Food & Function

ROYAL SOCIETY OF CHEMISTRY

REVIEW

View Article Online
View Journal | View Issue

Cite this: *Food Funct.*, 2021, **12**, 2850

Traditional plants from Asteraceae family as potential candidates for functional food industry

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Received 27th December 2020,
Accepted 9th February 2021

DOI: 10.1039/d0fo03433a

rsc.li/food-function

Traditional plants have been used in the treatment of disease and pain due to their beneficial properties such as antioxidant, antiinflammation, analgesic, and antibiotic activities. The Asteraceae family is one of the most common groups of plants used in folk medicine. The species *Achillea millefolium*, *Arnica montana*, *Bellis perennis*, *Calendula officinalis*, *Chamaemelum nobile*, *Eupatorium cannabinum*, *Helichrysum stoechas*, and *Taraxacum officinale* have been used in different remedies in Northwest Spain. Besides health benefits, some of them like *C. nobile* and *H. stoechas* are already employed in cooking and culinary uses, including cocktails, desserts, and savory dishes. This study aimed to review the current information on nutritive and beneficial properties and bioactive compounds of these plants, which are not mainly used as foods but are possible candidates for this purpose. The report highlights their current uses and suitability for the development of new functional food industrial applications. Phenolic compounds, essential oils, and sesquiterpene lactones are some of the most important compounds, being related to different bioactivities. Hence, they could be interesting for the development of new functional foods.

1. Introduction

Plants have been around human beings since ancient times. Throughout history, some plants have been chosen as food; some specific plants that were orally consumed ameliorated or had punctual benefits for the treatment or prevention of particular diseases, have been selected and described as "traditional plants" (TP).[1] These plants have been traditionally applied for the cure of some disorders, but they have also stood out as raw materials for the recovery of specific molecules, also known as bioactive compounds, and have shown the scientific evidences of promoting health beneficial properties.[2,3] In this sense, TP can be used for two different purposes. On one hand, there is the traditional part associated with the preservation of ancient knowledge and their use for therapeutic purposes under different consumption formulations (decoctions, infusions, ointment, *etc.*), which have been maintained over time. On the other hand, TP can be used in cooking and culinary applications, and they can be revalorized for recovering bioactive compounds intended for the food industry.[1]

TP are being increasingly consumed, according to two diametrically opposite realities. On one side, those countries or regions with a lower socioeconomic status choose to use medicinal plants instead of chemically synthesized drugs for different reasons. In some cases, these drugs are expensive and hardly accessible for these populations, while medicinal plants are natural, abundant, available, and a low-cost remedy. In addition, in these cases, the population can carry out its own collection and administration of plants as a legal practice.[2,4] The other reality—closer to Western and more developed populations—refers to the new trend of preference for consuming natural foods over processed ones. In this case, the choice of these products is usually related to the adverse effects associated with food, supplements, and additives of artificial origin.[5,6] The current risk perception of consumers regarding the food chain is influenced by food contamination accidents, the excessive use of pesticides, the introduction of genetically modified organisms, and the use of artificial ingredients. Moreover, their opinion is also motivated by an increase in cardiovascular diseases, where the lifestyle and food habits play a crucial role, as well as other disorders, such as allergies or intolerances also related to different food practices.[7] Therefore, there is a moving trend toward natural products.

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TP and aromatic plants have been widely used as a raw ingredient in human diet. Because of their demonstrable beneficial properties, they are used as food supplements, sold as capsules, powders, extracts or fresh/dried plants and consumed in salads, decoctions, and infusions.[1,5] Likewise, they have been included in animal diets as they entail a safe alternative for replacing or diminishing synthetic ingredients while enhancing the immune status of animals.[8,9] Apart from their primary use as natural medicines, TP are being proposed as a source of plant extracts and bioactive compounds with uses in the functional food industry.[10–12] In this regard, several studies have been conducted to evaluate the biological properties of TP, which range from antioxidants[13,14] to antiinflammatory products[15] such as antimicrobial[16,17] or antitumor[18] products. In the food industry, one of the main applications of TP is as a preservative due to their antioxidant and antimicrobial properties, which prevent oxidation, avoid microbial growth, and preserve the organoleptic characteristics of diverse products (such as meat, seafood, milk and dairy products[19–22]). New applications such as the incorporation of these natural compounds into food active packaging are also gaining importance.[23] Many of the described bioactive properties are due to the presence of phenolic compounds (PC). These compounds are the secondary metabolites of plants, which are principally well known for their strong antioxidant capacity, among other advantages.[24] In particular, these molecules have been highlighted as an alternative to synthetic antioxidants such as butylated hydroxytoluene (BHT).[13,25] On the other hand, several studies have included TP extracts and bioactive compounds in different food matrixes to develop enriched products.[26–30]

TP can be found along with many families and in different locations. Northwest Spain possesses varied flora and a high number of species can be used as functional ingredients.[1] Among other families, Asteraceae species are promising candidates due to their bioactive compounds and associated beneficial properties.[18,31–34] This family of cosmopolitan distribution and easiness of adaptability includes 8–10% of the known angiosperms and accounts for 24 000–25 000 species and 1600–1700 genera.[35,36] These plants are characterized by their great adaptability to different habitats or environmental conditions and their diversity of habits. They can be found in all continents, except Antarctica.[36] In fact, some plants of this family have already been used in the food industry for developing functional foods.[37,38] With regard to its chemical composition, Asteraceae is the family where a group of polyacetylenes is the most prevalent, which is an organic polymer present in the roots (R) of plants.[39] Asteraceae family is also rich in sesquiterpenes, a group of highly diverse 15-carbon terpenes, which are the major elements of essential oils (EO) and exert different biological activities, entailing medicinal and aromatic potential for the food industry.[40] Interest on EO from this and other families has been increasing in the last few years on the basis of their broad spectrum of bioactive components and associated activities.[41] For instance, sesquiterpene lactones (SL) identified in the Asteraceae family have exhibited antimicrobial and antiinflammatory properties, among others.[42] Furthermore, plants usually possess a wide collection of free-radical-scavenging molecules, highlighting the potential of PC as well as other molecules such as nitrogen compounds, vitamins, or terpenoids (Te).[43] Several species from the Asteraceae family are known for their Te (SL) and PC (flavonoids (F) and phenolic acids (PA)) contents—both responsible for their antioxidant activity.[43,44]

In particular, this review has focused on the following species: *Achillea millefolium*, *Arnica montana*, *Bellis perennis*, *Calendula officinalis*, *Chamaemelum nobile*, *Eupatorium cannabinum*, *Helichrysum stoechas*, and *Taraxacum officinale* (Fig. 1). These eight plants can be found in northwest Spain and the current knowledge of their beneficial properties depends on the target species. For instance, yarrow (*A. millefolium*), dandelion (*T. officinale*), and calendula (*C. officinalis*) have been comprehensively studied. Te (SL and pentacyclic triterpenes (Tt)), F, and PA—apart from carotenoids (Ca) in the case of *C. officinalis*—have been reported as the major components of these plants.[45–47] In the case of *A. montana* or *B. perennis*, their main bioactive compounds have been demonstrated to be SL in the case of *A. montana* (responsible for its antiinflammatory effects),[48] and Tt saponins (Sa), F, and aromatic and acyclic alcohol glycosides in the case of *B. perennis.*[49] Perhaps, the remaining species, namely, *C. nobile*, *E. cannabinum*, and *H. stoechas*, are less frