inflammation, inhibit oral pathogen growth, and trigger anti-inflammatory, antiseptic, antioxidant, and analgesic effects [3, 4]. Several phytochemical studies conducted on these plants have identified compounds such as flavonoids, alkaloids, and terpenes, which reduce toothache through their mechanism of action [3, 5–7].

Phytotherapy is the use of plants to treat diseases or as health-promoting agents. When used for this purpose, their original composition and integrity are generally preserved, so that an entire plant or a desired percentage of its components may be used for medicinal purposes, fulfilling a specific mechanism of action, generally, a specific pathway to relieve pain [8]. However, to our knowledge, no study has comprehensively tackled the mechanisms of action of the phytochemical compounds contained in medicinal plants used to treat toothache. This integrative review aimed to bridge this gap by compiling and analyzing the different studies available in the literature.

2. Materials and methods

The available literature in PubMed, PMC, and Scopus databases was searched to identify relevant articles on medicinal plants used to relieve toothache, published in English until July 31, 2021, using the search terms toothache, dental pain, medicinal plants, medicinal herbs, and phytochemicals. Articles unrelated to the use of plants that relieved toothache or lacking data for at least one of the following characteristics were excluded: family, scientific name, plant parts used, and method of preparation.

Of a total of 300 articles, 80 met the inclusion criteria and were comprehensively analyzed for this review. In addition, we performed a manual search of the reference lists of the initially selected articles to complement the available information and found 294 additional articles. Ten books with relevant information were also included. Regional medicinal plant types obtained from the articles and books were summarized by continents. Finally, owing to length issues, this review did not include information related to the possible adverse reactions and drug interactions resulting from the use of the plants included in this review.

3. Medicinal plants for toothache treatment

For several millennia, plants have been used in traditional dentistry to treat toothache, periodontal disease, herpetic ulcers, stomatitis, maxillary sinusitis, and other ailments [6]. In recent years, advances in science and technology have identified the phytochemical compounds in some of these plants and their mechanisms of action [3]. Phytochemicals are a large group of plant-derived chemical substances that have various biochemical and physiological effects that are beneficial for human health and nutrition [6, 9].

Phytochemicals found in plants vary greatly in number, structural heterogeneity, and distribution, and they are classified into polyphenols, carotenoids, alkaloids, terpenes, and terpenoids [10, 11]. All the tables in this review outline the phytochemicals described in previous reports on medicinal plants used to treat toothache, focusing on their analgesic mechanisms of action.

3.1 Plant parts and preparation method

As mentioned above, plants are used to treat diseases through phytotherapy, using either the entire plant or a desired percentage of its components [8]. The most commonly used parts of medicinal plants are the leaves, seeds, flowers, and roots. The roots, in particular, are highly important because they are higher in bioactive compounds than other plant parts [3, 12–14].

Leaves contain high concentrations of secondary metabolites, phytochemicals, and essential oils that have various health benefits [14]. Hence, most research supports the use of leaves instead of roots because root extraction threatens the conservation of several plant species, especially those that are widely used [3, 14].

There is considerable variation in the preparation methods of plants used to treat toothache, and the most common methods of administration are: using the plant extract, chewing, crushing, and drinking a decoction [3].

3.2 Mechanisms of action of phytochemical compounds

Phytochemicals such as flavonoids, alkaloids, and terpenes [3, 5] are biologically active compounds found in plants that work through various mechanisms of action [15, 16]. Based on the information gathered in this review, the most salient mechanisms of action of phytochemicals used to treat toothache were antioxidant activity [9, 17], action on transient receptor potential channels (TRP) [18], the γ-aminobutyric acid (GABA) mechanism [19, 20], and anti-inflammatory mechanisms (cyclooxygenase (COX) and lipoxygenase (LOX) pathways) [21].

3.2.1 Antioxidant activity

In living organisms, reactive oxygen species (ROS) are generated during metabolism and do not generally cause oxidative damage to cellular components due to the action of antioxidants present in these organisms [22].

Natural antioxidants are found in various plants and play a key role in stopping the generation of free radicals by preventing the oxidation of biomolecules in the body. Therefore, they are valuable therapeutic agents for preventing diseases caused by oxidative stress. This imbalance favors the production of prooxidants, represented by ROS, such as superoxide anions (O_2^-), hydrogen peroxide (H_2O_2), and hydroxyl radicals (OH^-) [23], which damage key cellular components, such as DNA, proteins, and membrane lipids, and can even trigger cell death [17, 24–27].

Conversely, during inflammatory processes, free radicals balance themselves by attacking the nearest stable molecule and “stealing” an electron. The attacked molecule then becomes a free radical by losing its electron and initiating a cascade of cell-damaging reactions [24]. Additionally, leukocytes present in damaged regions cause a “respiratory burst” from enhanced oxygen uptake, and inflammatory cells generate inflammatory mediators that act on the infection site to release more reactive species [24, 28, 29].

Therefore, the role of antioxidants is to delay, prevent, or eliminate oxidative damage of target molecules by controlling the levels of free radicals and other reactive species [30]. Plants are responsible for our oxygenated environment, and because they are exposed to high intracellular levels of oxygen and ROS, they have developed specialized defense systems (antioxidants) to protect their structures and tissues. Antioxidant activity is inherent to all plants as they act to prevent, destroy, or neutralize free radicals [17].

These antioxidant defense systems can be *enzymatic complexes and non-enzymatic systems.* Some enzymatic complexes are superoxide dismutase (SOD), catalase (CAT), glutathione peroxidase (GPx), and glutathione reductase (GR). *Non-enzymatic systems* consist of low-molecular-weight antioxidants such as ascorbic acid, glutathione, proline, carotenoids, phenolic acids, and flavonoids; and high-molecular-weight secondary metabolites, such as tannins, which efficiently prevent the toxic effects of free radicals [31, 32].

The phytochemicals in plants can act as antioxidants by directly eliminating ROS, chelating metals (Fe, Zn, Mg, and Mn), quenching the mitochondrial respiratory chain, and increasing the levels of endogenous antioxidant enzymes, such as SOD, CAT, and GPx [9, 31].

ROS and reactive nitrogen species (RNS) are key players in various types of pain [33]. Evidence suggests that tissue injury induces the production of both ROS and RNS, which causes pain by promoting neuronal excitability in pain pathways through neural interactions and by triggering mitochondrial dysfunction and neuro-inflammation [26, 34].

Peroxynitrite ($ONOO^-$) (PN) and its precursor superoxide (SO) are critical in the development of chronic pain and in the transition from acute to chronic pain [35]. An increase in SO/PN production triggers thermal hyperalgesia associated with acute and chronic inflammation in response to the activation of the *N*-methyl-D-aspartate receptor (NMDAR), leading to the development of orofacial pain [36].

PN improves protein kinase C (PKC) activity. This kinase is activated by peripheral and central sensitization and optimizes the translocation of regulatory subunits of NADPH oxidase to the membrane to increase the production of SO derived from NADPH oxidase. These two mechanisms together amplify the formation of SO-derived PN, leading to the development of central sensitization [35].

Thus, antioxidants can be administered for pain management to prevent the negative impact of ROS and RNS on nociception, which both play a key role in neuro-inflammatory processes both at the central and peripheral levels, leading to increased nociceptive and inflammatory responses [26, 33, 37, 38].

In addition to their antioxidant activity, flavonoids and phenolic compounds exhibit effective anti-inflammatory biological properties by blocking two main signaling pathways, NF-κB and mitogen-activated protein kinase (MAPK) [24]. These pathways initiate a cascade of phosphorylation events and result in the production of several pro-inflammatory mediators that mediate the transmission of extracellular signals from the membrane to the nucleus [24, 27, 39].

3.2.2 Action on TRP channels

TRP channels are involved in various homeostatic and sensory functions, such as nociception and temperature sensation, and are expressed in both neuronal and non-neuronal cells. They are grouped into six subfamilies: TRP ankyrin (TRPA), TRP canonical (TRPC), TRP melastatin (TRPM), TRP mucolipin (TRPML), TRP polycystin (TRPP), and TRP vanilloid (TRPV). They are mostly non-selective cation channels expressed on the cell membrane, including the TRPA1 channel, a Ca^{2+}-permeable channel expressed in sensory neurons and is activated by phytochemicals and multiple products of oxidative stress [18].

The Ca^{2+}-permeable TRP channels of presynaptic terminals can modulate synaptic transmission independent of action potentials. Thus, the TRP channels, TRPV1, and TRPA1 can cause the release of neurotransmitters at sensory nerve terminals where these channels are highly co-expressed and participate in inflammatory hyperalgesia [18, 40]. Capsaicin (hot pepper), allicin (garlic), camphor (*Cinnamomum camphora* and rosemary), and menthol (peppermint) are all categories of analgesics that excite and desensitize nociceptive sensory neurons by acting on the TRPA1 and TRPV1 channels [41–43].

Other phytochemicals also activate the TRP channels. For example, curcumin (*Curcuma longa*) activates TRPA1 channels; eugenol activates the TRPV1 and TRPV3 channels; menthol activates TRPM8 channels; ginger components activate the TRPV1 and TRPA1 channels; and the thymol and linalool compounds of thyme (*Thymus vulgaris*) activate the TRPV3 and TRPA1 channels [18].

3.2.3 GABA mechanism

GABA is a major inhibitory neurotransmitter [44] involved in most inhibitory actions in the central and peripheral nervous systems (CNS and PNS). GABA exerts its action through two types of receptors: ionotropic (GABAA and GABAC) and metabotropic (GABAB) receptors. GABAA and GABAC are ion channels found in CNS neurons that are permeable to chloride ions when activated by GABA. GABAB receptors belong to the superfamily of G protein-coupled receptors and are present at different levels of the pain neuraxis where they regulate nociceptive transmission and pain [19, 45, 46].

Some phytochemicals, including flavonoids and terpenes, modulate the function of ionotropic GABA receptors, and can act as positive, negative, and neutralizing allosteric modulators. Thus, herbal preparations such as *Heliopsis longipes*, *Acmella caulirhiza*, *Ginkgo biloba*, *Panax ginseng*, and *Scutellaria lateriflora* may help modulate toothache by crossing the blood–brain barrier and influencing brain function. Past research has suggested that an increase in GABAergic activity in the rostral agranular insular cortex may induce analgesia by enhancing descending inhibition of spinal cord nociceptive neurons [19, 47].

Spilanthes acmella is a species of a flowering herb also known as the "toothache plant" [48–50], which has been used for centuries to treat oral pain owing to its analgesic, anti-inflammatory, and anesthetic properties attributed to its bioactive compounds, especially phytosterols, phenolic compounds, and *N*-alkylamides [48, 50, 51]. Spilanthol, which is mainly present in the flowers and shoots of *S. acmella*, is the most representative compound found in this genus. This and other species such as *H. longipes* are used worldwide as traditional remedies for their analgesic, antinociceptive, antioxidant, and anti-inflammatory effects. The analgesic effect of this compound is attributed to GABA release in the temporal cerebral cortex, whereas the antinociceptive effect is caused by the activation of the opioid-adrenergic, serotonergic, and GABAergic systems [52].

The flavonoid baicalein, which can be extracted from *S. lateriflora*, exerts sedative and anxiolytic effects by binding to GABAA receptors and, hence, could be used to manage orofacial pain. This flavonoid is also believed to modulate both intra- and extracellular calcium levels, which play key roles in pain signaling and transmission [44].

GABA receptor systems are found in peripheral pathways and the spinal cord, which are both important sites for pain impulse formation and transmission. They are also located in brain regions such as the marginal zone and substantia gelatinosa of the dorsal horn, which are essential for interpreting and responding to these signals. These findings indicate that GABA plays a key role in nociceptive processing. Consequently, agents that modify the function of this inhibitory neurotransmitter are useful analgesics [46].

3.2.4 Anti-inflammatory mechanism (COX and LOX pathways)

Inflammation is mediated by several families of mediators such as eicosanoids, which are lipid mediators produced through arachidonic acid metabolism, primarily in the COX and LOX pathways [53]. The COX pathway leads to the formation of prostanoids (prostaglandins (PG), prostacyclin, and thromboxane), whereas the LOX pathway leads to the production of leukotrienes (LTs) [54].

Nonsteroidal anti-inflammatory drugs (NSAIDs) inhibit the COX pathway, whereas others such as licofelone are dual inhibitors that block both COX and LOX [54, 55]. However, the selective inhibition of the two COX isoforms by NSAIDs has several reported side effects. This has encouraged the search for a dual inhibitor of both COX-2 and 5-LOX that possesses improved anti-inflammatory potency and fewer side effects [53, 56].

This anti-inflammatory effect leads to the elimination of harmful stimuli and the restoration of normal physiology through the complex molecular cascade mentioned above [3, 21]. This is thought to be the mechanism by which herbal extracts act in the treatment of toothache [21]. Accordingly, medicinal plants, particularly herbs whose main component is curcumin, such as *C. longa*, seem to provide several advantages through their mediating action on the COX and LOX pathways. As a dual inhibitor, curcumin exhibits synergistic effects and optimal anti-inflammatory activity [57]. *Allium cepa* (onion), which also contains polyphenols and flavonoids, inhibits the COX and LOX pathways and prevents the formation of LTs, thromboxane B2 (TXB2), and prostaglandin E2 (PGE2) [58, 59].

Additionally, various ginger compounds, such as gingerols, shogaols, zingerones, gingerdiols, and paradols, exhibit antioxidant, analgesic, and anti-inflammatory activities. More specifically, they act through the inhibition of COX and LOX in addition to their antioxidant activity resulting in an analgesic effect [60]. *Allium sativum* also has antioxidant and anti-inflammatory properties, and its efficacy in reducing pro-inflammatory responses is based on its nature as a COX and LOX inhibitor [59].

3.3 Bioavailability of medicinal plants

In humans, most phytochemicals exhibit low bioavailability after ingestion [9]. Hence, polyphenols have a rather low bioavailability because they exert most of their antioxidant activity in the gastrointestinal tract [61]. Additionally, a challenge with flavonoids is their low water solubility, which leads to decreased absorption and consequently decreased bioavailability following oral administration [62].

Interindividual variability, which depends on several factors such as diet, genetic background, composition, and activity of the intestinal microbiota, must also be considered. For example, polyphenols are relatively poorly absorbed (0.3–43%), resulting in low circulating plasma concentrations of their metabolites [63]. Additionally, the quantity and composition of phytochemicals in plants are influenced by species, age, plant part, cultivation method, harvesting season, conservation method, and geographic distribution [9, 64].

To improve bioavailability, proper decoction practices and various plants combinations have been suggested [65] because of their different phytochemical components and since they may provide different health benefits without requiring an increase in the dose [9]. For example, *Piper sarmentosum* combined with ginger is used to soothe toothache [66]. Medicinal plants containing hundreds of phytochemicals can produce many metabolites in the body, exerting more efficient beneficial effects than individual phytochemicals [9]. However, their combination can also directly affect their bioavailability in the body via mechanisms such as the first-pass effect [18, 67].

3.4 Medicinal plants vs pharmaceutical drugs

Comparisons between the analgesic effects of medicinal plants and pharmaceutical drugs have shown that the rhizome of *Zingiber officinale* (ginger) has long been used in traditional Chinese and Indian medicine to treat a wide range of ailments, including toothache [68]. Fresh ginger extracts have been subjected to chromatographic purification, and the resulting fractions were analyzed to assess their effect on PG synthesis. Through this method, plant extracts belonging to the Zingiberaceae family were found to inhibit PG synthesis *in vitro* [69].

The rhizome of *Z. officinale* has pharmacological properties similar to those of dual-action NSAIDs [55]. It inhibits both enzymes (COX and LOX) and has significantly fewer side effects than conventional NSAIDs [69, 70]. Licofelone is an example of a dual-action NSAID (5-LOX/COX) that is currently in phase III clinical development [55]. Studies have shown that orally administered dry ginger or ginger extract can reduce acute inflammation [68, 71], *and in vitro* and *in vivo* comparisons have confirmed the anti-inflammatory and analgesic actions of ginger extract [69, 70].

However, most *in vitro* studies analyzed phytochemical profiles using indices such as the half-maximal inhibitory concentration (IC_{50}), and the medicinal plant extracts have been tested for only a single biological target, COX or LOX. This is insufficient to validate their anti-inflammatory and analgesic properties and hinders direct comparisons between plants and dual-action NSAIDs [72].

The anti-inflammatory properties of ginger extracts come from a mixture of biologically active components such as gingerols, shogaols, and paradols, which are phenolic compounds [73]. The inhibitory effects of ginger on PG synthesis can be attributed to the presence of hydroxymethoxyphenyl compounds in gingerols and shogaols, which in turn inhibit arachidonic acid metabolism via the COX pathway [69, 74]. Moreover, ginger components inhibit several genes encoding cytokines and chemokines involved in inflammatory responses [69, 75].

Essential oil from the fruit of the plant *Dennettia tripetala* (DT), commonly known as pepper fruit, has analgesic effects like those induced by opioids morphine, aspirin, and indomethacin. The analgesic mechanism of DT has been inferred from studies showing that naloxone, which inhibits the analgesic effect of morphine, could also inhibit DT. These findings suggest that DT can also be used for toothache relief [22].

3.5 Plant combinations

Mixtures of medicinal plants are a key field of research which accounts for a large volume of information because their polyvalent effects can be used to cure multicausal diseases [76]. In different regions and cultures, plants are used as the entire plant, a combination of plants, or a combination of a plant and a drug. When medicinal plants are mixed, side effects are more likely to happen because interactions can occur between individual components. The most desirable interactions provide additional therapeutic benefits. However, natural extracts also contain multiple components. Therefore, the effects of interactions between two plants are often unpredictable and complex [77].

Additionally, a combination of two or more phytochemicals does not always enhance a specific effect. Combining two or more active chemical substances can produce additive, synergistic, or antagonistic effects [9, 78]. An example of synergism in the use of medicinal plants is Iberogast®, a phyto-preparation used in European countries and consists of nine plant extracts. It is considered to have a multi-target effect (at the gastrointestinal level). Such a multi-target effect has advantages over that of synthetic single-target drugs [79, 80].

Another example is the phytotherapeutic drug Lenidase®, which, when compared to ibuprofen, more efficiently and safely controls postoperative pain and discomfort following third molar extraction. Lenidase® contains a blend of herbal extracts, such as baicalin (190 mg), bromelain (50 mg), and escin (30 mg) [81], which exhibit anti-inflammatory activities. Bromelain inhibits pain mediators such as PGE2 and substance P and exhibits anti-edematous activity. Baicalin regulates several genes associated with inflammation, such as *COX*, *LOX*, and the inducible nitric oxide synthase gene. Escin exerts anti-inflammatory and anti-edematous effects through antihistaminic and antiserotonergic activities [81].

4. Results and discussion

As discussed above, medicinal plants, their phytochemicals, and their mechanisms of action are key subjects of scientific research because they are used to treat and prevent various diseases. Further, plants are the basis of many drugs. Although they are highly complex compounds and are not always suitable substitutes for synthetic agents [82], phytochemicals have been used to provide relief from toothache in various regions of the world, as outlined in the five tables included in this review.

The components of the medicinal plants used and their preparations vary by location and between species. For example, a study conducted in America revealed that leaves were the most commonly used plant parts and that the most common preparations were pastes, extracts, and rinses [83]. Another study conducted in Africa found that *Datura stramonium* L. roots, leaves, stems, and seeds were often used to provide relief from toothache [3]. These findings demonstrate the need for further phytochemical and pharmacological studies to establish which part of the plant is most effective for toothache treatment and the optimal application method to increase its action.

The parts used may vary with the medicinal plant; however, we found the most commonly used plant parts were leaves and roots, followed by the bark, stem, and seeds (Fig. 1). Preferentially using the leaves instead of roots can also prevent detrimental effects on the plants.

The most common phytochemicals involved in the mechanism of action of medicinal plants for toothache treatment are polyphenols, more specifically, flavonoids and terpenes, which are the most abundant secondary metabolites and antioxidants in the human diet [3, 5–7]. Flavonoids are the most ubiquitous group of all plant phenolics, which could explain the implicit antioxidant capacity of all medicinal plants [84]. Furthermore, flavonoids can modulate the function of ionotropic GABA receptors, suggesting that these phytochemicals can exert different mechanisms of action to relieve pain [20].

Polyphenols are strong antioxidants that neutralize free radicals by donating an electron or a hydrogen atom [61], thus exerting antioxidant effects in plants and organisms that consume them. However, polyphenols decrease the concentrations of ROS and RNS far from the site of the primary response because the local concentrations of these radicals around the inflammatory site are substantially high (> 1 mM). Therefore, polyphenols are highly unlikely to be effective where these free radicals are produced but could be quantitatively more effective as antioxidants in the surrounding unaffected tissues [85].

Substances such as capsaicin, allicin, camphor, and menthol cause a state of activation and desensitization in the TRP receptor pathway through which pain may be reduced [18, 43]. Of these phytochemicals, only allicin was analyzed in the studies included in this review. Moreover, allicin and spilanthol, compounds present in *A. caulirhiza,* have various biological and pharmacological effects, which may cause analgesia [3, 52]. Further studies should be performed to better understand the roles of these phytochemicals.

The mechanisms of action of phytochemicals in toothache relief are only partly understood. This review shows that these mechanisms involve antioxidant activity, action on TRP receptors, the GABA mechanism, and COX/LOX inhibitory activity. The tables in this review outline 163 medicinal plants with antioxidant mechanisms of action, 20 with an anti-inflammatory mechanism (COX/LOX), four with the GABA mechanism, and two with a TRP mechanism. Some plants have two reported mechanisms of action. However, in general, there is insufficient literature addressing each mechanism responsible for the toothache relief.

Several reports cite the use of various plants for toothache treatment; however, in many of these reports, the mechanism of action underlying pain relief is not specified, as indicated in the tables of this review. Moreover, in several studies, the phytochemicals potentially responsible for the analgesic effect were not reported. Accordingly, future studies should focus on identifying the exact mechanisms that contribute to dental analgesia and the phytochemicals involved. Additionally, the “common names” of medicinal plants were not included in this research, considering the extensive information involved in the preparation of this manuscript.

As mentioned above, we found only one study comparing the pharmacological properties of medicinal plants with those of conventional pharmaceutical drugs [81]. However, 30 plants with dual anti-inflammatory mechanisms (COX/LOX) were identified, as outlined in the tables for each continent. This information could be useful in future comparative studies of conventional or dual NSAIDs.

Although dual inhibition of microsomal PGE2 synthetase (mPGES-1) and 5-LOX has not been described as a mechanism of action in the reports included in this review, several plants (some of which are indicated in our tables) contain acylphloroglucinols, phenolic compounds, and non-phenolic acidic structures that exhibit such dual action [86]. mPGES-1 is an inducible enzyme at inflammatory sites that preferentially receives its substrate from co-induced COX-2 and is responsible for the excessive formation of PGE2 during acute and chronic inflammation [87, 88]; thus, its inhibition could be a promising target for toothache treatment with medicinal plants. Furthermore, natural mPGES-1 inhibitors have advantages over NSAIDs since they are non-synthetic and safer because they do not inhibit COX-derived homeostatic eicosanoids [86].

However, in *several in vitro and in vivo* studies (utilizing indices such as IC_{50}), the vast majority of medicinal plant extracts have been tested only against one biological target (COX or LOX), which is insufficient to validate their anti-inflammatory and analgesic properties and hinders direct comparisons between plants and conventional or dual-action NSAIDs [72]. Therefore, further studies should be conducted to address this gap in the research and gather more relevant information.

Multiple experimental studies of COX-1/COX-2 inhibition have used IC_{50} (the concentration at which an NSAID produces 50% inhibition of both COX enzymes) to rank the relative inhibitory activity of NSAIDs on these enzymes, and consequently, establish their selectivity over COX, correlating this *in vitro* inhibition with clinical efficacy and toxicity levels [89]. However, IC_{50} values do not indicate the mechanism of enzyme inhibition and vary with substrate concentration. Furthermore, these values are not directly comparable unless identical experimental conditions are used, and they must be analyzed carefully when inhibition is time-dependent [89]. These drawbacks also (91) hinder direct comparison between medicinal plants and NSAIDs.

Only two studies on plant combinations were found for this review. The study on the phytotherapeutic Lenidase® [81] was already described above. The other reported on the use of seven popular medicinal plant mixtures for toothache in Europe (Catalonia), including several species [76] whose use was not found in other continents.

Although medicinal plants are distributed throughout the world [90], biodiversity could affect how intensely such plants are used for toothache, and thus the discovery of new drugs [91]. The 17 most megadiverse countries in the world are Brazil, Colombia, Mexico, Peru, Ecuador, Venezuela, the United States of America, Indonesia, Australia, Madagascar, China, the Philippines, India, New Guinea, Malaysia, South Africa, and the Democratic Republic of Congo; most of these are in the American continent [92]. However, in this present review, most of the information on medicinal plants was gathered from Asia (Table 4) and Africa (Table 5), possibly because herbal medicines remain a key component of healthcare systems in the developing cultures of these continents [90]. Oceania has only two of the 17 megadiverse countries, which may explain the scarcity of plants in this continent (Table 5). Nevertheless, in some regions, much of the traditional knowledge about medicinal plants is only spread verbally and, thus, remains unexplored and unreported [93].

In terms of plants used in different continents, *A. sativum* was found in America (Table 1), Europe (Table 2), and Africa (Table 3); *A. cepa* and *Syzygium aromaticum* were found in Europe, Africa, and Asia; and *Acmella oleracea, Jatropha curcas*, and *Jatropha gossypiifolia* were all found in America (Table 1), Africa (Table 3), and Asia (Table 4). Conversely, some species are found only in one continent, such as *Thymus schimperi* Ronniger in Africa, perhaps because this species is a rare plant highly localized in and endemic to Ethiopia [94].

Among the families of medicinal plants used worldwide, Asteraceae was the most common, followed by Solanaceae, Fabaceae, Lamiaceae, Euphorbiaceae, Rutaceae, and Myrtaceae (Fig. 2). The first three of these families have been widely reported as those most commonly used to treat inflammation and various types of pain [44, 44, 76].

5. Future perspectives

Although phytotherapy has a long history, natural medicines are considered a hidden source of drugs because many medicinal plants have not been studied in depth [79]. Accordingly, further studies should be conducted to better understand the role and benefits of phytotherapeutic drugs [81] for toothache treatment, particularly when combined based on the multi-objective therapeutic principle of phytotherapy [79, 95]. This principle would be analogous to the multimodal analgesic approach used for NSAIDs [96–98].

Aromatherapy also has non-pharmacological therapeutic potential for reducing toothache by combining highly complex mixtures of essential oils to produce a therapeutic effect [95]. Therefore, further research should be conducted in this field of alternative medicine.

Although polyphenols in organic food extracts (extractable polyphenols) have already been analyzed, significant amounts of potentially bioactive polyphenols that remain in the residues (non-extractable polyphenols) have been overlooked.

Additionally, significant amounts of non-extractable polyphenols are found in foods and vegetables [61, 99]. Therefore, these compounds should be considered for future studies.

A promising therapeutic option for the administration of flavonoids that may increase their bioavailability is to develop protective systems, such as microcapsules, nanoparticles, and nano-formulations, that improve water solubility, dissolution, absorption, and thermal stability. Accordingly, in the near future, such systems should be developed and administered for pain management [62].

Finally, human clinical trials are essential to confirm the effectiveness of traditional phytotherapy for toothache and to investigate the pharmacodynamic and pharmacokinetic interactions between medicinal plants and other synthetic drugs. Similarly, predictive (*in silico*) models, phytochemical analyses, and ethnopharmacological studies could be milestones for drug discovery in traditional medicinal plants for toothache treatment, because many of them lack information or have not been studied.

6. Conclusion

This is the first review to compile a large volume of data on the global use of medicinal plants for the treatment of toothache. A total of 21 species of medicinal plants were found in America (Table 1), 29 in Europe (Table 2), 192 in Africa (Table 3), 112 in Asia (Table 4), and 10 in Oceania (Table 5). Asia and Africa are the continents where the most research has been done on this topic. The Asteraceae was the most commonly found plant family in this review, followed by Solanaceae, Fabaceae, Lamiaceae, Euphorbiaceae, Rutaceae, and Myrtaceae.

In total, 364 medicinal plants used for toothache treatment were identified, of which 139 have not yet been scientifically studied, highlighting opportunities for ethnopharmacological research on toothache treatments. The most common species were *A. sativum, A. cepa, A. oleracea, J. curcas, J. gossypiifolia,* and *S. aromaticum.* These families and species were more commonly found in Africa and Asia, corroborating our previously reported findings. As determined in this review, the most commonly used plant parts were the leaves and roots, followed by the bark, stems, and seeds.

We identified four mechanisms of action of medicinal plants implied in toothache treatment, namely, the antioxidant effect, effects mediated through TRP receptors, the GABA mechanism, and the anti-inflammatory mechanism (COX/LOX). Flavonoids, terpenes, polyphenols, and alkaloids are the phytochemicals most commonly associated with toothache treatment. Many of the plants analyzed in this review have the potential to be used as agents for toothache treatment. Therefore, future studies must prioritize the analysis of their pharmacodynamic and pharmacokinetic interactions.

Finally, to more precisely clarify the usefulness of medicinal plants as a valid option for toothache treatment, comparative studies between medicinal plants and commonly used pharmaceutical drugs should be conducted. In addition, studies published in Spanish should be included in future reviews since we only analyzed studies published in English, and this may have limited our ability to gather additional information.

Ethical Statement: Ethical approval was not required for this review article.

Conflicts of Interest: The authors declare no conflicts of interest.

Acknowledgments: None

Credit authorship contribution statement

José Luis Álvarez-Vásquez: conceptualization, methodology, literature search, writing—original draft preparation, writing—review and editing, supervision, and project administration. **Nathaly Fernanda Parra-Solano**: Literature search, writing—original draft preparation, writing—review, and editing. **Gabriela Elizabeth Saavedra-Cornejo**: Literature search, writing—original draft preparation, writing—review, and editing. **Ximena Elizabeth Espinosa-Vásquez**: Writing -review and editing, supervision. All the authors have read and agreed to the published version of the manuscript.

TABLE 1. AMERICA

Family	Scientific name	Used part	Preparation	Phytochemicals	Analgesic effect	Anti-inflammatory effect	Mechanism of action	Ref.
Fabaceae	*Acacia farnesiana (L.) Willd.*	Stem, leaves	Filling, extract, rinse	Diterpenes, flavonoids	x	x	Antioxidant activity	[83]
Asclepiadaceae	*Asclepias curassavica L.*	Latex, leaves, stem	Filling, extract, rinse	Flavonoids, triterpenes, phenols, quinines, tannins	x	x	N/A	[83, 100]
Malpighiaceae	*Byrsonima crassifolia (L.)*	Leaves, flowers	Filling, extract, rinse	Triterpenes, sterols, flavonoids	x	x	Antioxidant activity	[83, 101, 102]
Solanaceae	*Capsicum frutescens L.*	Leaves	Filling, extract, rinse	Alkaloids, tannins, saponins, flavonoids, carotenoids, steroids	x	x	Antioxidant activity	[83, 103]
Chenopodiaceae	*Chenopodium graveolens (Willd.)*	Leaves	Filling, extract, rinse	Sterols, flavonoids	x	x	N/A	[83]
Sterculiaceae	*Chiranthodendron pentadactylon Lam.*	Root	Filling, extract, rinse	Flavonoids, phenolic compounds	x	x	Antioxidant activity	[83]
Moraceae	*Dorstenia contrajerva L.*	Root	Filling, extract, rinse	Flavonoids, alkaloids	x	x	N/A	[83, 104]

Asteraceae	*Heliopsis longipes*	Root	Filling, extract, rinse	Alkamides, affinin (spilanthol)	x	x	GABA mechanism, anti-inflammatory mechanism (COX and LOX)	[83, 105]
Campanulaceae	*Lobelia laxiflora Kunth.*	Whole plant	Filling, extract, rinse	N/A	x	x	N/A	[83]
Lauraceae	*Persea americana Miller.*	Fruit	Filling, extract, rinse	Phenolics, flavonoids	x	x	Antioxidant activity	[83, 106]
Malvaceae	*Sida rhombifolia L.*	Stem, leaves	Filling, extract, rinse	Flavonoids, terpenoids, alkaloids	x	x	N/A	[83, 107]
Sterculiaceae	*Theobroma cacao L.*	Grain	Filling, extract, rinse	Polyphenols (flavonoids, lignans, lignins.)	x	x	Antioxidant activity	[83]
Poligonacea	*Mexican Sanguinaria*	Root	Filling, extract, rinse	Flavonoids	x	x	N/A	[83]
Euphorbiaceae	*Jatropha gossypifolia*	Whole plant	Decoction	Alkaloids, terpenes, flavonoids, lignans, coumarins, phenolics	-	x	Antioxidant activity	[108]
Euphorbiaceae	*Jatropha curcas*	Sap	Topical	Alkaloids, terpenes, flavonoids, lignans, coumarins, phenolics	-	x	Antioxidant activity, anti-inflammatory mechanism	[108, 109]

							(COX and LOX)	
Amaryllidaceae	*Allium sativum L.*	Bulb	Crushed	Steroids, terpenoids, flavonoids, phenols	-	x	Antioxidant activity, TRP mechanism, anti-inflammatory mechanism (COX and LOX)	[18, 59, 110, 111]
Araliaceae	*Panax ginseng*	Leaves, seeds	Extract	Flavonoids, terpenes	-	x	GABA mechanism	[110]
Zingiberaceae	*Zingiber officinale roscoe*	Leaves, seeds	Extract	Flavonoids, terpenes	-	x	Anti-inflammatory mechanism (COX and LOX)	[60, 110]
Asteraceae	*Tagetes lucida*	Aerial parts	Decoction, infusion, rinse, direct application	Carotenoids, flavonoids, thiophenes	-	x	Antioxidant activity	[112, 113]
Onagraceae	*Lopezia racemosa*	Leaves, seeds	Infusion	Tannins, flavonoids	-	x	Antioxidant activity	[114, 115]
Asteraceae	*Acmella oleracea*	Flowers	Chewed	Spilanthol, sequesterpenes.	x	x	GABA mechanism, antioxidant activity	[51, 116]

N/A: no information available

TABLE 2. EUROPE

Family	Scientific name	Used part	Preparation	Phytochemicals	Analgesic effect	Anti-inflammatory effect	Mechanism of action	Ref.
Amaryllidaceae	*Allium cepa L.*	Bulb	Bandage	Saponin, quercetin, anthocyanin	-	x	Antioxidant activity, anti-inflammatory mechanism (COX and LOX)	[6, 59, 117]
Amaryllidaceae	*Allium sativum L.*	Bulb	Crushed	Alliin, allicin, flavonoids, terpenes	-	x	Antioxidant activity, TRP mechanism,	[6, 18, 59, 76, 111]

							anti-inflammatory mechanism (COX and LOX)	
Asteraceae.	*Antennaria dioica (L.)*	Leaves	Decoction	Phenolic, flavonoid	-	x	Antioxidant activity	[6, 118]
Brassicaceae	*Armoracia rusticana P.*	Root	Finely chopped, chew	Flavonoids	-	-	Antioxidant activity	[6, 119]
Brassicaceae	*Brassica oleracea L.*	Leaves	Rinse, gargle	Carotene, tocopherol, ascorbate	-	-	Antioxidant activity	[6, 120]
Lauraceae	*Cinnamomum verum J. Presl*	Bark	Mix with cinnamon powder, honey, rub and spread	Monoterpenes, diterpenes, sesquiterpenes, polyphenols	-	x	Antioxidant activity	[6, 121]
Myrtaceae	*Eucalyptus globulus Labill.*	Leaves	Infusion mixed with lemon, inhalation	Flavonoids	-	x	Antioxidant activity	[6, 122]
Solanaceae	*Hyoscyamus niger L.*	Leaves	Infusion, gargle	Alkaloids	x	x	Antioxidant activity	[6, 123]
Asteraceae	*Matricaria chamomilla L.*	Flowers	Infusion, gargle	Flavonoids, coumarins, sesquiterpenes, and polyacetylenes	-	x	Antioxidant activity	[6, 124, 125]

Ranunculaceae	*Nigella sativa L.*	Oil, seed	Dissolved in hot water	Phenols	-	x	Antioxidant activity	[6, 126]
Plantaginaceae	*Plantago lanceolata L.*	Leaves	Gargle	Phenolic compounds	-	x	Antioxidant activity, anti-inflammatory mechanism (COX and LOX)	[6, 127, 128]
Lamiaceae	*Salvia officinalis L.*	Leaves	Decoction, gargle	Phenolic compounds	-	x	Antioxidant activity, anti-inflammatory mechanism (COX and LOX)	[6, 129, 130]
Myrtaceae	*Syzygium aromaticum L.*	Flowers	Chewed	Phenolic compounds	-	x	Antioxidant activity, anti-inflammatory mechanism (COX and LOX)	[6, 131, 132]
Asteraceae	*Taraxacum sp.*	Leaves, root	Boil, drop, or chew	Phenolic compounds	x	x	Antioxidant activity	[6, 133]
Vitaceae	*Vitis vinifera L*	Fruit	Decoction, gargle	Polyphenols	-	x	Antioxidant activity	[6, 134]
Poaceae	*Zea mays L.*	Grain	Boil, gargle	Flavonoids, alkaloids, phenols, steroids, terpenoids, tannins.	x	X	Antioxidant activity	[6]

Malvaceae	*Althaea officinalis L*	Root	Tisane	N/A	-	-	N/A	[76]
Oleaceae	*Olea europaea L*	Fruit	Juice, aerosol	Phenolic compounds	x	X	Antioxidant activity, anti-inflammatory mechanism (COX and LOX)	[76, 135]
Asteraceae	*Calendula arvensis L*	Flowers	Poultice	N/A	-	-	N/A	[76]
Apiaceae	*Eryngium campestre L*	Root	Tisane	N/A	-	X	N/A	[76]
Anacardiaceae	*Pistacia lentiscus L*	Leaves	Mouthwash	N/A	x	X	N/A	[76]
Lamiaceae	*Origanum vulgare L.*	Flowers	Tisane	N/A	x	X	N/A	[76]
Rutaceae	*Ruta chalepensis L*	Aerial parts	Tisane	Alkaloids, flavonoids, phenols, saponins.	x	x	N/A	[76, 136]
Rosaceae	*Crataegus monogyna Jacq.*	Flowers	Poultice	N/A	-	x	N/A	[76]
Apiaceae	*Foeniculum vulgare Mill.*	Seed	Poultice	Flavonoids, phenolic compounds.	-	x	Antioxidant activity, anti-inflammatory mechanism (COX and LOX)	[76, 137, 138]
Fabaceae	*Glycyrrhiza glabra L.*	Root	Poultice	N/A	-	-	N/A	[76]

Papaveraceae	*Papaver rhoeas L*	Flowers	Poultice	N/A	-	-	N/A	[76]
Lamiaceae	*Thymus vulgaris L.*	Aerial parts	Fumigation	N/A	-	-	TRP mechanism	[18, 76]
Rutaceae	*Citrus limon L.*	Fruit	Juice, mouthwash	N/A	-	-	N/A	[76]

N/A: no information available

TABLE 3. AFRICA

Familia	Scientific name	Used part	Preparation	Phytochemicals	Analgesic effect	Anti-inflammatory effect	Mechanism of action	Ref.
Ebenaceae	*Euclea undulata thunb.*	Root, bark	Powder rubbed or root chewed	Flavonoids, saponins, diterpenes, alkaloids	-	x	Antioxidant activity	[139]
Fabaceae	*Millettia ferruginea (hochst.)*	Bark	Grind, mix with water, chew	Flavonoids	-	-	N/A	[140, 141]
Lamiaceae	*Salvia nilotica juss.*	Leaves, root, bark	Chewing, grinding, rubbing	N/A	-	x	N/A	[140, 142]
Lamiaceae	*Rotheca myricoides (hochst.)*	Leaves, root, bark	Rubbing, grinding, eating, boiling	N/A	-	-	N/A	[140]

Malvaceae	*Ceiba pentandra L. Gaertn*	Fruit	Grinding, hold on teeth	Flavonoids	x	x	N/A	[140, 143]
Acanthaceae	*Blepharis linariifolia pers.*	Aerial part	Filling with powder	Flavonoids, phenolic acids	-	x	N/A	[144, 145]
Acanthaceae	*Barleria homoiotrichac. B. Clarke*	Bark	Drink	N/A	-	-	N/A	[3]
Acanthaceae	*Dyschoriste radicans (hochst. Ex. Rich.) Nees*	Whole plant	N/A	N/A	-	-	N/A	[3]
Acanthaceae	*Justicia Schimperiana (Hochst. ex Nees) T. Anderson*	Twigs	Chewed	Saponins, alkaloids, terpenoids and flavonoids	-	-	Antioxidant activity	[3, 146]
Amaryllidaceae	*Allium sativum L.*	Bulb	Crushed	Alliin, allicin, flavonoids, terpenes	-	x	Antioxidant activity, TRP mechanism, anti-inflammatory mechanism (COX and LOX)	[3, 18, 111]

Amaranthaceae	*Amaranthus caudatus L.*	Bark, leaves	Chewed	Flavonoids, phenols	-	-	Antioxidant activity	[140, 147]
Amaryllidaceae	*Allium cepa L.*	Leaves	Paste	Flavonoids, saponin	-	x	Antioxidant activity, anti-inflammatory mechanism (COX and LOX)	[59, 148, 149]
Anacardiaceae	*Mangifera indica L.*	Stem, root, leaves	Solution	N/A	-	x	N/A	[148, 150]
Anacardiaceae	*Rhus natalensis bernh. Ex. Krauss*	Leaves	Chewed	Flavonoids	-	x	Antioxidant activity	[3, 151–153]
Anacardiaceae	*Schinus molle L.*	Stem	Brushing	Monoterpenes.	x	x	Antioxidant activity	[3, 154]
Ancistrocladaceae	*Ancistrocladus abbreviatua*	Bark	Boil crust	Naphthylisoquinoline alkaloids	-	-	N/A	[148, 155]
Annonaceae	*Dennettia tripetala*	Fruits, leaves, seeds, roots	Extract	Tannins, alkaloids, flavonids, terpenoids, saponins	x	x	N/A	[22]
Apiaceae	*Ammi visnaga*	Fruit	Raw, decoction, direct	Tannins, coumarins, flavonoids, phenolic acids	x	x	Antioxidant activity	[156, 157]

			application, rinse					
Apiaceae	*Coriandrum sativum L.*	Fruit	Raw, direct application	Polyphenols: flavonoids	x	x	Antioxidant activity	[156, 158]
Apiaceae	*Foeniculum vulgare mill.*	Roots	Decoction	Flavonoids, phenolic compounds.	-	x	Antioxidant activity, anti-inflammatory mechanism (COX and LOX)	[3, 137, 138]
Apiaceae	*Oenanthe palustris (chiov.) C. Norman*	Leaves	Chewed	N/A	-	-	N/A	[3]
Apocynaceae	*Carissa edulis (forssk.) Vahl*	Root, leaves	Pound, boil and press on tooth	Lignans, sesquiterpenes, phenols	-	x	Antioxidant activity	[159, 160]
Apocynaceae	*Nerium oleander*	Leaves, root	Raw, direct application	Triterpene, flavonoids	-	x	Antioxidant activity, anti-inflammatory mechanism (COX and LOX)	[156, 161, 162]
Apocynaceae	*Carissa spinarum l.*	Bark	Chew or hold on teeth for 5-10 min.	Coumarin, lignans	-	-	Antioxidant activity	[163, 164]

Apocynaceae	*Calotropis procera (ait.) Dryand.*	Bark	Pounded	Triterpenoids	x	x	Antioxidant activity	[3, 165]
Aquifoliaceae	*Ilex mitis (l.) Radlk.*	Twigs	N/A	N/A	-	-	N/A	[3]
Araliaceae	*Scheffliera abyssinian (hochst. Ex a. Rich.) Harms*	Bark	Chewed	Saponins	-	-	N/A	[3]
Arecaceae	*Cocos nucifera L.*	Root	Powder and whole root	Phenols, tannins, flavonoids, triterpenes, steroids, alkaloid	-	x	Antioxidant activity, anti-inflammatory mechanism (COX and LOX)	[148, 166–168]
Asclepiadaceae	*Gomphocarpus purpurascens a. Rich.*	Root	Mix with honey and chew	N/A	-	-	N/A	[169, 170]
Asparagaceae	*Asparagus africanus lam.*	Root	Drink	Saponins, flavonoids, tannins.	x	x	N/A	[3, 171]
Asteraceae	*Echinops kebericho, mesfin*	Root	Pounded dry root is mixed with coffee	N/A	x	x	N/A	[172, 173]
Asteraceae	*Erlangea tomentosa*	Leaves	Crush and press on the tooth	Alkaloids, saponins, coumarins, tannins	-	-	N/A	[159]

Asteraceae	*Chamaemelum nobile l*	Flowers	Decoction, mouthwash	Flavonoids	-	x	Antioxidant activity	[156, 174]
Asteraceae	*Artemisia absinthium L.*	Leaves	Decoction, mouthwash	Phenolic compounds	-	x	Antioxidant activity	[156, 175]
Asteraceae	*Atractylis gummifera*	Root	Raw, direct application	Polyphenols, flavonoids, tannins	-	-	Antioxidant activity	[156, 176]
Asteraceae	*Spilanthes africana*	Flowers	All parts	Alkaloids, saponins and glycosides	x	x	N/A	[148, 177]
Asteraceae	*Echinaceae purpurea*	Leaves, stem	Paste	N/A	-	x	Antioxidant activity	[148]
Asteraceae	*Ageratum conyzoides*	Whole plant	Dust	Alkaloids, flavonoids, terpenoids	x	x	N/A	[148, 178]
Asteraceae	*Dichrocephala integrifolia*	Whole plant	Paste	Alkaloids, glycoside, flavanoids, phytosterols, saponins, tannins, carotenoids	_	x	N/A	[148, 179]
Asteraceae	*Acmella caulirhiza del.*	Flowers	Chewed, topical application	Lipophilic alkylamides, spilanthol	x	-	N/A	[3, 152]
Asteraceae	*Acmella oleracea*	Flowers	Chewed	Spilanthol, sequesterpenes.	x	x	GABA mechanism, antioxidant activity	[51, 51, 51, 180]
Asteraceae	*Artemisia abyssinica*	Stem	Chewed	Alkaloids, saponins, flavonoids and tannins.	x	x	Antioxidant activity	[3, 181]

	sch.bip. Ex a. Rich.							
Asteraceae	*Artemisia afra jack. Ex wild.*	Leaves	Chewed	N/A	-	-	N/A	[3]
Asteraceae	*Echinops kebericho mesfin*	Roots	Powdering	Flavonoids	x	x	Antioxidant activity	[3, 182]
Asteraceae	*Echinops macrochaetus fresen.*	Roots	Hold in mouth	N/A	-	-	N/A	[3]
Asteraceae	*Galinsoga parviflora cav.*	Flowers	Rubbing	Polyphenols and flavonoids, phenolic acids	-	x	Antioxidant activity, anti-inflammatory mechanism (COX and LOX)	[3, 183, 184]
Asteraceae	*Inula confertiflora a. Rich.*	Leaves	Chewed	N/A	-	-	N/A	[3]
Asteraceae	*Kleinia squarrosa cufod.*	Stem	Brushing	N/A	-	-	N/A	[3]
Asteraceae	*Laggera intermedia c. B. Clarke*	Leaves	Crushed	N/A	-	-	N/A	[3]
Asteraceae	*Parthenium hysterophorus L.*	Roots	Chewed	N/A	-	-	N/A	[3]

Asteraceae	*Vernonia auriculifera hiern*	Roots	Chewed	Tannins, flavonoids, terpenoids, saponins	-	-	N/A	[3, 185]
Balanitaceae	*Balanites aegyptiaca (l.) Del.*	Bark	Chewed	Saponins	-	x	Antioxidant activity, anti-inflamatory mechanism (COX and LOX)	[3, 186, 187]
Bignoniaceae.	*Stereospermum kunthianum cham*	Stem	Chewed	Flavonoids and phenolic acids	x	x	Antioxidant activity	[3, 188]
Boraginaceae	*Ehretia cymosa thonn.*	Bark, leaves	Chew, grind, boil, squeeze	Phenols, flavonoids, tannins, alkaloids, terpenes	-	-	Antioxidant activity	[140, 189]
Boraginaceae	*Cordia africana lam.*	Bark	Chewed	Flavonoids and phenolic compounds	-	x	Antioxidant activity	[3, 190]
Boraginaceae	*Cynoglossum coeruleum hochst. Ex a. Dc*	Leaves	Hold in mouth	N/A	-	-	N/A	[3]
Brassicaceae	*Lepidium sativum L.*	Seeds	Chewed	Flavonoids, saponosides, tannins, alkaloids, stereol and polyterpene.	-	x	Antioxidant activity	[3, 191]

Burseraceae	*Commiphora hodai Sprague*	Roots	Inhaling	N/A	-	-	N/A	[3]
Capparaceae	*Boscia salicifilia oliv.*	Leaves	Chew	Alkaloids, flavonoids, sesquiterpenes and their glycosides.	-	-	Antioxidant activity	[169, 192]
Capparaceae	*Capparis tomentosa lam.*	Roots	Chewed	Alkaloids, saponin glycosides, alkaloids, phytosterols, terpenoids, tannins, sterol, polyphenols, flavonoids	x	x	Antioxidant activity	[3, 193]
Capparaceae	*Capparis fascicularis dc.*	Roots	Chewed	N/A	-	-	N/A	[3]
Capparidaceae	*Cadaba rotundifolia forssk.*	Leaves	Chewed	Alkaloids, terpenoids and flavonoids	-	-	Antioxidant activity	[3, 194]
Capparidaceae	*Crateva adansonii dc.*	Leaves	Heating	Tannins, triterpenoids	-	-	Antioxidant activity	[3, 195]
Caricaceae	*Carica papaya*	Leaves	Solution	Alkaloids, saponins, glycosides, tannins	-	x	N/A	[148, 150, 196]
Caryophyllaceae	*Drymaria cordata*	Leaves	N/A	Alkaloid, glycosides, saponins, tannins	x	x	N/A	[3, 197]

Celastraceae	*Catha edulis (vahl) endl*	Leaves	Eat, boil, chew, mix with water.	N/A	-	-	N/A	[140]
Chenopodiaceae	*Chenopodium opulifolium*	Leaves	Drink	Flavonoids, saponins, terpenes, sterols, alkaloids	-	-	Antioxidant activity	[3, 159, 198]
Chenopodiaceae	*Chenopodium ambrosioides*	Whole plant, seeds	Paste	N/A	-	-	Antioxidant activity	[148, 199]
Clusiaceae	*Clusia lanceolata cambess.*	Leaves	N/A	N/A	-	-	N/A	[3]
Clusiaceae	*Garcinia livingstonei t. Anderson*	Stem	Chewed	Benzophenone derivatives, biflavonoids	-	-	Antioxidant activity	[3, 200, 201]
Colchicaceae	*Gloriosa superba L.*	Leaves	Crushed	Polyphenols, sterols and resinous substances	-	-	Antioxidant activity	[3, 202]
Combretaceae	*Anogeissus leiocarpus (dc.)*	Bark	Filling with powder	Flavonoids, terpenes, saponins	-	-	Antioxidant activity	[144, 203]
Asteraceae	*African Aspilia*	Whole plant	Paste	Terpenoids, sterols	-	x	N/A	[148, 204]
Asteraceae	*Vernonia amygdalina*	Leaves	Solution, chewed	Flavonoids, saponins, alkaloids, tannins, phenolics, terpenes	-	x	Antioxidant activity	[148, 205]
Asteraceae	*Arnica montana*	Leaves	Solution	Flavonoids, carotenoids,	-	x	Antioxidant activity	

				diterpenes, alkaloids, coumarins, lignans				[148, 206]
Convolvulaceae	*Ipomoea batatas*	Leaves	Paste	Polyphenol	_	x	N/A	[148]
Crassulaceae	*Kalanchoe laciniata (l.) Dc*	Roots	Chewed	Flavonoids, carotenoids	x	x	Antioxidant activity	[3, 207]
Cucurbitaceae	*Cucumis ficifolius*	Roots	Chewed	N/A	-	-	N/A	[169]
Cucurbitaceae	*Momordica foetida schumach.*	Roots	Chewed	Ucurbitan triterpenes	-	-	Antioxidant activity	[3, 208]
Cupressaceae	*Cupressus bethanis*	Seed, bark	Solution / rinse	N/A	-	-	N/A	[148]
Cupressaceae	*Cupressus lusitanica mill.*	Leaves	Decoction	Ascorbic acid, tocopherols	-	-	Antioxidant activity	[3, 209]
Cupressaceae	*Juniperus procera hochst. Ex endl.*	Bark	Hold	N/A	x	x	Antioxidant activity	[3, 210]
Dracaenaceae	*Dracaena fragrans L.*	Bark	Chewed	Flavonoids, alkaloids, carotenoids, saponins	-	-	N/A	[159, 211]
Dracaenaceae	*Dracaena diesteliana*	Root	Solution	N/A	-	-	N/A	[148]

Ebenaceae	*Euclea racemosa*	Whole plant	Chewed	Flavonoids, glycosides, phenols, saponins, steroids, tannins and triterpenes	-	-	Antioxidant activity	[3, 169]
Ebenaceae	*Euclea divinorum hiern*	Roots	Drink	Alkaloids, flavonoids, tannins, saponins	x	x	Antioxidant activity	[3, 212]
Euphorbiaceae	*Jatropha gossypifolia*	Whole plant	Decoction	Alkaloids, terpenes, flavonoids, lignans, coumarins, phenolics	-	x	Antioxidant activity	[108]
Euphorbiaceae	*Jatropha curcas*	Sap	Topical	Alkaloids, terpenes, flavonoids, lignans, coumarins, phenolics	-	x	Antioxidant activity, anti-inflammatory mechanism (COX-LOX)	[108, 109]
Euphorbiaceae	*Ricinus communis*	Leaves	Solution	steroids, saponins, alkaloids, flavonoids and glycosides	x	x	Antioxidant activity	[148, 213]
Euphorbiaceae	*Alchornea cordifolia*	Stem, bark	Boiled	Alkaloids, terpenes, steroids, phenolic acid, saponins	-	-	N/A	[148, 214]
Euphorbiaceae	*Ricinodendron heudelotii*	Seeds	Paste	Tannins, flavonoids	-	x	Antioxidant activity	[148, 215]
Euphorbiaceae	*Clutia abyssinica*	Leaves	Hold in mouth	Flavonoids, alkaloids, terpenoids and saponins	-	x	Anti-inflammatory	[163, 216]

	joub. & spach.						mechanism (COX-LOX)	
Euphorbiaceae	*Phyllanthus sepialis mull. Arg*	Roots	Chewed	N/A	-	-	N/A	[3]
Euphorbiaceae	*Acalypha sp.*	Leaves	Boil	Tannins, flavonoids, phenolics, saponins, alkaloids, terpenoids, coumarins, anthocyanins and anthraquinones.	x	x	Antioxidant activity	[148, 217]
Fabaceae	*Calpurnia aurea (aiton) benth.*	Leaves, root	Chewing, rubbing, powdering, grinding	N/A	-	-	N/A	[140]
Fabaceae	*Acacia albida delile*	Stem	Chewing, blow drying	Triterpenoids, tannins, sterols	-	x	Antioxidant activity	[140, 218]
Fabaceae	*Albizia gummiffera (j. F. Gmel.) Ca Sm.*	Leaves	Crushed, rubbed	N/A	-	-	N/A	[163]
Fabaceae	*Acacia nilotica*	Stem, bark	Decoction	Alkaloids, flavonoid phenols, tannins, terpenes	-	-	Antioxidant activity	[3, 219–221]
Fabaceae	*Abyssinian inlet a. Rich.*	Bark	Chewed	Tannins, saponins and flavonoids	-	-	N/A	[222]

Fabaceae	*Erythrina brucei schweinf.*	Bark	Chewed	Isoflavones	-	-	N/A	[3, 223]
Fabaceae	*Indigofera spicata forssk.*	Roots	Chewed	N/A	-	-	N/A	[3]
Flacourtiaceae	*Dovyalis abyssinica (a. Rich.) Warb.*	Seeds	Chewed	N/A	-	-	N/A	[3]
Flacourtiaceae	*Monsonia parvifolia schinz*	Leaves	Heated	N/A	-	-	N/A	[3]
Geraniaceae	*Geranium sp.*	Leaves	Rubbing	Terpenes	-	x	Antioxidant activity	[3, 224]
Clusiaceae	*Garcinia kola*	Bark and seeds	Rinse, paste	Flavonoids, phenol, alkaloids, saponin, tannin	-	X	Antioxidant activity	[148, 225]
Lamiaceae	*Coleus blumei*	Leaves	Paste	Rosmarinic acid	-	X	Antioxidant activity	[148, 226]
Lamiaceae	*Thymus schimperi ronniger*	Whole plant	Chew	N/A	-	-	N/A	[169]
Lamiaceae	*Clerodendrum myricoides (hochst.)*	Roots, seeds	Crushed	Alkaloid, phenols, anthraquinones, terpenoids, and flavonoids.	-	-	N/A	[3, 227]

Lamiaceae	*Isodon ramosissimus (hook.f.)*	Roots, leaves	Chewed	N/A	-	-	N/A	[3]
Lamiaceae	*Mentha pulegium L.*	Leaves	Chewed, infusion	-	-	-	TRP mechanism	[3, 18, 156]
Lamiaceae	*Ocimum urticifolium roth*	Leaves	Chewed	Tannins, glycosides, saponins, flavonoids, steroids, terpenoids, phenols	-	-	N/A	[3, 228]
Lamiaceae	*Oymus schimperi ronniger*	Whole plant	Chewed		-	-	N/A	[3]
Lauraceae	*Persea americana*	Seeds, stem	Decoction / hot solution	Flavonoids, saponins, tannins, steroids, alkaloids, terpenoids.	-	X	Antioxidant activity	[106, 148, 229]
Fabaceae	*Acacia oerfota (forssk.) Schweinf.,*	Root	Paste	Alkaloids, terpenes, flavonoids	-	-	N/A	[144]
Fabaceae	*Acacia senegal (l.) Willd.,*	Leaves, thorns	Filling with powder and bowling	Flavonoids, alkaloids, terpenoids, steroids	-	-	Antioxidant activity	[144]
Fabaceae	*Cassia arereh delile*	Root	Filling with powder	Flavonoids, phenols, terpenoids, saponins, tannins	-	-	Antioxidant activity	[144, 230]
Loranthaceae	*Plicosepalus robustus*	Leaves	Pulverized	N/A	-	-	N/A	[3]

	wiens & polhill							
Loranthaceae	*Tapinanthus globiferus (a. Rich.) Tiegh.*	Leaves	Rub	N/A	x	-	Antioxidant activity	[3, 231]
Malvaceae	*Cola nitida*	Bark and fruit	Solution and paste	Alkaloids, tannin, saponin, flavonoids	-	X	Antioxidant activity	[148, 232]
Malvaceae	*Pavonia urens cav.*	Root	Decoction	N/A	-	-	N/A	[3]
Malvaceae	*sida tenuicarpa vollesen*	Root	Brushed	N/A	-	-	N/A	[3]
Malvaceae	*Sida ovata forssk.*	Leaves, root	Liquid form	N/A	-	-	N/A	[140]
Malvaceae	*Azadirachta indica A.*	Leaves root, bark	Grinding, chewing, boiling, liquid form	Alkaloids, flavonoids, triterpenes, steroids, phenolic compounds.	-	X	Antioxidant activity	[140, 233–235]
Meliaceae	*Melia azedarach L.*	Leaves	Chewed	Alkaloids, terpenoids, flavonoids	-	-	Antioxidant activity	[3, 236]
Menispermaceae	*Stephania abyssinica*	Root	Brushed	N/A	-	-	N/A	[3]
Lamiaceae	Marrubium vulgare L	Whole plant	Decoction, mouthwash	Phenolic compounds	x	X	Antioxidant activity, anti-inflammatory	[156, 237, 238]

							mechanisms (COX-LOX)	
Lamiaceae	Origanum majorana	Whole plant	Mouthwash	Terpenoids, flavonoids, phenolic acids.	x	X	Antioxidant activity	[156, 239]
Moraceae	*Ficus palmata forssk.*	Root	Chewed	Phenolic compounds, flavonoid	-	-	Antioxidant activity	[3, 240]
Moraceae	*Ficus sur forssk.*	Bark	Chewed	Tannins, saponins, steroids, tannins	-	-	N/A	[3, 241]
Moraceae	*Ficus vasta forssk.*	Bark	Eating, chewing	Phenolic compounds, flavonoids	-	-	Antioxidant activity	[140, 242]
Moringaceae	*Moringa oleifera*	Root	Decoction	Alkaloids, protein, quinine, saponins, flavonoids, tannin, steroids, glycosides	x	X	Antioxidant activity	[148, 243]
Myristicaceae	*Pycnanthus angolensis*	Stem, bark, leaves	Decoction / mouthwash	N/A	-	-	N/A	[148]
Myrtaceae	*Eucalyptus globulus Labill.*	Leaves	Infusion mixed with lemon, inhalation	Flavonoids	-	X	Antioxidant activity	[6, 122, 156]
Myrtaceae	*Myrtus communis l*	Leaves	Decoction, mouthwash	Phenolic compounds, flavonoids	-	-	Antioxidant activity	[156, 244]

Myrtaceae	*Syzygium aromaticum L.*	Flowers	Chewed	Phenolic compounds	-	X	Antioxidant activity, anti-inflammatory mechanism (COX and LOX)	[6, 132, 156, 245]
Myrtaceae	*Eucalyptus saligna*	Leaves	Solution, paste	Flavonoids, derived from phenylpropene	-	-	N/A	[148]
Myrtaceae	*Psidium guajava L.*	Leaves	Hot rinse, chewed	Flavonids, triterpenes, tannins	x	X	Antioxidant activity	[93, 148, 219, 246]
Myrtaceae	*Eucalyptus sp*	Roots	Rub	N/A	-	X	Antioxidant activity	[3, 247]
Myrtaceae	*Eucalyptus camaldulensis*	Leaves	Rubbing, hold on teeth, filling with powder	N/A	x	X	Antioxidant activity	[140, 144, 248]
Nitrariaceae	*Peganum harmala L.*	Seeds	Decoction, mouthwash	Flavonoids, alkaloids, saponins, tannins, glycosides, terpenoids and steroids	x	-	N/A	[156, 249–251]
Olacaceae	*Ximenia americana L.*	Bark	Pulverized	Flavonoids, polyphenols	-	-	Antioxidant activity	[3, 252]
Oleaceae	*Olea europaea l.*	Leaves	Chewed	Phenolic compounds	-	X	Antioxidant activity, anti-inflammatory	[130, 135, 169]

							mechanism (COX and LOX)	
Oleaceae	*Jasminum abyssinicum hochst*	Roots	Chewed	Alkaloids, flavonoids, terpenes, phenol	-	-	Antioxidant activity	[3, 253]
Oleaceae	*Jasminum grandiflorum L.*	Leaves, stem	Crushed	Flavonoids, alkaloids, glycosides	-	-	Antioxidant activity	[3, 254]
Oliniaceae	*Olinia rochetiana a. Juss.*	Leaves, bark	N/A	N/A	-	-	N/A	[3]
Opiliaceae	*Ziziphus mauritiana lam*	Stem	Boiled	Flavonoids glycoside, phenol, lignin, saponins, sterols and tannins	-	X	Antioxidant activity	[3, 255]
Orobanchaceae	*Orobanche ramosa L.*	Roots	Chewed	N/A	-	-	N/A	[3]
Oxalidaceae	*Oxalis corniculata L.*	Leaves	Chewed	Flavonoids, alkaloids, tannins, phenols	-	X	Antioxidant activity	[3, 256]
Oxalidaceae	*Oxalis radicosa A. Rich.*	Leaves, stem	Chewed	N/A	-	-	N/A	[3, 152]
Phytolaccaceae	*Phytolacca dodecandra L'her*	Stem	Chewed	Triterpenoids, saponins, alkaloid, phenolics, steroids, terpenoids	x	X	N/A	[3, 257, 258]

Plumbaginaceae	*Plumbago zeylanica L.*	Roots, bark	Crushed root, direct application	Alkaloids, glycosides, steroids, triterpenoids, tannins, phenolic compounds, flavanoids, saponins, coumarins	-	X	N/A	[152, 259, 260]
Polygalaceae	*Securidaca longepedunculata fresen.*	Leaves	Chewed	Flavonoids, tannins, triterpenoids	x	X	N/A	[3, 261]
Polygonaceae	*Rumex abyssinicus jacq*	Roots	Crushed, drink	Phenolic compounds, tannins, saponins, flavonoids, terpenoids, steroids, alkaloids,	x	X	N/A	[3, 169, 262]
Polygonaceae	*Rumex nepalensis spreng.*	Roots	Chewed	Flavonoids, terpenoids, alkaloids, saponins, tannins	-	X	Antioxidant activity	[3, 263]
Polypodiaceae	*Drynaria volkensii Heiron*	Roots	Chewed, heat	N/A	-	-	N/A	[3, 163]
Proteaceae	*Faurea speciosa welw*	Roots, leaves	Chewed, Topical application	N/A	-	-	N/A	[3, 152]

Ranunculaceae	*Clematis longicauda steud.*	Leaves	Crushed	Tannins, saponins, flavonoids, and steroids	-	-	N/A	[3, 264]
Ranunculaceae	*Clematis simensis fresen.*	Bark, seed, roots	Chewed	Triterpenoids, saponins, alkaloids, polyphenol	-	X	N/A	[3, 265]
Ranunculaceae	*Ranunculus multifidus forssk.*	Roots	Chewed	N/A	-	-	N/A	[3]
Ranunculaceae	*Thalictrum rhynchocarpum dill*	Roots	Chewed	N/A	-	-	N/A	[3]
Rosaceae	*Prunus africana (hook.f.)*	Bark	Chewed	Phenolic, flavonoid	-	-	Antioxidant activity	[3, 266]
Rosaceae	*Prunus persica (l.) Batsch*	Bark	Chewed	Phenolic compounds, carotenoids	-	X	N/A	[3, 267]
Rubiaceae	*Galium boreo-aethiopicum*	Roots	Chewed	N/A	-	-	N/A	[169]
Rubiaceae	*Gardenia ternifolia schumach.*	Roots	Chewed	Saponins, sterols, triterpenes, tannins, flavonoids	-	-	Antioxidant activity	[3]
Rubiaceae	*Pavetta gardeniifolia hochst.*	Roots	Crushed	N/A	-	-	N/A	[3]

Rubiaceae	*Pentas lanceolata (forssk.)*	Roots	Chewed	Saponins, alkaloids	-	-	N/A	[3, 152, 268]
Rutaceae	*Clausena anisata (willd.)*	Roots, stem, seeds, leaves	Chewed	Phenolic, alkaloid, flavonoid, saponins, tannin	-	-	Antioxidant activity	[3, 269]
Rutaceae	*Ruta chalepensis L*	Leaves	Chewed	Alkaloids, flavonoids, phenols, saponins.	x	X	N/A	[3, 136]
Rutaceae	*Vepris dainellii (pichi-serm.) Kokwaro*	Bark	Chewed	N/A	-	-	N/A	[3]
Rutaceae	*Zanthoxylum chalybeum engl.*	Bark	Hold	Alkaloids, phenolic	x	-	N/A	[3, 270]
Salvadoraceae	*Salvadora persica L.*	Stem	Brushed	Saponins, alkaloids	x	-	N/A	[3, 271]
Sapindaceae	*Dodonaea angustifolia*	Roots, leaves	Brushed	Di and triterpenes, saponins, flavonoids, phenolic compound.	x	X	Antioxidant activity	[3, 272, 273]
Scrophulariaceae	*Verbascum sinaiticum benth.*	Roots	Chewed	Alkaloids, phenolic compounds, anthraquinones, flavonoids,	-	-	Antioxidant activity	[169, 274]

				saponins, tannins, steroids, terpenes.				
Simaroubaceae	*Brucea antidysenterica J.F.Mill.*	Roots, bark	Chewed	Alkaloids, flavonoids, glycosides, phenols, quinones, saponins, steroids, tannins, terpenoids	-	X	N/A	[3, 275]
Solanaceae	*Solanum americanum mill.*	Leaves, fruits	Grind, boiled, chewed	Alkaloids, flavonoids, tannins, saponins	-	-	N/A	[140]
Solanaceae	*Datura stramonium L.*	Fruits, leaves, stem, seeds	Grind, rub, liquid form, boiled, squeezed	Alkaloids, tannins, flavonoids, phenols	x	X	Antioxidant activity	[152, 276, 277]
Solanaceae	*Nicotiana tabacum L.*	Leaves	Boiled, chewed	Flavonoids, alkaloids, tannins, phenolic compounds, terpenoids	-	-	N/A	[140, 278]
Solanaceae	*Solanum hastifollium hochst.*	Roots	Chewed	N/A	-	-	N/A	[169]
Solanaceae	*Solanum incanum l.*	Fruits, roots	Chewed	Alkaloids, flavonoids, saponins, steroids	-	-	Antioxidant activity	[3, 279]

Solanaceae	*Solanum marginatum l. F.*	Roots	Chewed	Alkaloids, saponins, flavonoids, glycosides, terpenoids, steroid	-	-	N/A	[3, 280]
Solanaceae	*Capsicum frutescens L.*	Fruits	Paste	Alkaloids, tannins, saponins, flavonoids, carotenoids, steroids	x	X	N/A	[103, 148]
Tiliaceae	*Grewia bicolor juss*	Stem	Brushed	Alkaloids, triterpenes	-	-	N/A	[3, 281]
Tiliaceae	*Grewia ferruginea hochst.*	Roots	Shredded	N/A	-	-	N/A	[3]
Verbenaceae	*Premna schimperi engl.*	Leaves, root, stem	Grind, chewed, rub, boiled	Flavonoids, diterpenoids, triterpenes, sterols, alkaloids	-	X	Antioxidant activity	[140, 282]
Verbenaceae	*Stachytarpheta angustifolia*	Leaves	Decoction	Phenolic, tannin compounds	-	X	Antioxidant activity	[148, 283]
Verbenaceae	*Premna oligotricha*	Leaves	Chewed	Flavonoids, alkaloids, triterpenoids, resins, tannins, saponins and steroids,	-	-	N/A	[3, 169, 284]
Verbenaceae	*Premna resinosa (hochst.)*	Roots	Chewed	Alkaloids, phenols, terpenids, flavonoids	-	-	Antioxidant activity	[3, 285]

Vitaceae	*Cyphostemma junceum (webb)*	Whole plant	Chewed	N/A	-	-	N/A	[169]
Vitaceae	*Cissus quadrangularis L..*	Roots	Chewed	Sterols, tannins, alkaloids	-	-	Antioxidant activity	[3, 286]
Xanthorrhoeaceae	*Aloe vera L.*	Leaves	Chewed	Phenolic compounds, alkaloids	-	x	Antioxidant activity, anti-inflammatory mechanism (COX and LOX)	[287–290]
Zingiberaceae	*Aframomum corrorima*	Seeds, rhizome	Chewed	Flavonoids, phenolics, terpenoids	-	-	Antioxidant activity	[3, 291]
Zingiberaceae	*Zingiber officinale roscoe*	Rhizome	Chewed	Flavonoids, alkaloids, saponins, steroids, terpenoids, tannin.	x	X	Antioxidant activity, Anti-inflammatory mechanism (COX and LOX)	[3, 60, 70, 292]

N/A: no information available

TABLE 4. ASIA

Family	Scientific name	Used part	Preparation	Phytochemicals	Analgesic effect	Anti-inflammatory effect	Mechanism of action	Ref.
Acanthaceae	*Barleria Cristata*	Leaves, roots	Chewed, infusion	Triterpenoids, flavonoids, phenolic compounds	-	x	Antioxidant activity	[293]
Acanthaceae	Hygrophila auriculata	Roots, leaves	N/A	N/A	-	-	N/A	[294]
Actinidiaceae	*Saurauia tristyla DC.*	Roots	Decoction	Phenolic compounds, flavonoids, alkaloids, steroids, saponins	-	-	N/A	[295, 296]
Amaryllidaceae	*Allium cepa L.*	Bulb	Raw, cooked	Phenolic acids, flavonoids, anthocyanins	X	x	Antioxidant activity, Anti-inflammatory mechanism (COX and LOX)	[6, 59, 297, 298]
Amaranthaceae	*Beta vulgaris L*	Leaves	Juice	N/A	-	-	Antioxidant activity	[298, 299]

Amaranthaceae	*Achyranthes aspera*	Leaves, roots	Decoction	Saponins, alkaloids	X	x	Antioxidant activity	[14, 219, 294]
Anacardiaceae	*Mangifera indica L.*	Bark	Powdered inner bark, keep in mouth	N/A	-	-	N/A	[219]
Apocynaceae	*Wrightia tinctoria*	Leaves	Chewed	Flavonoids, glycoflavonoids, phenolic acids	-	x	Antioxidant activity	[300]
Apocynaceae	Plumeria rubra L	Stem, bark	N/A	N/A	-	-	N/A	[294]
Araliaceae	*Panax ginseng*	Leaves, seeds	Extract	Flavonoids, terpenes	-	x	GABA mechanism	[110]
Aristolochiaceae	*Asarum longerhizomatosum C.*	Whole plant	Ground, decoction	Flavonoids	-	x	N/A	[296, 301]
Aristolochiaceae	*Asarum caudigerum*	Whole plant	Direct application	N/A	-	-	N/A	[302]
Asclepiadaceae	*Pergularia daemia*	Latex	Direct application	Alkaloids, saponins, tannins, flavonoids, terpenoids, phenols	-	x	Antioxidant activity	[219, 303]
Asteraceae	*Achillea biebersteinii*	Leaves	N/A	N/A	-	-	N/A	[250, 298, 304]

Asteraceae	*Bidens biternate*	Roots	Paste	Glycosides, flavonoids, alkaloids, tannins, steroids, terpenoids, coumarins	-	-	N/A	[14, 305]
Asteraceae	*Parthenium hysterophorus L.*	Flowers	Chewed	Phenols, flavonoids	-	-	N/A	[3, 14, 306]
Asteraceae	*Achillea biebersteinii*	Flowers, leaves	N/A	Terpenes, flavonoids, phenolic acids	-	x	Antioxidant activity	[250, 304]
Asteraceae	*Acmella oleracea*	Flowers	Chewed	Spilanthol, sequesterpenes.	X	x	GABA mechanism, antioxidant activity	[51, 51, 180]
Berberidaceae	*Berberis wuliangshanensis*	Roots	N/A	N/A	-	-	N/A	[307]
Biebersteiniaceae	*Biebersteinia multifida*	Leaves, stem	Extract	Alkaloids	X	x	N/A	[298, 308]
Bignoniaceae	*Incarvillea sinensis Lam.*	Roots (fresh or dried)	Gargle	Alkaloids	-	-	N/A	[309, 310]
Boraginaceae	*Cynoglossum lanceolatum*	Fruits, leaves, seeds	Chewed	Alkaloids	X	x	Antioxidant activity	[14, 311, 312]

Caesalpiniaceae	*Caesalpinia coriaria*	Fruits	Powder	Tannins	-	-	Antioxidant activity	[219, 313]
Capparidaceae	*Capparis spinosa*	Stem, fruits	N/A	Alkaloids, flavonoids, steroids, terpenoids, tocopherol, phenolic compounds	X	x	Antioxidant activity	[250, 298, 314, 315]
Caryophyllaceae	*Dianthus crinitus*	Seeds	N/A	Flavonoids	-	x	Antioxidant activity	[298]
Caryophyllaceae	*Dianthus orientalis*	Seed, leaves, flowers, fruits.	Extract	Flavonoids, phenols	-	-	Antioxidant activity	[250, 298]
Cannaceae	Canna indica L	Roots	Direct aplication	N/A	-	-	N/A	[294]
Cleomaceae	*Cleome gynandra, L.*	Leaves	Extract	Polyphenols, oleic acid, linoleic acid	X	-	Antioxidant activity	[219, 316]
Convolvulaceae	*Merremia chryseides*	Whole plant	Decoction	N/A	-	-	N/A	[219]
Ebenaceae	*Diospyros lotus*	Branch, roots	Rub	Phenolic compounds	X	x	Antioxidant activity	[14, 317]
Elaeagnaceae	*Elaeagnus umbellate*	Branch	Rub	Alkaloids, steroids, terpenoids, saponins	-	-	Antioxidant activity	[14, 318]

Eriocaulaceae	*Eriocaulon buergerianum*	Flowers	Decoction	Flavonoids, phenolic compounds	-	x	N/A	[302, 319]
Euphorbiaceae	*Jatropha gossypifolia*	Whole plant	Decoction	alkaloids, terpenes, flavonoids, phenolics	-	x	Antioxidant activity	[108]
Euphorbiaceae	*Jatropha curcas*	Sap	Topical	alkaloids, terpenes, flavonoids, phenolics	-	x	Antioxidant activity, anti-inflammatory mechanism (COX-LOX)	[108, 109, 294]
Fabaceae	*Acacia nilótica*	Bark	Decoction	Alkaloids, flavonoid phenols, tannins, terpenes	-	-	Antioxidant activity	[219–221]
Fabaceae	*Lespedeza juncea*	Whole plant	Decoction	Flavonoids, alkaloids	-	-	Antioxidant activity	[14, 320]
Fabaceae	Senna tora (L.)	Leaves, Stem, Fruit, Root, Seed	N/A	N/A	-	-	N/A	[294]
Geraniaceae	*Erodium cicutarium*	Aerial parts	Boiled	Polyphenols	-	-	Antioxidant activity	[298, 321]
Ginkgoaceae	*Ginkgo biloba*	Leaves, seeds	Extract	flavonoids, terpenes	-	x	N/A	

								[110, 322]
Hypericaceae	*Hypericum perforatum*	Flowers	N/A	Flavonoids	-	x	N/A	[298, 323]
Iridaceae	*Iris dichotoma Pall.*	Roots, bark	Chop and chew	Phenolic compound, flavonoids or isoflavones	-	x	N/A	[310, 324]
Lamiaceae	*Leucas aspera, (Willd.)*	Leaves	Extract	Triterpenoids, diterpenoids, phenolic compounds, alkaloids	-	-	Antioxidant activity	[219, 325]
Lamiaceae	*Teucrium polium L*	Aerial parts	Extract	Flavonoids, terpenoids	-	x	Antioxidant activity	[298, 326]
Lamiaceae	*Stachys pilifera*	Leaves	Extract	Flavonoids, diterpenes, saponins, terpenoids	-	x	Antioxidant activity	[298, 327]
Lamiaceae	*Micromeria biflora*	Roots	Paste	N/A	-	-	N/A	[14]
Lamiaceae	*Plectranthus*	Bud, flowers	Chewed	Monoterpenoids, sesquiterpenoids, diterpenoids, phenolics	-	x	N/A	[14, 328]

Lauraceae	*Litsea cubeba (Lour.) Pers.*	Fruits	Decoction	Flavonoids, Terpenoids, Alkaloids	-	x	Antioxidant activity	[296, 329]
Liliaceae	*Allium condensatum Turcz.*	Aerial parts	Smell after calcination	N/A	-	-	N/A	[310]
Liliaceae	*Fritillaria imperialis L.*	Fruits	N/A	Alkaloids, terpenoids, saponins	x	x	Antioxidant activity	[298, 330]
Liliaceae	*Allium tuberosum Rottl. ex*	Whole plant	Ground, decoction	Alkaloids, flavonoids, terpenoids, tannins, saponins	-	x	Antioxidant activity	[296, 331]
Loganiaceae	*Strychnos nux-vomica L.*	Seeds	Chewed	Phenolic compounds	x	x	N/A	[302, 332]
Meliaceae	*Azadirachta indica A.*	Bark, leaves, branches	Powdered inner bark keep in mouth, extract	Alkaloids, flavonoids, triterpenoids, phenolic compounds	-	x	Antioxidant activity	[219, 233, 235]
Menispermaceae	*Cyclea hypoglauca (Schauer)*	Roots	Infusion	N/A	-	-	N/A	[296]
Moraceae	*Streblus asper, Lour.*	Bark	Powdered inner bark keep in mouth	N/A	-	-	N/A	[219]

Myrtaceae	*Syzygium aromaticum L.*	Flowers	Decoction, powder and hydrodistillate	Monoterpenes, sesquiterpenes, phenolics, hydrocarbon compounds.	x	x	Antioxidant activity, anti-inflammatory mechanism (COX and LOX)	[132, 288, 333]
Myrtaceae	*Psidium guajava L.*	Leaves, bark	Chewed	Flavonoids, triterpenes, tannins	x	x	Antioxidant activity	[93, 219, 246]
Fabaceae	Mimosa pudica L.	Roots	Boiled	N/A	-	-	N/A	[294]
Malpighiaceae	Hiptage benghalensis	Stem	N/A	N/A	-	-	N/A	[294]
Nyctaginaceae	*Mirabilis jalapa Linn.*	Whole plant	N/A	Alkaloids, tannins, flavonoids, glycosides, phenols, steroids, triterpenoids, saponins	-	X	Antioxidant activity	[307, 334]
Oleaceae	*Olea ferruginea (Sol.)*	Fruits, leaves, seeds and bark	Decoction	Phenolic compounds	-	-	N/A	[335, 335, 336]

Oxalidaceae	*Oxalis corniculate L.*	Flowers	Chewed	Flavonoids, phytosterols, phenolic compounds, tannins	-	-	N/A	[14, 337]
Fabaceae	*Astragalus verus Oliv.*	Resin	N/A	N/A	-	-	N/A	[298]
Fabaceae	Clitoria ternatea L.	Roots	Paste	N/A	-	-	N/A	[294]
Fabaceae	Pongamia pinnata L.	Seeds	Oil	N/A	-	-	N/A	[294]
Pinaceae	*Pinus roxburghii Sarg.*	Aerial parts	Extract, juice	Flavonoids	x	X	Antioxidant activity	[335, 338]
Plantaginaceae	*Plantago lanceolata L.*	Leaves	Grind and keep in mouth	Phenols, flavonoids	-	X	Antioxidant activity, anti-inflammatory mechanism (COX and LOX)	[127, 335, 339]
Polypodiaceae	*Drynaria roosii Nakaike*	Rhizome	Cooked with water, sliced, dried, medicinal liquor	Flavonoids	-	-	N/A	[302]
Poaceae	Cynodon dactylon (L.	Roots, leaves	N/A	N/A	-	-	N/A	[294]

Poaceae	Desmostachya bipinnata	Roots	N/A	N/A	-	-	N/A	[294]
Poaceae	Vetiveria zizanoides (L.)	Roots	N/A	N/A	-	-	N/A	[294]
Rhamnaceae	*Rhamnus persica*	Fruits, leaves	Decoction, infusion, powder	Monoterpenes , sesquiterpenes, aldehydes, phenols	-	-	Antioxidant activity	[298]
Rosaceae	*Sanguisorba minor*	Stem, aerial parts, roots	N/A	Flavonoids, phenols, triterpenoids	X	x	Antioxidant activity	[298, 340, 341]
Rosaceae	*Prunus pérsica*	Branch	Chewed	N/A	-	-	N/A	[14]
Rosaceae	*Rubus parvifolius L.*	Whole plant	Ground, decoction	Phenolic compounds	-	x	Antioxidant activity	[296, 342]
Rosaceae	*Geum japonicum Thunb.*	Whole plant	Decoction	Triterpenoids, sterols, tannins	-	x	N/A	[302, 343]
Rosaceae	*Amygdalus davidiana*	Bark, leaves	N/A	N/A	-	-	N/A	[307]
Rosaceae	*Prunus humilis Bunge*	Roots (fresh or dried)	Chop and chew, decoction	Flavonoids and phenolic compounds	-	-	Antioxidant activity	[310, 344]
Rubiaceae	*Gailonia Aucheri*	Leaves, flowers	N/A	N/A	-	-	N/A	[298]
Rutaceae	*Zanthoxylum nitidum*	Stem, branches, leaves, roots	Decoction	Alkaloids, coumarins, lignans,	x	x	Antioxidant activity	[345]

				flavonoids, terpenes, steroids, alkylamides				
Rutaceae	*Zanthoxylum bungeanum*	Stem, leaves, seeds, roots, bark	Liquid, powder	Alkaloids, flavonoids, terpenoids	x	x	Antioxidant activity	[307, 346]
Rutaceae	*Zanthoxylum alatum*	Branch	Rub, dust	Linalol	-	x	Antioxidant activity	[14, 347]
Rutaceae	*Murraya exotica L.*	Roots, leaves	Ground, decoction	Alkaloids, tannins, alkalis	-	x	Antioxidant activity	[296, 348]
Solanaceae	*Solanum melongena L.*	Roots, stem	Direct application	Flavonoids, tropane, glycoalkaloids	x	x	Antioxidant activity	[302, 349]
Solanaceae	*Solanum verbascifolium L.*	Whole plant	Decoction	Flavonoids	-	-	N/A	[302, 350]
Solanaceae	*Solanum nigrum, L.*	Leaves	Extract	N/A	-	-	Antioxidant activity	[219, 351]
Solanaceae	*Solanum surattense.*	Seeds	Steam from the seeds keep in the mouth	Alkaloids	-	-	N/A	[219, 352]
Solanaceae	*Hyoscyamus niger L.*	Leaves, seeds	Infusion, gargle	Alkaloids: atropine, tropane and scopolamine.	x	x	Antioxidant activity	[123, 298, 353]

Solanaceae	*Lycopersicum esculentum*	Fruits, leaves and flowers	N/A	Flavonoids, phenols	-	-	Antioxidant activity	[298, 354]
Solanaceae	*Hyoscyamus muticus*	Seeds, roots	N/A	Alkaloids	-	-	N/A	[298]
Thymelaeaceae	*Daphne mucronata*	Leaves, stem	N/A	Coumarins, flavonoids, triterpenoids	-	-	N/A	[298, 355]
Verbenaceae	*Vitex negundo, L.*	Leaves	Chewed	Flavonoids	x	x	Antioxidant activity, anti-inflammatory mechanism (COX and LOX)	[219, 356]
Vitaceae	*Cayratia albifolia C. L. Li*	Root, leaves	Chewed	N/A	-	-	N/A	[302]
Xanthorrhoeaceae	*Aloe vera L.*	Leaves	Decoction	Lignin, anthraquinones, saponins	-	x	Antioxidant activity, anti-inflammatory mechanism (COX and LOX)	[287, 288, 290]
Zygophyllaceae	*Tribulus terrestris, L.*	Fruit	Powder, massage	Alkaloids, tannins, saponins	x	-	N/A	[219, 357]

Zygophyllaceae	*Peganum harmala L.*	Seeds, fruit	Incense	Flavonoids, alkaloids, saponins, tannins, glycosides, terpenoids and steroids	x	-	Antioxidant activity	[249–251, 298]
Zygophyllaceae	*Fagonia olivieri*	Roots, fruits, stem, flowers	N/A	Flavonoids, alkaloids, tannins, saponins, terpenoids	-	x	Antioxidant activity, anti-inflammatory mechanism (COX and LOX)	[358–360]
Asteraceae	Emilia sonchifolia (L.)	Flowers	Paste	Alkaloids	x	x	N/A	[93, 361]
Asteraceae	Galinsoga parviflora Cav.	Leaves	Decoction	Polyphenols and flavonoids, phenolic acids.	-	x	Antioxidant activity, anti-inflammatory mechanism (COX and LOX)	[93, 183]
Asteraceae	Xanthium strumarium L	Leaves, roots	Juice	Sesquiterpenic lactones, glycosides,	x	x	Antioxidant activity	[93, 362]

				phenols, polyesterols				
Fabaceae	Mimosa pudica	Seeds	Powder	Alkaloids, flavonoids, glycosides, sterols, terpenoids, tannins and fatty acids.	x	-	Antioxidant activity	[93, 363]
Myricaceae	Myrica adenophora	Bark	Decoction	Flavonoids, triterpenoids, tannins, monoterpenoids, and benzenoids	x	x	Antioxidant activity	[93, 364]
Plantaginaceae	Plantago major L	Flowers	Paste	Polysaccharides, flavonoids, glycosides, terpenoids, alkaloids, organic acids.	x	x	Antioxidant activity	[93, 341]
Rubiaceae	Spermacoce neohispida Govaerts	Flowers	Paste	N/A	-	-	N/A	[93]
Rutaceae	Zanthoxylum oxyphyllum	Leaves, fruits	Juice	N/A	-	-	N/A	[93]

Sapindaceae	Sapindus mukorossi Gaert	Seeds	Powder	Saponins	-	-	N/A	[93, 365]
Solanaceae	Nicotiana plumbaginifolia Viv	Leaves	Paste	Alkaloids, saponin, tannin, flavonoids, phenolic compounds, steroids, terpenoids and carbohydrates.	-	-	N/A	[93, 366]
Solanaceae	Solanum aculeatissimum Jacq	Leaves, Fruits	Decoction	Steroidal saponins	-	-	N/A	[93, 294, 367]
Solanaceae	Solanum virginianum Dunal	Leaves, seeds	N/A	N/A	-	-	N/A	[294]
Urticaceae	Urtica parviflora Roxb	Fruits	Boiled juice	Alkaloids, polysaccharides, saponins, flavonoids, phenolic compounds, glycosides and tannins.	-	-	Antioxidant activity	[93, 368]

Arecaceae	Borassus flabellifer	Roots	Boiled, gargling	N/A	-	-	N/A	[294]
Verbenaceae	Vitex negundo L.	Leaves, bark	N/A	N/A	-	-	N/A	[294]

N/A: no information available

TABLE 5. OCEANIA

Family	Scientific name	Used part	Preparation	Phytochemicals	Analgesic effect	Anti-inflammatory effect	Mechanism of action	Ref.
Euphorbiaceae	*Petalostigma pubescens*	Fruits, bark	Hold in the mouth	Saponins, phenolic compounds, flavonoids, triterpenoids, tannins and alkaloids	-	-	Antioxidant activity	[90, 369]
Euphorbiaceae	*Petalostigma quadriloculare*	Fruits, bark	N/A	Saponins, phenolic compounds, flavonoids, triterpenoids, tannins and alkaloids	-	-	Antioxidant activity	[90, 369]
Myoporaceae	*Eremophilia fraseri*	Leaves	N/A	Diterpenes, triterpenoids,	-	x	Antioxidant activity	[90, 370]

				phenylpropanoids, lignans, flavonoids				
Myrtaceae	*Melaleuca cajuputi*	Bark, leaves	Extract	Flavonoids, phenolic compounds	-	-	Antioxidant activity	[90, 371]
Rhamnaceae	*Ventilago viminalis*	Bark, roots	N/A	N/A	-	-	N/A	[90]
Rutaceae	*Geijera parviflora*	Leaves	N/A	Alkaloids, flavonoids	-	x	N/A	[90, 372]
Rutaceae	*Melicope vitoflora*	Bark	N/A	N/A	-	-	N/A	[90]
Sapindaceae	*Dodonaea viscosa*	Roots, leaves	N/A	Alkaloids, flavonoids, steroids, phenolics, saponins, tannins	x	x	Antioxidant activity	[90, 373]
Tiliaceae	*Grewia retusifolia*	Fruit, roots, leaves	N/A	N/A	-	-	N/A	[90]
Asteraceae	*Acmella grandiflora*	Roots, flowers	Crushed	Spilanthol, acmellonate, tannins, flavonoids, and phenolic compounds	x	X	Antioxidant activity, GABA mechanism	[90, 374]

N/A: no information available

Figure 1. Relative frequency of global use of plants parts for the treatment of toothache.

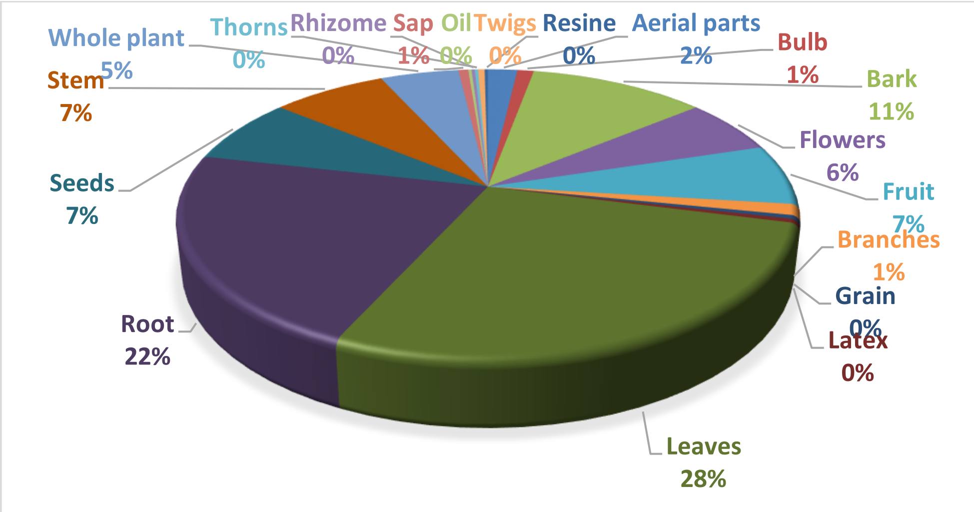
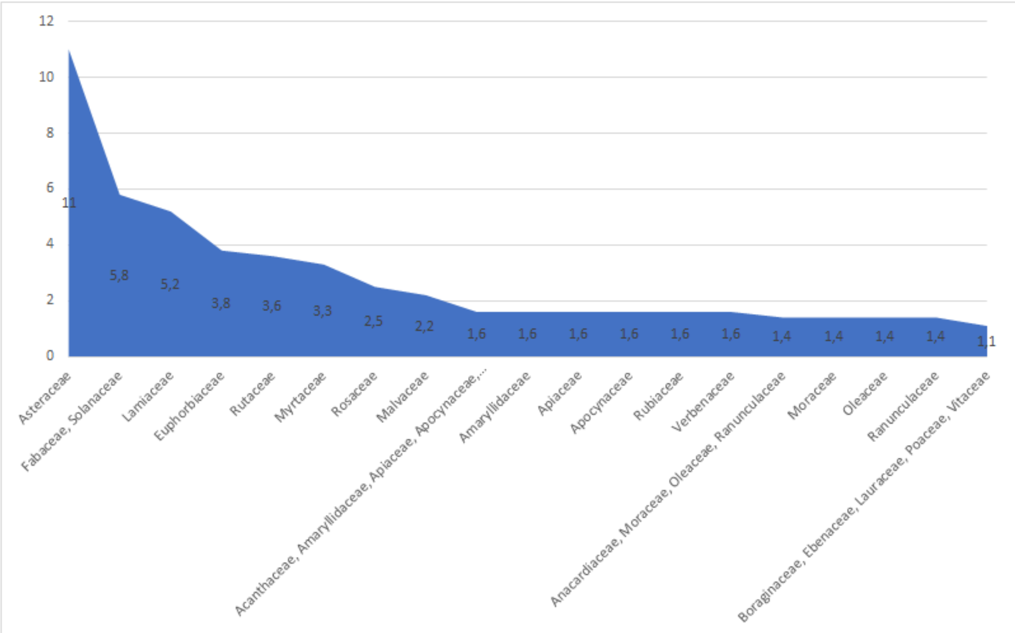


Figure 2. Families of medicinal plants globally used for the treatment of toothache.



REFERENCES

[1] Heir GM. The Emerging Specialty of Orofacial Pain. *J Indian Prosthodont Soc* 2013; 13: 140–141.

[2] Cohen LA, Bonito AJ, Akin DR, et al. Toothache pain: behavioral impact and self-care strategies. *Spec Care Dent* 2009; 29: 85–95.

[3] Megersa M, Jima TT, Goro KK. The Use of Medicinal Plants for the Treatment of Toothache in Ethiopia. *Evid Based Complement Alternat Med* 2019; 2019: 2645174.

[4] Palombo EA. Traditional Medicinal Plant Extracts and Natural Products with Activity against Oral Bacteria: Potential Application in the Prevention and Treatment of Oral Diseases. *Evid Based Complement Alternat Med* 2011; 2011: 680354.

[5] Sharifi-Rad M, Yılmaz YB, Antika G, et al. Phytochemical constituents, biological activities, and health-promoting effects of the genus Origanum. *Phytother Res* 2021; 35: 95–121.

[6] Ilic DV, Radicevic BA, Nedelcheva A, et al. Traditional dentistry knowledge among Serbs in several Balkan countries. *J Intercult Ethnopharmacol* 2017; 6: 223–233.

[7] Yadav R, Agarwala M. Phytochemical analysis of some medicinal plants. *J Phytol* 2011; 3: 10–14.

[8] Falzon CC, Balabanova A. Phytotherapy: An Introduction to Herbal Medicine. *Prim Care* 2017; 44: 217–227.

[9] Zhang L, Virgous C, Si H. Synergistic anti-inflammatory effects and mechanisms of combined phytochemicals. *J Nutr Biochem* 2019; 69: 19–30.

[10] B.K. Tiwari, Nigel P. Bruton, Charles S. Brennan. *Handbook of Plant Food Phytochemicals: Sources, Stability and Extraction*. 2013.

[11] Prakash Bhanu. *Functional and Preservative Properties of Phytochemicals*. 1st ed. Elsevier, 2020.

[12] Mahmood A, Mahmood A, Malik RN, et al. Indigenous knowledge of medicinal plants from Gujranwala district, Pakistan. *J Ethnopharmacol* 2013; 148: 714–723.

[13] Kunwar RM, Nepal BK, Kshhetri HB, et al. Ethnomedicine in Himalaya: a case study from Dolpa, Humla, Jumla and Mustang districts of Nepal. *J Ethnobiol Ethnomed* 2006; 2: 27.

[14] Farooq A, Amjad MS, Ahmad K, et al. Ethnomedicinal knowledge of the rural communities of Dhirkot, Azad Jammu and Kashmir, Pakistan. *J Ethnobiol Ethnomed* 2019; 15: 45.

[15] Luna-Vázquez FJ, Ibarra-Alvarado C, Rojas-Molina A, et al. Vasodilator compounds derived from plants and their mechanisms of action. *Molecules* 2013; 18: 5814–5857.

[16] Liu RH. Potential synergy of phytochemicals in cancer prevention: mechanism of action. *J Nutr* 2004; 134: 3479S-3485S.

[17] Benzie IF, Choi SW. Antioxidants in food: content, measurement, significance, action, cautions, caveats, and research needs. *Adv Food Nutr Res* 2014; 71: 1–53.

[18] Premkumar LS. Transient receptor potential channels as targets for phytochemicals. *ACS Chem Neurosci* 2014; 5: 1117–1130.

[19] Johnston GAR, Hanrahan JR, Chebib M, et al. Modulation of ionotropic GABA receptors by natural products of plant origin. *Adv Pharmacol* 2006; 54: 285–316.

[20] Hanrahan JR, Chebib M, Johnston GAR. Interactions of flavonoids with ionotropic GABA receptors. *Adv Pharmacol* 2015; 72: 189–200.

[21] Tasneem S, Liu B, Li B, et al. Molecular pharmacology of inflammation: Medicinal plants as anti-inflammatory agents. *Pharmacol Res* 2019; 139: 126–140.

[22] Iseghohi SO. A Review of the Uses and Medicinal Properties of Dennettia tripetala (Pepperfruit). *Med Sci Basel* 2015; 3: 104–111.

[23] Nilius B, Flockerzi V. *Mammalian Transient Receptor Potential (TRP) Cation Channels.* Handb Exp Pharmacol, 2014. Epub ahead of print 2014. DOI: 10.1007/978-3-319-05161-1.

[24] Arulselvan P, Fard MT, Tan WS, et al. Role of Antioxidants and Natural Products in Inflammation. *Oxid Med Cell Longev* 2016; 2016: 5276130.

[25] Becker EM, Nissen LR, Skibsted LH. Antioxidant evaluation protocols: Food quality or health effects. *Eur Food Res Technol* 2004; 219: 561–571.

[26] Tobore TO. Towards a Comprehensive Theory of Non-Cancer Acute and Chronic Pain Management: The Critical Role of Reactive Oxygen and Nitrogen Species in Pain, and Opioid Dependence, Addiction, Hyperalgesia, and Tolerance. *Adv Redox Res* 2021; 2: 100003.

[27] Thannickal VJ, Fanburg BL. Reactive oxygen species in cell signaling. *Am J Physiol Lung Cell Mol Physiol* 2000; 279: L1005–L1028.

[28] Federico A, Morgillo F, Tuccillo C, et al. Chronic inflammation and oxidative stress in human carcinogenesis. *Int J Cancer* 2007; 121: 2381–2386.

[29] Hussain SP, Hofseth LJ, Harris CC. Radical causes of cancer. *Nat Rev Cancer* 2003; 3: 276–285.

[30] Tang SY, Halliwell B. Medicinal plants and antioxidants: what do we learn from cell culture and Caenorhabditis elegans studies? *Biochem Biophys Res Commun* 2010; 394: 1–5.

[31] Chanda S, Dave R. In vitro models for antioxidant activity evaluation and some medicinal plants possessing antioxidant properties: An overview. *Afr J Microbiol Res* 2009; 3: 981–996.

[32] Kasote DM, Katyare SS, Hegde MV, et al. Significance of Antioxidant Potential of Plants and its Relevance to Therapeutic Applications. *Int J Biol Sci* 2015; 11: 982–991.

[33] Little JW, Doyle T, Salvemini D. Reactive nitroxidative species and nociceptive processing: determining the roles for nitric oxide, superoxide, and peroxynitrite in pain. *Amino Acids* 2012; 42: 75–94.

[34] Grace PM, Gaudet AD, Staikopoulos V, et al. Nitroxidative Signaling Mechanisms in Pathological Pain. *Trends Neurosci* 2016; 39: 862–879.

[35] Salvemini D, Little JW, Doyle T, et al. Roles of reactive oxygen and nitrogen species in pain. *Free Radic Biol Med* 2011; 51: 951–966.

[36] Yeo JF, Ling SF, Tang N, et al. Antinociceptive effect of CNS peroxynitrite scavenger in a mouse model of orofacial pain. *Exp Brain Res* 2008; 184: 435–438.

[37] Bruno R, Ghiadoni L. Polyphenols, Antioxidants and the Sympathetic Nervous System. *Curr Pharm Des* 2018; 24: 130–139.

[38] Rokyta R, Holecek V, Pekárkova I, et al. Free radicals after painful stimulation are influenced by antioxidants and analgesics. *Neuro Endocrinol Lett* 2003; 24: 304–309.

[39] Boutros T, Chevet E, Metrakos P. Mitogen-Activated Protein (MAP) Kinase/MAP Kinase Phosphatase Regulation: Roles in Cell Growth, Death, and Cancer. *Pharmacol Rev* 2008; 60: 261–310.

[40] Tominaga M, Wada M, Masu M. Potentiation of capsaicin receptor activity by metabotropic ATP receptors as a possible mechanism for ATP-evoked pain and hyperalgesia. *Proc Natl Acad Sci U S A* 2001; 98: 6951–6956.

[41] Ruparel NB, Patwardhan AM, Akopian AN, et al. Homologous and heterologous desensitization of capsaicin and mustard oil responses utilize different cellular pathways in nociceptors. *Pain* 2008; 135: 271–279.

[42] Bautista DM, Movahed P, Hinman A, et al. Pungent products from garlic activate the sensory ion channel TRPA1. *Proc Natl Acad Sci U S A* 2005; 102: 12248–12252.

[43] Hossain MZ, Bakri MM, Yahya F, et al. The Role of Transient Receptor Potential (TRP) Channels in the Transduction of Dental Pain. *Int J Mol Sci* 2019; 20: 526.

[44] Uritu CM, Mihai CT, Stanciu GD, et al. Medicinal Plants of the Family Lamiaceae in Pain Therapy: A Review. *Pain Res Manag* 2018; 2018: 7801543.

[45] Goudet C, Magnaghi V, Landry M, et al. Metabotropic receptors for glutamate and GABA in pain. *Brain Res Rev* 2009; 60: 43–56.

[46] Enna SJ, McCarson KE. The Role of GABA in the Mediation and Perception of Pain. *Adv Pharmacol* 2006; 54: 1–27.

[47] Jasmin L, Rabkin SD, Granato A, et al. Analgesia and hyperalgesia from GABA-mediated modulation of the cerebral cortex. *Nature* 2003; 424: 316–320.

[48] Dubey S, Maity S, Singh M, et al. Phytochemistry, Pharmacology and Toxicology of Spilanthes acmella: A Review. *Adv Pharmacol Sci* 2013; 2013: 423750.

[49] Prachayasittikul V, Prachayasittikul S, Ruchirawat S, et al. High therapeutic potential of Spilanthes acmella: A review. *EXCLI J* 2013; 12: 291–312.

[50] Abdul Rahim R, Jayusman PA, Muhammad N, et al. Potential Antioxidant and Anti-Inflammatory Effects of Spilanthes acmella and Its Health Beneficial Effects: A Review. *Int J Environ Res Public Health* 2021; 18: 3532.

[51] Rondanelli M, Fossari F, Vecchio V, et al. Acmella oleracea for pain management. *Fitoterapia* 2020; 140: 104419.

[52] Barbosa AF, Carvalho MG de, Smith RE, et al. Spilanthol: occurrence, extraction, chemistry and biological activities. *Rev Bras Farmacogn* 2016; 26: 128–133.

[53] Julémont F, Dogné JM, Pirotte B, et al. Recent development in the field of dual COX / 5-LOX inhibitors. *Mini Rev Med Chem* 2004; 4: 633–638.

[54] Yahfoufi N, Alsadi N, Jambi M, et al. The Immunomodulatory and Anti-Inflammatory Role of Polyphenols. *Nutrients* 2018; 10: 1618.

[55] Martel-Pelletier J, Lajeunesse D, Reboul P, et al. Therapeutic role of dual inhibitors of 5-LOX and COX, selective and non-selective non-steroidal anti-inflammatory drugs. *Ann Rheum Dis* 2003; 62: 501–509.

[56] Leval X d, Julemont F, Delarge J, et al. New trends in dual 5-LOX/COX inhibition. *Curr Med Chem* 2002; 9: 941–962.

[57] Rao CV. Regulation of COX and LOX by curcumin. *Adv Exp Med Biol* 2007; 595: 213–226.

[58] Marefati N, Ghorani V, Shakeri F, et al. A review of anti-inflammatory, antioxidant, and immunomodulatory effects of Allium cepa and its main constituents. *Pharm Biol* 2021; 59: 287–302.

[59] Wilson EA, Demmig-Adams B. Antioxidant, anti-inflammatory, and antimicrobial properties of garlic and onions. *Nutr Food Sci* 2007; 37: 178–183.

[60] Rondanelli M, Fossari F, Vecchio V, et al. Clinical trials on pain lowering effect of ginger: A narrative review. *Phytother Res* 2020; 34: 2843–2856.

[61] Belščak-Cvitanović A, Durgo K, Huđek A, et al. Overview of polyphenols and their properties. In: Galanakis CM (ed) *Polyphenols: Properties, Recovery, and Applications*. Woodhead Publishing, 2018, pp. 3–44.

[62] Ferraz CR, Carvalho TT, Manchope MF, et al. Therapeutic Potential of Flavonoids in Pain and Inflammation: Mechanisms of Action, Pre-Clinical and Clinical Data, and Pharmaceutical Development. *Molecules* 2020; 25: 762.

[63] Rein MJ, Renouf M, Cruz-Hernandez C, et al. Bioavailability of bioactive food compounds: a challenging journey to bioefficacy. *Br J Clin Pharmacol* 2013; 75: 588–602.

[64] Lim W, Mudge KW, Vermeylen F. Effects of population, age, and cultivation methods on ginsenoside content of wild American ginseng (Panax quinquefolium). *J Agric Food Chem* 2005; 53: 8498–8505.

[65] Platel K, Srinivasan K. Bioavailability of Micronutrients from Plant Foods: An Update. *Crit Rev Food Sci Nutr* 2016; 56: 1608–1619.

[66] Sun X, Chen W, Dai W, et al. Piper sarmentosum Roxb.: A review on its botany, traditional uses, phytochemistry, and pharmacological activities. *J Ethnopharmacol* 2020; 263: 112897.

[67] Hewlings SJ, Kalman DS. Curcumin: A Review of Its Effects on Human Health. *Foods* 2017; 6: 92.

[68] Rayati F, Hajmanouchehri F, Najafi E. Comparison of anti-inflammatory and analgesic effects of Ginger powder and Ibuprofen in postsurgical pain model: A randomized, double-blind, case-control clinical trial. *Dent Res J Isfahan* 2017; 14: 1–7.

[69] Grzanna R, Lindmark L, Frondoza CG. Ginger--an herbal medicinal product with broad anti-inflammatory actions. *J Med Food* 2005; 8: 125–132.

[70] Ali BH, Blunden G, Tanira MO, et al. Some phytochemical, pharmacological and toxicological properties of ginger (Zingiber officinale Roscoe): a review of recent research. *Food Chem Toxicol* 2008; 46: 409–420.

[71] Chrubasik S, Pittler MH, Roufogalis BD. Zingiberis rhizoma: a comprehensive review on the ginger effect and efficacy profiles. *Phytomedicine* 2005; 12: 684–701.

[72] Khumalo GP, Van Wyk BE, Feng Y, et al. A review of the traditional use of southern African medicinal plants for the treatment of inflammation and inflammatory pain. *J Ethnopharmacol* 2022; 283: 114436.

[73] Mao QQ, Xu XY, Cao SY, et al. Bioactive Compounds and Bioactivities of Ginger (Zingiber officinale Roscoe). *Foods* 2019; 8: 185.

[74] Tjendraputra E, Tran VH, Liu-Brennan D, et al. Effect of ginger constituents and synthetic analogues on cyclooxygenase-2 enzyme in intact cells. *Bioorg Chem* 2001; 29: 156–163.

[75] Flynn DL, Rafferty MF, Boctor AM. Inhibition of human neutrophil 5-lipoxygenase activity by gingerdione, shogaol, capsaicin and related pungent compounds. *Prostaglandins Leukot Med* 1986; 24: 195–198.

[76] Gras A, Parada M, Rigat M, et al. Folk medicinal plant mixtures: Establishing a protocol for further studies. *J Ethnopharmacol* 2018; 214: 244–273.

[77] Che CT, Wang ZJ, Chow MSS, et al. Herb-Herb Combination for Therapeutic Enhancement and Advancement: Theory, Practice and Future Perspectives. *Molecules* 2013; 18: 5125–5141.

[78] Vijayalakshmi G, Adinarayana M, Jayaprakash Rao P. A synergistic approach to kinetic and mechanistic studies of regeneration of β-carotene from tert-butoxyl radical induced β-carotene radical cation by chlorogenic acid. *Int J Pharm Life Sci* 2014; 5: 942–950.

[79] Rather MA, Bhat BA, Qurishi MA. Multicomponent phytotherapeutic approach gaining momentum: Is the ‘one drug to fit all’ model breaking down?. *Phytomedicine* 2013; 21: 1–14.

[80] Allescher HD. Functional dyspepsia--a multicausal disease and its therapy. *Phytomedicine* 2006; 13 Suppl 5: 2–11.

[81] Isola G, Matarese M, Ramaglia L, et al. Efficacy of a drug composed of herbal extracts on postoperative discomfort after surgical removal of impacted mandibular third molar: a randomized, triple-blind, controlled clinical trial. *Clin Oral Investig* 2019; 23: 2443–2453.

[82] Szyszkowska A, Koper J, Szczerba J, et al. The use of medicinal plants in dental treatment. *Herba Pol* 2010; 56: 97–107.

[83] Cruz Martínez C, Diaz Gómez M, Oh MS. Use of traditional herbal medicine as an alternative in dental treatment in Mexican dentistry: a review. *Pharm Biol* 2017; 55: 1992–1998.

[84] Campos-Vega R, Oomah BD. Chemistry and classification of phytochemicals. In: Tiwari BK, Brunton NP, Brennan CS (eds) *Handbook of Plant Food Phytochemicals*. John Wiley & Sons Ltd, 2013, pp. 5–48.

[85] Mark S. Meskin, Wayne R. Bidlack, Audra J. Davies, et al. *Phytochemicals: Mechanisms of Action*. 1st ed. 2003.

[86] Koeberle A, Werz O. Natural products as inhibitors of prostaglandin E2 and pro-inflammatory 5-lipoxygenase-derived lipid mediator biosynthesis. *Biotechnol Adv* 2018; 36: 1709–1723.

[87] Koeberle A, Northoff H, Werz O. Curcumin blocks prostaglandin E2 biosynthesis through direct inhibition of the microsomal prostaglandin E2 synthase-1. *Mol Cancer Ther* 2009; 8: 2348–2355.

[88] Samuelsson B, Morgenstern R, Jakobsson PJ. Membrane prostaglandin E synthase-1: a novel therapeutic target. *Pharmacol Rev* 2007; 59: 207–224.

[89] Knights KM, Mangoni AA, Miners JO. Defining the COX inhibitor selectivity of NSAIDs: implications for understanding toxicity. *Expert Rev Clin Pharmacol* 2010; 3: 769–776.

[90] Cock I. *Medicinal and aromatic plants – Australia.* Ethnopharmacology. 2011.

[91] Cordell GA. Biodiversity and drug discovery--a symbiotic relationship. *Phytochemistry* 2000; 55: 463–480.

[92] Harding K, Benson EE, Nunes E da C, et al. Can Biospecimen Science Expedite the Ex Situ Conservation of Plants in Megadiverse Countries? A Focus on the Flora of Brazil. *Crit Rev Plant Sci* 2013; 32: 411–444.

[93] Jamir K, Seshagirirao K, Meitei MD. Indigenous oral knowledge of wild medicinal plants from the Peren district of Nagaland, India in the Indo Burma hot-spot. *Acta Ecol Sin* 2021; 18.

[94] Desta KT, Kim GS, Abd El-Aty AM, et al. Flavone polyphenols dominate in Thymus schimperi Ronniger: LC-ESI-MS/MS characterization and study of anti-proliferative effects of plant extract on AGS and HepG2 cancer cells. *J Chromatogr B Analyt Technol Biomed Life Sci* 2017; 1053: 1–8.

[95] Efferth T, Koch E. Complex interactions between phytochemicals. The multi-target therapeutic concept of phytotherapy. *Curr Drug Targets* 2011; 12: 122–132.

[96] Manworren RC. Multimodal pain management and the future of a personalized medicine approach to pain. *AORN J* 2015; 101: 308–318.

[97] Young A, Buvanendran A. Recent advances in multimodal analgesia. *Anesthesiol Clin* 2012; 30: 91–100.

[98] Helander EM, Menard BL, Harmon CM, et al. Multimodal Analgesia, Current Concepts, and Acute Pain Considerations. *Curr Pain Headache Rep* 2017; 21: 3.

[99] Gavarić N, Kladar N, Mišan A, et al. Postdistillation waste material of thyme (Thymus vulgaris L., Lamiaceae) as a potential source of biologically active compounds. *Ind Crops Prod* 2015; 74: 457–464.

[100] Al-Snafi A. Chemical constituents and pharmacological effects of Asclepias curassavica – A review. *Asian J Pharm Res* 2015; 5: 83–87.

[101] Rezende CM, Fraga SRG. Chemical and aroma determination of the pulp and seeds of murici (Byrsonima crassifolia L.). *J Braz Chem Soc* 2003; 14: 425–428.

[102] Maldini M, Sosa S, Montoro P, et al. Screening of the topical anti-inflammatory activity of the bark of Acacia cornigera Willdenow, Byrsonima crassifolia Kunth, Sweetia panamensis Yakovlev and the leaves of Sphagneticola trilobata Hitchcock. *J Ethnopharmacol* 2009; 122: 430–433.

[103] Otunola GA, Oloyede OB, Oladiji AT, et al. Comparative analysis of the chemical composition of three spices – Allium sativum L. Zingiber officinale Rosc. and Capsicum frutescens L. commonly consumed in Nigeria. *Afr J Biotechnol* 2010; 9: 6927–6931.

[104] Peraza-Sánchez SR, Cen-Pacheco F, Noh-Chimal A, et al. Leishmanicidal evaluation of extracts from native plants of the Yucatan peninsula. *Fitoterapia* 2007; 78: 315–318.

[105] Hernández I, Márquez L, Martínez I, et al. Anti-inflammatory effects of ethanolic extract and alkamides-derived from Heliopsis longipes roots. *J Ethnopharmacol* 2009; 124: 649–652.

[106] Srianthie D, Udayangani DN, Chamari H. Antioxidant, antibacterial and anti-inflammatory potential of the aqueous extract of the raw leaves of sri lankan variety of persea americana miller (avocado). *Int J Ayurveda Pharma Res* 2020; 8: 1–11.

[107] Chaves OS, Gomes RA, Tomaz AC de A, et al. Secondary Metabolites from Sida rhombifolia L. (Malvaceae) and the Vasorelaxant Activity of Cryptolepinone. *Molecules* 2013; 18: 2769–2777.

[108] Sabandar CW, Ahmat N, Jaafar FM, et al. Medicinal property, phytochemistry and pharmacology of several Jatropha species (Euphorbiaceae): a review. *Phytochemistry* 2013; 85: 7–29.

[109] Pudji A. The ability of anti-inflammatory jatropha curcas leaf extract at cox-2 expression on monocytes were exposed LPS. *UNEJ E-Proceeding* 2017; 154–157.

[110] Shankland WE 2nd. Four common herbs seen in dental practice: properties and potential adverse effects. *Cranio* 2009; 27: 118–124.

[111] Kim S, Kim DB, Jin W, et al. Comparative studies of bioactive organosulphur compounds and antioxidant activities in garlic (Allium sativum L.), elephant garlic (Allium ampeloprasum L.) and onion (Allium cepa L.). *Nat Prod Res* 2018; 32: 1193–1197.

[112] Salehi B, Valussi M, Morais-Braga MFB, et al. Tagetes spp. Essential Oils and Other Extracts: Chemical Characterization and Biological Activity. *Molecules* 2018; 23: 2847.

[113] Céspedes CL, Avila JG, Martínez A, et al. Antifungal and antibacterial activities of Mexican tarragon (Tagetes lucida). *J Agric Food Chem* 2006; 54: 3521–3527.

[114] Vergara Barragán E, Bach H, Meza-Reyes S, et al. Bioactivities of Flavonoids from Lopezia racemosa. *BioMed Res Int* 2019; 2019: 3286489.

[115] Cruz Paredes C, Bolívar Balbás P, Gómez-Velasco A, et al. Antimicrobial, antiparasitic, anti-inflammatory, and cytotoxic activities of Lopezia racemosa. *ScientificWorldJournal* 2013; 2013: 237438.

[116] Srinath J. Therapeutic Potential of Spilanthes acmella – A Dental Note. *Int J Pharm Sci Rev Res* 2014; 151–153.

[117] Pareek S, Sagar NA, Sharma S, et al. Onion (Allium cepa L.). In: Yahia EM (ed) *Fruit and Vegetable Phytochemicals*. Chichester, UK: John Wiley & Sons, Ltd, 2017, pp. 1145–1162.

[118] Babotă M, Mocan A, Vlase L, et al. Phytochemical Analysis, Antioxidant and Antimicrobial Activities of Helichrysum arenarium (L.) Moench. and Antennaria dioica (L.) Gaertn. Flowers. *Molecules* 2018; 23: 409.

[119] Gafrikova M, Galova E, Sevcovicova A, et al. Extract from Armoracia rusticana and Its Flavonoid Components Protect Human Lymphocytes against Oxidative Damage Induced by Hydrogen Peroxide. *Molecules* 2014; 19: 3160–3172.

[120] Singh J, Upadhyay AK, Bahadur A, et al. Antioxidant phytochemicals in cabbage (Brassica oleracea L. var. capitata). *Sci Hortic* 2006; 108: 233–237.

[121] Singh N, Rao AS, Nandal A, et al. Phytochemical and pharmacological review of Cinnamomum verum J. Presl-a versatile spice used in food and nutrition. *Food Chem* 2021; 338: 127773.

[122] Dezsi Ș., Bădărău AS, Bischin C, et al. Antimicrobial and Antioxidant Activities and Phenolic Profile of Eucalyptus globulus Labill. and Corymbia ficifolia (F. Muell.) K.D. Hill & L.A.S. Johnson Leaves. *Molecules* 2015; 20: 4720–4734.

[123] Al-Snafi A. Therapeutic importance of Hyoscyamus species grown in Iraq (Hyoscyamus albus, Hyoscyamus niger and Hyoscyamus reticulates)-A review. *IOSR J Pharm* 2018; 8: 18–32.

[124] Singh O, Khanam Z, Misra N, et al. Chamomile (Matricaria chamomilla L.): An overview. *Pharmacogn Rev* 2011; 5: 82–95.

[125] Roby MHH, Sarhan MA, Selim KA-H, et al. Antioxidant and antimicrobial activities of essential oil and extracts of fennel (Foeniculum vulgare L.) and chamomile (Matricaria chamomilla L.). *Ind Crops Prod* 2013; 44: 437–445.

[126] Cheikh-Rouhou S, Besbes S, Hentati B, et al. Nigella sativa L.: Chemical composition and physicochemical characteristics of lipid fraction. *Food Chem* 2007; 101: 673–681.

[127] Beara IN, Lesjak MM, Orčić DZ, et al. Comparative analysis of phenolic profile, antioxidant, anti-inflammatory and cytotoxic activity of two closely-related Plantain species: Plantago altissima L. and Plantago lanceolata L. *LWT - Food Sci Technol* 2012; 47: 64–70.

[128] Beara IN, Orcić DZ, Lesjak MM, et al. Liquid chromatography/tandem mass spectrometry study of anti-inflammatory activity of Plantain (Plantago L.) species. *J Pharm Biomed Anal* 2010; 52: 701–706.

[129] Afonso AF, Pereira OR, Fernandes Â, et al. Phytochemical Composition and Bioactive Effects of Salvia africana, Salvia officinalis 'Icterina' and Salvia mexicana Aqueous Extracts. *Molecules* 2019; 24: 4327.

[130] Ghasemian M, Owlia S, Owlia MB. Review of Anti-Inflammatory Herbal Medicines. *Adv Pharmacol Sci* 2016; 2016: 9130979.

[131] Kaur K, Kaushal S. Phytochemistry and pharmacological aspects of Syzygium aromaticum: A review. *J Pharmacogn Phytochem* 2019; 8: 398–406.

[132] Déciga-Campos M, Beltrán-Villalobos KL, Aguilar-Mariscal H, et al. Synergistic Herb-Herb Interaction of the Antinociceptive and Anti-Inflammatory Effects of Syzygium aromaticum and Rosmarinus officinalis Combination. *Evid Based Complement Alternat Med* 2021; 2021: 8916618.

[133] Kisiel W, Barszcz B. Further sesquiterpenoids and phenolics from Taraxacum officinale. *Fitoterapia* 2000; 71: 269–273.

[134] Moldovan ML, Carpa R, Fizeșan I, et al. Phytochemical Profile and Biological Activities of Tendrils and Leaves Extracts from a Variety of Vitis vinifera L. *Antioxidants* 2020; 9: 373.

[135] Nicolì F, Negro C, Vergine M, et al. Evaluation of Phytochemical and Antioxidant Properties of 15 Italian Olea europaea L. Cultivar Leaves. *Molecules* 2019; 24: 1998.

[136] Günaydin K, Savci S. Phytochemical studies on Ruta chalepensİs (Lam.) Lamarck. *Nat Prod Res* 2005; 19: 203–210.

[137] Badgujar SB, Patel VV, Bandivdekar AH. Foeniculum vulgare Mill: a review of its botany, phytochemistry, pharmacology, contemporary application, and toxicology. *Biomed Res Int* 2014; 2014: 842674.

[138] Choi EM, Hwang JK. Antiinflammatory, analgesic and antioxidant activities of the fruit of Foeniculum vulgare. *Fitoterapia* 2004; 75: 557–565.

[139] Maroyi A. Euclea undulata Thunb.: Review of its botany, ethnomedicinal uses, phytochemistry and biological activities. *Asian Pac J Trop Med* 2017; 10: 1030–1036.

[140] Tefera BN, Kim YD. Ethnobotanical study of medicinal plants in the Hawassa Zuria District, Sidama zone, Southern Ethiopia. *J Ethnobiol Ethnomed* 2019; 15: 25.

[141] Buyinza D, Chalo DM, Derese S, et al. Flavonoids and Isoflavonoids of Millettia dura and Millettia ferruginea: Phytochemical review and chemotaxonomic values. *Biochem Syst Ecol* 2020; 91: 104053.

[142] Wondimieneh S, Asres K. In Vivo Anti-inflammatory and Antinociceptive Activities of Salvia nilotica and Rosa abyssinica. *Ethiop Pharm J* 2008; 26: 75–82.

[143] Itou RDGE, Sanogo R, Ossibi AWE, et al. Anti-Inflammatory and Analgesic Effects of Aqueous Extract of Stem Bark of Ceiba pentandra Gaertn. *Pharmacol Pharm* 2014; 05: 1113–1118.

[144] Issa TO, Mohamed YS, Yagi S, et al. Ethnobotanical investigation on medicinal plants in Algoz area (South Kordofan), Sudan. *J Ethnobiol Ethnomed* 2018; 14: 31.

[145] Dirar AI, Adhikari-Devkota A, Kunwar RM, et al. Genus Blepharis (Acanthaceae): A review of ethnomedicinally used species, and their phytochemistry and pharmacological activities. *J Ethnopharmacol* 2021; 265: 113255.

[146] Tesfaye S, Belete A, Engidawork E, et al. Ethnobotanical Study of Medicinal Plants Used by Traditional Healers to Treat Cancer-Like Symptoms in Eleven Districts, Ethiopia. *Evid Based Complement Alternat Med* 2020; 2020: 7683450.

[147] Jimoh MO, Afolayan AJ, Lewu FB. Antioxidant and phytochemical activities of Amaranthus caudatus L. harvested from different soils at various growth stages. *Sci Rep* 2019; 9: 12965.

[148] Ashu Agbor M, Naidoo S. Ethnomedicinal Plants Used by Traditional Healers to Treat Oral Health Problems in Cameroon. *Evid Based Complement Alternat Med* 2015; 2015: 649832.

[149] Pareek S, Sagar N, Sharma S, et al. Onion (Allium cepa L.): Chemistry and Human Health. In: *Fruit and Vegetable Phytochemicals*. 2017, pp. 1145–1162.

[150] Elgorashi EE, McGaw LJ. African plants with in vitro anti-inflammatory activities: A review. *South Afr J Bot* 2019; 126: 142–169.

[151] Matata DZ, Moshi MJ, Machumi F, et al. Isolation of a new cytotoxic compound, 3-((Z)-heptadec-14-enyl) benzene - 1-ol from Rhus natalensis root extract. *Phytochem Lett* 2020; 36: 120–126.

[152] Kidane B, van Andel T, van der Maesen LJG, et al. Use and management of traditional medicinal plants by Maale and Ari ethnic communities in southern Ethiopia. *J Ethnobiol Ethnomed* 2014; 10: 46.

[153] Alqasoumi SI, Basudan OA, Alam P, et al. Antioxidant study of flavonoid derivatives from the aerial parts of Rhus natalensis growing in Saudi Arabia. *Pak J Pharm Sci* 2016; 29: 97–103.

[154] Martins MR, Arantes S, Candeias F, et al. Antioxidant, antimicrobial and toxicological properties of Schinus molle L. essential oils. *J Ethnopharmacol* 2014; 151: 485–492.

[155] Bringmann G, Rüdenauer S, Irmer A, et al. Antitumoral and antileishmanial dioncoquinones and ancistroquinones from cell cultures of Triphyophyllum peltatum (Dioncophyllaceae) and Ancistrocladus abbreviatus (Ancistrocladaceae). *Phytochemistry* 2008; 69: 2501–2509.

[156] Zougagh S, Belghiti A, Rochd T, et al. Medicinal and Aromatic Plants Used in Traditional Treatment of the Oral Pathology: The Ethnobotanical Survey in the Economic Capital Casablanca, Morocco (North Africa). *Nat Prod Bioprospect* 2019; 9: 35–48.

[157] Khalil N, Bishr M, Desouky S, et al. Ammi Visnaga L., a Potential Medicinal Plant: A Review. *Molecules* 2020; 25: 301.

[158] Laribi B, Kouki K, M’Hamdi M, et al. Coriander (Coriandrum sativum L.) and its bioactive constituents. *Fitoterapia* 2015; 103: 9–26.

[159] Tugume P, Kakudidi EK, Buyinza M, et al. Ethnobotanical survey of medicinal plant species used by communities around Mabira Central Forest Reserve, Uganda. *J Ethnobiol Ethnomed* 2016; 12: 5.

[160] Woode E, Ansah C, Ainooson GK, et al. Anti-inflammatory and antioxidant properties of the root extract of Carissa edulis (forsk.) Vahl (apocynaceae). *J Sci Technol Ghana* 2007; 27: 5–15.

[161] Farkhondeh T, Kianmehr M, Kazemi T, et al. Toxicity effects of Nerium oleander, basic and clinical evidence: A comprehensive review. *Hum Exp Toxicol* 2020; 39: 773–784.

[162] Shafiq Y, Naqvi SBS, Rizwani GH, et al. A mechanistic study on the inhibition of bacterial growth and inflammation by Nerium oleander extract with comprehensive in vivo safety profile. *BMC Complement Med Ther* 2021; 21: 135.

[163] Megersa M, Asfaw Z, Kelbessa E, et al. An ethnobotanical study of medicinal plants in Wayu Tuka District, East Welega Zone of Oromia Regional State, West Ethiopia. *J Ethnobiol Ethnomed* 2013; 9: 68.

[164] Wangteeraprasert R, Lipipun V, Gunaratnam M, et al. Bioactive Compounds from Carissa spinarum. *Phytother Res* 2012; 26: 1496–1499.

[165] Punia DP. A review on varieties of Arka Calotropis procera (AITON) Dryand and Calotropis gigantea (L.) Dryand. *Global J Res Med Plants & Indigen Med* 2013; 2: 392–400.

[166] Ghosh PK, Bhattacharjee P, Mitra S, et al. Physicochemical and Phytochemical Analyses of Copra and Oil of Cocos nucifera L. (West Coast Tall Variety). *Int J Food Sci* 2014; 2014: 310852.

[167] Lima EB, Sousa CN, Meneses LN, et al. Cocos nucifera (L.) (Arecaceae): A phytochemical and pharmacological review. *Braz J Med Biol Res* 2015; 48: 953–964.

[168] Chithra MA, Ijinu TP, Kharkwal H, et al. Phenolic rich Cocos nucifera inflorescence extract ameliorates inflammatory responses in LPS-stimulated RAW264.7 macrophages and toxin-induced murine models. *Inflammopharmacology* 2020; 28: 1073–1089.

[169] Teklay A, Abera B, Giday M. An ethnobotanical study of medicinal plants used in Kilte Awulaelo District, Tigray Region of Ethiopia. *J Ethnobiol Ethnomed* 2013; 9: 65.

[170] Misganaw D, Sahile S, Negash W. Invitro antimicrobial effects of gomphocarpus purpurascens a. rich against standard and clinically isolated microorganisms. *Glob J Sci Res* 2019; 7: 121–136.

[171] Hassan H, Ahmadu AA, Hassan AS. Analgesic and anti-inflammatory activities of Asparagus africanus root extract. *Afr J Tradit Complement Altern Med* 2007; 5: 27–31.

[172] Abera B. Medicinal plants used in traditional medicine by Oromo people, Ghimbi District, Southwest Ethiopia. *J Ethnobiol Ethnomed* 2014; 10: 40.

[173] Yimer T, Birru EM, Adugna M, et al. Evaluation of Analgesic and Anti-Inflammatory Activities of 80% Methanol Root Extract of Echinops kebericho M. (Asteraceae). *J Inflamm Res* 2020; 13: 647–658.

[174] Liu X, Wang X, Chen Z, et al. De novo assembly and comparative transcriptome analysis: novel insights into terpenoid biosynthesis in Chamaemelum nobile L. *Plant Cell Rep* 2019; 38: 101–116.

[175] Msaada K, Salem N, Bachrouch O, et al. Chemical Composition and Antioxidant and Antimicrobial Activities of Wormwood (*Artemisia absinthium* L.) Essential Oils and Phenolics. *J Chem* 2015; 2015: 1–12.

[176] Bouabid K, Lamchouri F, Toufik H, et al. Phytochemical investigation, in vitro and in vivo antioxidant properties of aqueous and organic extracts of toxic plant: Atractylis gummifera L. *J Ethnopharmacol* 2020; 253: 112640.

[177] Ngueguim TF, Djouwoug Noussi C, Donfack JH, et al. Acute and sub-acute toxicity of a lyophilised aqueous extract of the aerial part of Spilanthes africana Delile in rats. *J Ethnopharmacol* 2015; 172: 145–154.

[178] Okunade AL. Ageratum conyzoides L. (Asteraceae). *Fitoterapia* 2002; 73: 1–16.

[179] Mohammed T, Teshale C. Preliminary phytochemical screening and evaluation of antibacterial activity of Dichrocepala integrifolia (L.f) O. kuntze. *J Intercult Ethnopharmacol* 2012; 1: 30–34.

[180] Uthpala TGG, Navaratne SB. Acmella oleracea Plant; Identification, Applications and Use as an Emerging Food Source – Review. *Food Rev Int* 2021; 37: 399–414.

[181] Letha N, Ganesan K, Kumar S, et al. Studies on phytochemical screening and in vitro antioxidant activity of Ethiopian indigenous medicinal plants, Artemisia abyssinica Sch.Bip. Ex A.Rich. *World J Pharm Res* 2016; 5: 1048–1058.

[182] Tariku Y, Hymete A, Hailu A, et al. In vitro evaluation of antileishmanial activity and toxicity of essential oils of Artemisia absinthium and Echinops kebericho. *Chem Biodivers* 2011; 8: 614–623.

[183] Studzińska-Sroka E, Dudek-Makuch M, Chanaj-Kaczmarek J, et al. Anti-inflammatory Activity and Phytochemical Profile of Galinsoga Parviflora Cav. *Molecules* 2018; 23: 2133.

[184] Ali S, Zameer S, Yaqoob M. Ethnobotanical, phytochemical and pharmacological properties of Galinsoga parviflora (Asteraceae): A review. *Trop J Pharm Res* 2017; 16: 3023–3033.

[185] Albejo B, Endale M, Kibret B, et al. Phytochemical investigation and antimicrobial activity of leaves extract of Vernonia auriculifera Hiern. *J Pharm Pharmacogn Res* 2015; 3: 141–147.

[186] Speroni E, Cervellati R, Innocenti G, et al. Anti-inflammatory, anti-nociceptive and antioxidant activities of Balanites aegyptiaca (L.) Delile. *J Ethnopharmacol* 2005; 98: 117–125.

[187] Traore KT, Ouédraogo N, Belemnaba L, et al. Anti-inflammatory and analgesic activities of extracts from Balanites aegyptiaca L. Delile (Balanitaceae) root bark: Plant used against liver diseases in Bukina Faso. *Afr J Pharm Pharmacol* 2019; 13: 322–329.

[188] Compaoré M, Lamien-Meda A, Mogoşan C, et al. Antioxidant, diuretic activities and polyphenol content of Stereospermum kunthianum Cham. (Bignoniaceae). *Nat Prod Res* 2011; 25: 1777–1788.

[189] Ogundajo A, Ashafa AT. Phytochemical Compositions and In vitro Assessments of Antioxidant and Antidiabetic Potentials of Fractions from Ehretia cymosa Thonn. *Pharmacogn Mag* 2017; 13: S470–S480.

[190] Yismaw YE, Abdelwuhab M, Ambikar DB, et al. Phytochemical and Antiulcer Activity Screening of Seed Extract of Cordia africana Lam (Boraginaceae) in Pyloric Ligated Rats. *Clin Pharmacol Adv Appl* 2020; 12: 67–73.

[191] Riazullah, Hussain I, Badrullah. Phytochemical and anti-microbial activity of Lepidium sativum L. *J Med Plants Res* 2012; 6: 4358–4361.

[192] Maroyi A. Boscia salicifolia: review of its botany, medicinal uses, phytochemistry and biological activities. *J Pharm Sci* 2019; 11: 3055–3060.

[193] Tekulu GH, Hiluf T, Brhanu H, et al. Anti-inflammatory and anti-nociceptive property of Capparis tomentosa Lam. root extracts. *J Ethnopharmacol* 2020; 253: 112654.

[194] Abdulaziz Al-Hamoud G, Saud Orfali R, Sugimoto S, et al. Four New Flavonoids Isolated from the Aerial Parts of Cadaba rotundifolia Forssk. (Qadab). *Molecules* 2019; 24: 2167.

[195] Martial N, Dah-Nouvlessounon D, Christine N tcha, et al. Phytochemistry and biological activities of crateva adansonii extracts. *Int J Pharm Pharm Sci* 2018; 10: 62–67.

[196] Zunjar V, Mammen D, Trivedi B, et al. Pharmacognostic, Physicochemical and Phytochemical Studies on Carica papaya Linn. Leaves. *Pharmacogn J* 2011; 3: 5–8.

[197] Kashyap K, Sarkar P, Kalita MC, et al. A review on the widespread therapeutic application of the traditional herb Drymaria cordata. *Int J Pharma Bio Sci* 2014; 5: 696–705.

[198] Kokanova-Nedialkova Z, Nedialkov PT, Nikolov SD. The Genus Chenopodium: Phytochemistry, Ethnopharmacology and Pharmacology. *Pharmacogn Rev* 2009; 3: 280–306.

[199] Kumar R, Mishra AK, Dubey NK, et al. Evaluation of Chenopodium ambrosioides oil as a potential source of antifungal, antiaflatoxigenic and antioxidant activity. *Int J Food Microbiol* 2007; 115: 159–164.

[200] Muriithi E, Bojase-Moleta G, Majinda RRT. Benzophenone derivatives from Garcinia livingstonei and their antioxidant activities. *Phytochem Lett* 2016; 18: 29–34.

[201] Yang H, Figueroa M, To S, et al. Benzophenones and biflavonoids from Garcinia livingstonei fruits. *J Agric Food Chem* 2010; 58: 4749–4755.

[202] Ashokkumar K. Gloriosa superba (L.): A Brief Review of its Phytochemical Properties and Pharmacology. *Int J Pharmacogn Phytochem Res* 2015; 7: 1190–1193.

[203] Arbab A. Review on anogeissus leiocarpus a potent african traditional drug. *Int J Res Pharm Chem* 2014; 4: 496–500.

[204] Okoli CO, Akah PA, Nwafor SV, et al. Anti-inflammatory activity of hexane leaf extract of Aspilia africana C.D. Adams. *J Ethnopharmacol* 2007; 109: 219–225.

[205] Alara OR, Abdurahman NH, Mudalip SKA, et al. Phytochemical and pharmacological properties of Vernonia amygdalina: A review. *J Chem Eng Ind Biotechnol* 2017; 2: 80–96.

[206] Kriplani P, Guarve K, Baghael US. Arnica montana L. – a plant of healing: review. *J Pharm Pharmacol* 2017; 69: 925–945.

[207] Fernandes JM, Cunha LM, Azevedo EP, et al. Kalanchoe laciniata and Bryophyllum pinnatum: an updated review about ethnopharmacology, phytochemistry, pharmacology and toxicology. *Rev Bras Farmacogn* 2019; 29: 529–558.

[208] Soh D, Bakang BT, Tchouboun EN, et al. New cucurbitane type triterpenes from Momordica foetida Schumach. (Cucurbitaceae). *Phytochem Lett* 2020; 38: 90–95.

[209] Guimarães R, Barros L, Carvalho AM, et al. Aromatic plants as a source of important phytochemicals: Vitamins, sugars and fatty acids in Cistus ladanifer, Cupressus lusitanica and Eucalyptus gunnii leaves. *Ind Crops Prod* 2009; 30: 427–430.

[210] Salih AM, Al-Qurainy F, Khan S, et al. Mass propagation of Juniperus procera Hoechst. Ex Endl. From seedling and screening of bioactive compounds in shoot and callus extract. *BMC Plant Biol* 2021; 21: 192.

[211] Ilodibia* CV, Ugwu RU, Okeke CU, et al. Phytochemical evaluation of various parts of Dracaena arborea Link. and Dracaena mannii Bak. *Afr J Plant Sci* 2015; 9: 287–292.

[212] Kilonzo M, Rubanza C, Richard U, et al. Antimicrobial activities and phytochemical analysis of extracts from Ormocarpum trichocarpum (Taub.) and Euclea divinorum (Hiern) used as traditional medicine in Tanzania. *Tanzan J Health Res* 2019; 21: 1–12.

[213] Jena J, Gupta A. Ricinus communis linn: A phytopharmacological review. *Int J Pharm Pharm Sci* 2012; 4: 25–29.

[214] Martínez CA, Mosquera OM, Niño J. Medicinal plants from the genus Alchornea (Euphorbiaceae): A review of their ethnopharmacology uses and phytochemistry. *Bol Latinoam Caribe Plant Med Aromat* 2017; 16: 162–205.

[215] Yakubu OF, Adebayo AH, Iweala EEJ, et al. Anti-inflammatory and antioxidant activities of fractions and compound from Ricinodendron heudelotii (Baill.). *Heliyon* 2019; 5: e02779.

[216] Koech S, Maoga J, Sindani A, et al. Anti-Inflammatory Activity of Dichloromethanolic Root Extract of Clutia abyssinica in Swiss Albino Mice. *J Pharmacogn Nat Prod* 2017; 3: 1000132.

[217] Seebaluck R, Gurib-Fakim A, Mahomoodally F. Medicinal plants from the genus Acalypha (Euphorbiaceae)–A review of their ethnopharmacology and phytochemistry. *J Ethnopharmacol* 2015; 159: 137–157.

[218] Bruno T, Soh D, Ernestine N, et al. Phytochemical Composition and Biological Activity of Faidherbia albida (Mimosaceae) Roots and Leaves. *Int J Pharm Sci Rev Res* 2020; 65(1): 124–130.

[219] Hebbar SS, Harsha VH, Shripathi V, et al. Ethnomedicine of Dharwad district in Karnataka, India—plants used in oral health care. *J Ethnopharmacol* 2004; 94: 261–266.

[220] Kalaivani T, Mathew L. Free radical scavenging activity from leaves of Acacia nilotica (L.) Wild. ex Delile, an Indian medicinal tree. *Food Chem Toxicol* 2010; 48: 298–305.

[221] Ali A, Naveed A, Khan B, et al. Acacia nilotica: A plant of multipurpose medicinal uses. *J Med Plants* 2012; 6: 1492–1496.

[222] Mariita RM, Orodho JA, Okemo PO, et al. Antifungal, antibacterial and antimycobacterial activity of Entada abysinnica Steudel ex A. Rich (Fabaceae) methanol extract. *Pharmacogn Res* 2010; 2: 163–168.

[223] Gurmessa GT, Kusari S, Laatsch H, et al. Chemical constituents of root and stem bark of Erythrina brucei. *Phytochem Lett* 2018; 25: 37–42.

[224] Narnoliya LK, Jadaun JS, Singh SP. The Phytochemical Composition, Biological Effects and Biotechnological Approaches to the Production of High-Value Essential Oil from Geranium. In: Malik S (ed) *Essential Oil Research: Trends in Biosynthesis, Analytics, Industrial Applications and Biotechnological Production*. 2019, pp. 327–352.

[225] Adesuyi A, Elumm I, Adaramola F, et al. Nutritional and Phytochemical Screening of Garcinia kola. *Adv J Food Sci Technol* 2012; 4: 9–14.

[226] Petersen M, Simmonds MS. Rosmarinic acid. *Phytochemistry* 2003; 62: 121–125.

[227] Njeru SN, Obonyo M, Nyambati S, et al. Antimicrobial and cytotoxicity properties of the organic solvent fractions of Clerodendrum myricoides (Hochst.) R. Br. ex Vatke: Kenyan traditional medicinal plant. *J Intercult Ethnopharmacol* 2016; 5: 226–232.

[228] Alemayehu K, Anza M, Engdaw D, et al. Chemical constituents, physicochemical properties and antibacterial activity of leaves essential oil of Ocimum urticifolium. *J Coast Life Med* 2016; 4: 955–960.

[229] Idris S, Ndukwe G, Gimba C. Preliminary phytochemical screening and antimicrobial activity of seed extracts of Persea americana (avocado pear). *Bayero J Pure Appl Sci* 2009; 2: 173–176.

[230] Tirfe M, Gebrehiwot M, Gebrelibanos M, et al. Radical Scavenging Activity and Preliminary Phytochemical Screening of Pods of Cassia arereh Del. (Fabaceae). *Momona Ethiop J Sci* 2015; 7: 125–133.

[231] Jeremiah C, Aliyu N, Dijie H, et al. Pharmacognostic and Elemental Analysis of the Leaves of Tapinanthus globifer (A. Rich). Tiegh. *Res J Pharmacol* 2018; 6: 11–18.

[232] Abiche E, Habila J. Phytochemistry, pharmacology and medicinal uses of Cola (Malvaceae) family: a review. *Med Chem Res* 2020; 29: 2089–2105.

[233] Imam H, et al. Neem (Azadirachta indica A. Juss)-A Nature's Drugstore: An overview. *Int Res J Biol Sci* 2012; 1: 76–79.

[234] Sahrawat A, Sharma J, Rahul S, et al. Phytochemical analysis and Antibacterial properties of Azadirachta indica (Neem) leaves extract against E.coli. *J Pharmacogn Phytochem* 2018; 7: 1368–1371.

[235] Lakshmi T, Krishnan V, Rajendran R, et al. Azadirachta indica: A herbal panacea in dentistry – An update. *Pharmacogn Rev* 2015; 9: 41–44.

[236] Qureshi H, Arshad M, Akram A, et al. Ethnopharmacological and phytochemical account of paradise tree (Melia azedarach L.: Meliaceae). *Pure Appl Biol* 2015; 5: 5–14.

[237] Aćimović M, Jeremić K, Salaj N, et al. Marrubium vulgare L.: A Phytochemical and Pharmacological Overview. *Molecules* 2020; 25: 2898.

[238] Pascal DrMK, my el abbes F, Meddah B, et al. Assessment of methanolic extract of Marrubium vulgare for antiinflammatory, analgesic and anti-microbiologic activities. *J Chem Pharm Res* 2011; 3: 199–204.

[239] Bouyahya A, Chamkhi I, Benali T, et al. Traditional use, phytochemistry, toxicology, and pharmacology of Origanum majorana L. *J Ethnopharmacol* 2021; 265: 113318.

[240] Negi A, Dobhal K, Ghildiyal P. Antioxidant Potential and Effect of Extraction Solvent on Total Phenol Content, Flavonoids Content and Tannin Content of Ficus palmata Forssk. *Int J Pharm Sci Rev Res* 2018; 49: 19–24.

[241] Anibasa G. Antimicrobial And Phytochemical Screening Activities Of Ficus Sur (Forssk). *N Y Sci J* 2011; 4(1): 15–18.

[242] Taviano MF, Rashed K, Filocamo A, et al. Phenolic profile and biological properties of the leaves of Ficus vasta Forssk. (Moraceae) growing in Egypt. *BMC Complement Altern Med* 2018; 18: 161.

[243] Paikra BK, Dhongade H kumar J, Gidwani B. Phytochemistry and Pharmacology of Moringa oleifera Lam. *J Pharmacopuncture* 2017; 20: 194–200.

[244] Messaoud C, Laabidi A, Boussaid M. Myrtus communis L. infusions: the effect of infusion time on phytochemical composition, antioxidant, and antimicrobial activities. *J Food Sci* 2012; 77: C941–C947.

[245] Kaushal S. Phytochemistry and pharmacological aspects of Syzygium aromaticum: A review. *J Pharmacogn Phytochem* 2019; 8: 398–406.

[246] Kamath JV, Rahul N, Kumar CKA, et al. Psidium guajava L: A review. *Int J Green Pharm*; 2. Epub ahead of print 2008. DOI: 10.22377/ijgp.v2i1.386.

[247] Dhakad AK, Pandey VV, Beg S, et al. Biological, medicinal and toxicological significance of Eucalyptus leaf essential oil: a review. *J Sci Food Agric* 2018; 98: 833–848.

[248] Al-Snafi A. The pharmacological and therapeutic importance of Eucalyptus species grown in Iraq. *IOSR J Pharm* 2017; 7: 72–91.

[249] Fatma B, Fatiha M, Elattafia B, et al. Phytochemical and antimicrobial study of the seeds and leaves of Peganum harmala L. against urinary tract infection pathogens. *Asian Pac J Trop Dis* 2016; 6: 822–826.

[250] Ghasemi Pirbalouti A, Momeni M, Bahmani M. Ethnobotanical study of medicinal plants used by Kurd tribe in Dehloran and Abdanan Districts, Ilam Province, Iran. *Afr J Tradit Complement Altern Med* 2013; 10: 368–385.

[251] Mina CN, Farzaei MH, Gholamreza A. Medicinal properties of Peganum harmala L. in traditional Iranian medicine and modern phytotherapy: a review. *J Tradit Chin Med* 2015; 35: 104–109.

[252] Almeida ML, Freitas WE, de Morais PL, et al. Bioactive compounds and antioxidant potential fruit of Ximenia americana L. *Food Chem* 2016; 192: 1078–1082.

[253] Balkrishna A, Rohela A, Kumar A, et al. Mechanistic Insight into Antimicrobial and Antioxidant Potential of Jasminum Species: A Herbal Approach for Disease Management. *Plants* 2021; 10: 1089.

[254] Sekharan TR, Mohan MS, Venkatnarayanan R, et al. Pharmacognostical and Preliminary Phytochemical Screening the Leaves of Jasminum grandiflorum Linn. *Res J Pharmacogn Phytochem* 2010; 2: 438–440.

[255] Rathore S, Bhatt S, Dhyani D, et al. Preliminary phytochemical screening of medicinal plant Ziziphus mauritiana Lam fruits. *Int J Curr Pharm Res* 2012; 4: 160–162.

[256] Aruna K, Devi P, Rajeswari R, et al. Quantitative phytochemical analysis of oxalis corniculata l. (oxalidaceae). *World J Pharm Pharm Sci* 2014; 3: 711–716.

[257] Desta KT, Abd El-Aty AM. Triterpenoid and Saponin Rich Phytolacca dodecandra L'Herit (Endod): A Review on Its Phytochemistry and Pharmacological Properties. *Mini Rev Med Chem* 2021; 21: 23–34.

[258] Nakalembe L, Kasolo JN, Nyatia E, et al. Analgesic and Anti-Inflammatory Activity of Total Crude Leaf Extract of Phytolacca dodecandra in Wistar Albino Rats. *Neurosci Med* 2019; 10: 259–271.

[259] Manu P, Lal A, Rana S, et al. Plumbago zeylanica L.: A mini review. *Int J Pharm Appl* 2012; 3: 399-405.

[260] Rajakrishnan R, Lekshmi R, Benil PB, et al. Phytochemical evaluation of roots of Plumbago zeylanica L. and assessment of its potential as a nephroprotective agent. *Saudi J Biol Sci* 2017; 24: 760–766.

[261] Ojewole JA. Analgesic, anti-inflammatory and hypoglycaemic effects of Securidaca longepedunculata (Fresen.) [Polygalaceae] root-bark aqueous extract. *Inflammopharmacology* 2008; 16: 174–181.

[262] Mekonnen T, Urga K, Engidawork E. Evaluation of the diuretic and analgesic activities of the rhizomes of Rumex abyssinicus Jacq in mice. *J Ethnopharmacol* 2010; 127: 433–439.

[263] Kumar S, Singh PK. Phytochemical investigation and antioxidant characterization of essential oil from roots of Rumex nepalensis Spreng high altitude of North India. *Mater Today Proc* 2020; 26: 3442–3448.

[264] Hawaze S, Deti H, Suleman S. In vitro Antimicrobial Activity and Phytochemical Screening of Clematis Species Indigenous to Ethiopia. *Indian J Pharm Sci* 2012; 74: 29–35.

[265] Tadele A, Asres K, Melaku D, et al. In vivo anti-inflammatory and antinociceptive activities of the leaf extracts of Clematis simensis Fresen. *Ethiop Pharm J* 2010; 27: 33–41.

[266] Madivoli ES, Maina EG, Kairigo PK, et al. In vitro antioxidant and antimicrobial activity of Prunus africana (Hook. f.) Kalkman (bark extracts) and Harrisonia abyssinica Oliv. extracts (bark extracts): A comparative study. *J Med Plants Econ Dev* 2018; 2: 1–9.

[267] Bento C, Gonçalves AC, Silva B, et al. Peach (Prunus Persica): Phytochemicals and Health Benefits. *Food Rev Int* 2020; 1–32.

[268] Venditti A, Guarcini L, Ballero M, et al. Iridoid glucosides from Pentas lanceolata (Forssk.) Deflers growing on the Island of Sardinia. *Plant Syst Evol* 2015; 301: 685–690.

[269] Lawal IO, Grierson DS, Afolayan AJ. Phytochemical and antioxidant investigations of a Clausena anisata hook, a South African medicinal plant. *Afr J Tradit Complement Altern Med* 2015; 12: 28–37.

[270] Nantongo JS, Odoi JB, Abigaba G, et al. Variability of phenolic and alkaloid content in different plant parts of Carissa edulis Vahl and Zanthoxylum chalybeum Engl. *BMC Res Notes* 2018; 11: 125.

[271] Dutta S, Shaikh A. The Active chemical constituent and biological activity of salvadora persica (Miswak). *Int J Curr Pharm Rev Res* 2012; 3: 1–14.

[272] Rani MS, Pippalla RS, Mohan K. Dodonaea Viscosa Linn. - An Overview. *Asian J Pharm Res Health Care* 2009; 1: 97–112.

[273] Jima T, Megersa M. Ethnobotanical Study of Medicinal Plants Used to Treat Human Diseases in Berbere District, Bale Zone of Oromia Regional State, South East Ethiopia. *Evid Based Complement Alternat Med* 2018; 2018: 8602945.

[274] Mergia E, Shibeshi W, Terefe G, et al. Antitrypanosomal activity of Verbascum sinaiticum Benth. (Scrophulariaceae) against Trypanosoma congolense isolates. *BMC Complement Altern Med* 2016; 16: 362.

[275] Guluma T, G NB, Teju E, et al. Phytochemical investigation and evaluation of antimicrobial activities of Brucea antidysenterica leaves. *Chem Data Collect* 2020; 28: 100433.

[276] Soni P, Siddiqui AA, Dwivedi J, et al. Pharmacological properties of Datura stramonium L. as a potential medicinal tree: An overview. *Asian Pac J Trop Biomed* 2012; 2: 1002–1008.

[277] Sayyed A. Phytochemistry, pharmacological and traditional uses of Datura stramonium L. *J Pharmacogn Phytochem* 2013; 2: 123–125.

[278] Oyekunle I, Nwogu U, Orababa O, et al. Phytochemical, Antimicrobial and Proximate Composition of Nicotiana tabacum Leaves Extract. *Int J Innov Res Sci Eng Technol*; 4.

[279] Sambo H, Olatunde A, Kiyawa S. Phytochemical, Proximate and Mineral Analyses of Solanum incanum Fruit. *Int J Chem Mater Environ Res* 2016; 3: 8–13.

[280] Sbhatu D, Abraha H. Preliminary Antimicrobial Profile of Solanum incanum L.: A Common Medicinal Plant. *Evid Based Complement Alternat Med* 2020; 2020: 3647065.

[281] Jaspers MW, Bashir AK, Zwaving JH, et al. Investigation of Grewia bicolor juss. *J Ethnopharmacol* 1986; 17: 205–211.

[282] Dianita R, Jantan I. Ethnomedicinal uses, phytochemistry and pharmacological aspects of the genus Premna: a review. *Pharm Biol* 2017; 55: 1715–1739.

[283] Awah FM, Uzoegwu PN, Oyugi JO, et al. Free radical scavenging activity and immunomodulatory effect of Stachytarpheta angustifolia leaf extract. *Food Chem* 2010; 119: 1409–1416.

[284] Seyfe S, Toma A, Etisso A, et al. Journal of Medicinal Plants Research Phytochemical screening and in vivo antimalarial activities of crude extracts of Lantana trifolia root and Premna oligotricha leaves in Plasmodium berghei infected mice. *J Med Plants Res* 2017; 11: 763–769.

[285] Njeru SN, Obonyo MA, Nyambati SO, et al. Antimicrobial and cytotoxicity properties of the crude extracts and fractions of Premna resinosa (Hochst.) Schauer (Compositae): Kenyan traditional medicinal plant. *BMC Complement Altern Med* 2015; 15: 295.

[286] Chidambara Murthy KN, Vanitha A, Mahadeva Swamy M, et al. Antioxidant and antimicrobial activity of Cissus quadrangularis L. *J Med Food* 2003; 6: 99–105.

[287] Kumar S, Yadav M, Yadav A, et al. Impact of spatial and climatic conditions on phytochemical diversity and in vitro antioxidant activity of Indian Aloe vera (L.) Burm.f. *South Afr J Bot* 2017; 111: 50–59.

[288] Ahmed H. Ethnopharmacobotanical study on the medicinal plants used by herbalists in Sulaymaniyah Province, Kurdistan, Iraq. *J Ethnobiol Ethnomed* 2016; 12: 8.

[289] Salehi B, Albayrak S, Antolak H, et al. Aloe Genus Plants: From Farm to Food Applications and Phytopharmacotherapy. *Int J Mol Sci* 2018; 19: 2843.

[290] Sánchez-Machado DI, López-Cervantes J, Sendón R, et al. Aloe vera: Ancient knowledge with new frontiers. *Trends Food Sci Technol* 2017; 61: 94–102.

[291] Eyob S, Martinsen BK, Tsegaye A, et al. Antioxidant and antimicrobial activities of extract and essential oil of korarima (Aframomum corrorima (Braun) P.C.M. Jansen). *Afr J Biotechnol* 2008; 7: 2585–2592.

[292] Kumar G, Loganathan K, Rao B. A Review on Pharmacological and Phytochemical Properties of Zingiber officinale Roscoe (Zingiberaceae). *J Pharm Res* 2011; 4: 2963–2966.

[293] Kumar H, Agrawal R, Kumar V. Barleria cristata: perspective towards phytopharmacological aspects. *J Pharm Pharmacol* 2018; 70: 475–487.

[294] Muñoz-Acevedo A, Martinez JL, Rai M. *Ethnobotany: Local Knowledge and Traditions*. 1st ed. CRC Press, 2019.

[295] Pasaribu G, Budianto E, Cahyana H, et al. A Review on Genus Saurauia: Chemical Compounds and their Biological Activity. *Pharmacogn J* 2020; 12: 657–666.

[296] Hong L, Guo Z, Huang K, et al. Ethnobotanical study on medicinal plants used by Maonan people in China. *J Ethnobiol Ethnomed* 2015; 11: 32.

[297] Ye CL, Dai DH, Hu WL. Antimicrobial and antioxidant activities of the essential oil from onion (Allium cepa L.). *Food Control* 2013; 30: 48–53.

[298] Ghamari S, Mohammadrezaei Khorramabadi R, Mardani M, et al. An overview of the most important medicinal plants with anti-toothache property based on ethnobotanical sources in Iran. *J Pharm Sci Res* 2017; 9: 796–799.

[299] Bor M, Özdemir F, Türkan I. The effect of salt stress on lipid peroxidation and antioxidants in leaves of sugar beet Beta vulgaris L. and wild beet Beta maritima L. *Plant Sci* 2003; 164: 77–84.

[300] Srivastava R. A review on phytochemical, pharmacological, and pharmacognostical profile of Wrightia tinctoria: Adulterant of kurchi. *Pharmacogn Rev* 2014; 8: 36–44.

[301] Zhang SX, Tani T, Yamaji S, et al. Glycosyl flavonoids from the roots and rhizomes of Asarum longerhizomatosum. *J Asian Nat Prod Res* 2003; 5: 25–30.

[302] Hu R, Lin C, Xu W, et al. Ethnobotanical study on medicinal plants used by Mulam people in Guangxi, China. *J Ethnobiol Ethnomed* 2020; 16: 40.

[303] Doss A, Anand SP. Preliminary phytochemical screening of Asteracantha longifolia and Pergularia daemia. *World Appl Sci J* 2012; 18: 233–235.

[304] Abd-Alla HI, Shalaby NMM, Hamed MA, et al. Phytochemical composition, protective and therapeutic effect on gastric ulcer and α-amylase inhibitory activity of Achillea biebersteinii Afan. *Arch Pharm Res* 2016; 39: 10–20.

[305] Sukumaran P, Nair AG, Chinmayee DM, et al. Phytochemical Investigation of Bidens biternata (Lour.) Merr. and Sheriff. - -a nutrient-rich leafy vegetable from Western Ghats of India. *Appl Biochem Biotechnol* 2012; 167: 1795–1801.

[306] Patel S. Harmful and beneficial aspects of Parthenium hysterophorus: an update. *3 Biotech* 2011; 1: 1–9.

[307] Lunlun G, Wei N, Yang G, et al. Ethnomedicine study on traditional medicinal plants in the Wuliang Mountains of Jingdong, Yunnan, China. *J Ethnobiol Ethnomed* 2019; 15: 20.

[308] Farsam H, Amanlou M, Reza Dehpour A, et al. Anti-inflammatory and analgesic activity of Biebersteinia multifida DC. root extract. *J Ethnopharmacol* 2000; 71: 443–447.

[309] Chi YM, Nakamura M, Zhao XY, et al. A monoterpene alkaloid from incarvillea sinensis. *Chem Pharm Bull (Tokyo)* 2005; 53: 1178–1179.

[310] Wurchaih, Huar, Menggenqiqig, et al. Medicinal wild plants used by the Mongol herdsmen in Bairin Area of Inner Mongolia and its comparative study between TMM and TCM. *J Ethnobiol Ethnomed* 2019; 15: 32.

[311] Yu CH, Tang WZ, Peng C, et al. Diuretic, anti-inflammatory, and analgesic activities of the ethanol extract from Cynoglossum lanceolatum. *J Ethnopharmacol* 2012; 139: 149–154.

[312] Joshi K. Cynoglossum L.: A review on phytochemistry and chemotherapeutic potential. *J Pharmacogn Phytochem* 2016; 5: 32–39.

[313] Jeeva K, Thiyagarajan M, Elangovan V, et al. Caesalpinia coriaria leaf extracts mediated biosynthesis of metallic silver nanoparticles and their antibacterial activity against clinically isolated pathogens. *Ind Crops Prod* 2014; 52: 714–720.

[314] Jiménez-López J, Ruiz-Medina A, Ortega-Barrales P, et al. Phytochemical profile and antioxidant activity of caper berries (Capparis spinosa L.): Evaluation of the influence of the fermentation process. *Food Chem* 2018; 250: 54–59.

[315] Zhang H, Ma ZF. Phytochemical and Pharmacological Properties of Capparis spinosa as a Medicinal Plant. *Nutrients* 2018; 10: 116.

[316] Mishra S, Moharana S, Dash M. Review on Cleome gynandra. *Int J Res Pharm Chem* 2011; 1: 681–689.

[317] Uddin G, Rauf A, Siddiqui BS, et al. Anti-nociceptive, anti-inflammatory and sedative activities of the extracts and chemical constituents of Diospyros lotus L. *Phytomedicine* 2014; 21: 954–959.

[318] Rauf A. Phytochemical screening and biological activity of the aerial parts of Elaeagnus umbellata. *Sci Res Essays* 2012; 7: 3690–3694.

[319] Ho JC, Chen CM. Flavonoids from the aquatic plant Eriocaulon buergerianum. *Phytochemistry* 2002; 61: 405–408.

[320] Tantray MA, Khan R, Shawl AS, et al. Phenolic glycosides from Lespedeza juncea. *Chem Nat Compd* 2008; 44: 591–593.

[321] Sroka Z, Bodalska HR, Mażol I. Antioxidative Effect of Extracts from Erodium cicutarium L. *Z Naturforsch C J Biosci* 1994; 49: 881–884.

[322] Di Lorenzo C, Ceschi A, Kupferschmidt H, et al. Adverse effects of plant food supplements and botanical preparations: a systematic review with critical evaluation of causality. *Br J Clin Pharmacol* 2015; 79: 578–592.

[323] Raak C, Büssing A, Gassmann G, et al. A systematic review and meta-analysis on the use of Hypericum perforatum (St. John’s Wort) for pain conditions in dental practice. *Homeopathy* 2012; 101: 204–210.

[324] Wei Y, Shu P, Hong J, et al. Qualitative and quantitative evaluation of phenolic compounds in Iris dichotoma Pall. *Phytochem Anal* 2012; 23: 197–207.

[325] Prajapati MS, Patel JB, Modi K, et al. Leucas aspera: A review. *Pharmacogn Rev* 2010; 4: 85–87.

[326] Bahramikia S, Yazdanparast R. Phytochemistry and medicinal properties of Teucrium polium L. (Lamiaceae). *Phytother Res* 2012; 26: 1581–1593.

[327] Sadeghi H, Zarezade V, Sadeghi H, et al. Anti-inflammatory Activity of Stachys Pilifera Benth. *Iran Red Crescent Med J* 2014; 16: e19259.

[328] Lukhoba CW, Simmonds MSJ, Paton AJ. Plectranthus: A review of ethnobotanical uses. *J Ethnopharmacol* 2006; 103: 1–24.

[329] Kong DG, Zhao Y, Li GH, et al. The genus Litsea in traditional Chinese medicine: An ethnomedical, phytochemical and pharmacological review. *J Ethnopharmacol* 2015; 164: 256–264.

[330] Al-Snafi A. Fritillaria Imperialis-A Review. *IOSR J Pharm* 2019; 9: 47–51.

[331] Nhut P, An TN, Minh LV, et al. Phytochemical screening of Allium Tuberosum Rottler. ex Spreng as food spice. *IOP Conf Ser Mater Sci Eng* 2020; 991: 012021.

[332] Eldahshan OA, Abdel-Daim MM. Phytochemical study, cytotoxic, analgesic, antipyretic and anti-inflammatory activities of Strychnos nux-vomica. *Cytotechnology* 2015; 67: 831–844.

[333] Mittal M, Gupta N, Parashar P, et al. Phytochemical evaluation and pharmacological activity of syzygium aromaticum: A comprehensive review. *Int J Pharm Pharm Sci* 2014; 6: 67–72.

[334] Hanani E, Prastiwi R, Karlina L, et al. Indonesian Mirabilis jalapa Linn.: A Pharmacognostical and Preliminary Phytochemical Investigations. *Pharmacogn J* 2017; 9: 683–688.

[335] Khan I, AbdElsalam NM, Fouad H, et al. Application of Ethnobotanical Indices on the Use of Traditional Medicines against Common Diseases. *Evid Based Complement Alternat Med* 2014; 2014: 635371.

[336] Shan S, Huang X, Shah M, et al. Evaluation of Polyphenolics Content and Antioxidant Activity in Edible Wild Fruits. *BioMed Res Int* 2019; 2019: 1–11.

[337] Raghavendra MP, Satish S, Raveesha KA. Phytochemical analysis and antibacterial activity of Oxalis corniculata; a known medicinal plant. *My Sci* 2006; 1: 72–78.

[338] Kaushik P, Kaushik D, Khokra SL. Ethnobotany and phytopharmacology of Pinus roxburghii Sargent: a plant review. *J Integr Med* 2013; 11: 371–376.

[339] Bahadori MB, Sarikurkcu C, Kocak MS, et al. Plantago lanceolata as a source of health-beneficial phytochemicals: Phenolics profile and antioxidant capacity. *Food Biosci* 2020; 34: 100536.

[340] C. Karkanis A, Fernandes Â, Vaz J, et al. Chemical composition and bioactive properties of Sanguisorba minor Scop. under Mediterranean growing conditions. *Food Funct* 2019; 10: 1340–1351.

[341] Zhao Z, He X, Zhang Q, et al. Traditional Uses, Chemical Constituents and Biological Activities of Plants from the Genus *Sanguisorba* L. *Am J Chin Med* 2017; 45: 199–224.

[342] Gao J, Sun C, Yang J, et al. Evaluation of the hepatoprotective and antioxidant activities of Rubus parvifolius L. *J Zhejiang Univ Sci B* 2011; 12: 135–142.

[343] Cheng X, Qin J, Zeng Q, et al. Taraxasterane-Type Triterpene and Neolignans from Geum japonicum Thunb. var. chinense F. Bolle. *Planta Med* 2011; 77: 2061–2065.

[344] Fu H, Mu X, Wang P, et al. Fruit quality and antioxidant potential of Prunus humilis Bunge accessions. *PLoS One* 2020; 15: e0244445.

[345] Lu Q, Ma R, Yang Y, et al. Zanthoxylum nitidum (Roxb.) DC: Traditional uses, phytochemistry, pharmacological activities and toxicology. *J Ethnopharmacol* 2020; 260: 112946.

[346] Zhang M, Wang J, Zhu L, et al. Zanthoxylum bungeanum Maxim. (Rutaceae): A Systematic Review of Its Traditional Uses, Botany, Phytochemistry, Pharmacology, Pharmacokinetics, and Toxicology. *Int J Mol Sci* 2017; 18: 2172.

[347] Prakash B, Singh P, Mishra PK, et al. Safety assessment of Zanthoxylum alatum Roxb. essential oil, its antifungal, antiaflatoxin, antioxidant activity and efficacy as antimicrobial in preservation of Piper nigrum L. fruits. *Int J Food Microbiol* 2012; 153: 183–191.

[348] Khatun A, Rahman M, Jahan S. Preliminary phytochemical, cytotoxic, thrombolytic and antioxidant activities of the methanol extract of Murraya exotica Linn. leaves. *Orient Pharm Exp Med* 2014; 14: 223–229.

[349] Solanke SB. Phytochemical Information and Pharmacological Activities of Eggplant (Solanum Melongena L.): A Comprehensive Review. *EAS J Pharm Pharmacol* 2019; 1: 103–114.

[350] Ohtsuki T, Miyagawa T, Koyano T, et al. Isolation and structure elucidation of flavonoid glycosides from Solanum verbascifolium. *Phytochem Lett* 2010; 3: 88–92.

[351] Son YO, Kim J, Lim JC, et al. Ripe fruits of Solanum nigrum L. inhibits cell growth and induces apoptosis in MCF-7 cells. *Food Chem Toxicol* 2003; 41: 1421–1428.

[352] Tekuri SK, Pasupuleti SK, Kranthi KK, et al. Phytochemical and pharmacological activities of Solanum surattense Burm. f.–A review. *J App Pharm Sci* 2019; 9: 126–136.

[353] Alizadeh A, Moshiri M, Alizadeh J, et al. Black henbane and its toxicity - a descriptive review. *Avicenna J Phytomed* 2014; 4: 297–311.

[354] Martínez-Valverde I, Periago MJ, Provan G, et al. A. Phenolic compounds, lycopene and antioxidant activity in commercial varieties of tomato (Lycopersicum esculentum): Phenolics, lycopene and antioxidant activity in tomatoes. *J Sci Food Agric* 2002; 82: 323–330.

[355] Zaidi A, Bukhari S, Khan F, et al. Ethnobotanical, phytochemical and pharmacological aspects of *daphne mucronata* (thymeleaceae). *Trop J Pharm Res* 2015; 14: 1517–1523.

[356] Zheng CJ, Zhao XX, Ai HW, et al. Therapeutic effects of standardized Vitex negundo seeds extract on complete Freund's adjuvant induced arthritis in rats. *Phytomedicine* 2014; 21: 838–846.

[357] Usman H, Abdulrahman FI, A.A L. Phytochemical and Antimicrobial Evaluation of Tribulus terrestris L. (Zygophylaceae). Growing in Nigeria. *Res J Biol Sci* 2007; 2: 244–247.

[358] Rashid U, Khan MR, Jan S, et al. Assessment of phytochemicals, antimicrobial and cytotoxic activities of extract and fractions from Fagonia olivieri (Zygophyllaceae). *BMC Complement Altern Med* 2013; 13: 167.

[359] Rashid U, Khan MR, Sajid M. Antioxidant, anti-inflammatory and hypoglycemic effects of Fagonia olivieri DC on STZ-nicotinamide induced diabetic rats - In vivo and in vitro study. *J Ethnopharmacol* 2019; 242: 112038.

[360] Abbasi BH, Khan T, Khurshid R, et al. UV-C mediated accumulation of pharmacologically significant phytochemicals under light regimes in in vitro culture of Fagonia indica (L.). *Sci Rep* 2021; 11: 679.

[361] Joshi RK. Volatile Constituents of *Emilia sonchifolia* from India. *Nat Prod Commun* 2018; 13: 1355–1356.

[362] Kamboj A, Saluja AK. Phytopharmacological review of Xanthium strumarium L. (Cocklebur). *Int J Green Pharm* 2010; 4: 129–139.

[363] Ahmad H, Sehgal S, Mishra A, et al. Mimosa pudica L. (Laajvanti): An overview. *Pharmacogn Rev* 2012; 6: 115–124.

[364] Ting YC, Ko HH, Wang HC, et al. Biological evaluation of secondary metabolites from the roots of Myrica adenophora. *Phytochemistry* 2014; 103: 89–98.

[365] Suhagia B, Rathod I, Sindhu S. Sapindus mukorossi (areetha): An overview. *Int J Pharm Sci Res* 2011; 2: 1905–1913.

[366] Daboriya V, Kumar S, Singh S. Antibacterial activity and phytochemical investigations on nicotiana plumbaginifolia viv. (wild tobacco). *Rom J Biol - Plant Biol* 2010; 55: 135–142.

[367] Ikenaga T, Handayani R, Oyama T. Steroidal saponin production in callus cultures of Solanum aculeatissimum Jacq. *Plant Cell Rep* 2000; 19: 1240–1244.

[368] Pandey S, Sah SP, Sah ML, et al. An antioxidant potential of hydromethanolic extract of Urtica parviflora Roxb. *J Basic Clin Pharm* 2010; 1: 191–195.

[369] Kalt FR, Cock IE. Gas chromatography-mass spectroscopy analysis of bioactive petalostigma extracts: Toxicity, antibacterial and antiviral activities. *Pharmacogn Mag* 2014; 10: S37–S49.

[370] Singab AN, Youssef FS, Ashour ML, et al. The genus *Eremophila* (Scrophulariaceae): an ethnobotanical, biological and phytochemical review. *J Pharm Pharmacol* 2013; 65: 1239–1279.

[371] Al-Abd NM, Mohamed Nor Z, Mansor M, et al. Antioxidant, antibacterial activity, and phytochemical characterization of Melaleuca cajuputi extract. *BMC Complement Altern Med* 2015; 15: 385.

[372] Banbury LK, Shou Q, Renshaw DE, et al. Compounds from Geijera parviflora with prostaglandin E2 inhibitory activity may explain its traditional use for pain relief. *J Ethnopharmacol* 2015; 163: 251–255.

[373] Al-Snafi A. A review on Dodonaea viscosa: A potential medicinal plant. *IOSR J Pharm* 2017; 7: 10–21.

[374] Dapar MLG, Meve U, Liede-Schumann S, et al. Ethnomedicinal plants used for the treatment of cuts and wounds by the Agusan Manobo of Sibagat, Agusan del Sur, Philippines. *Ethnobot Res Appl* 2020; 19: 1–18.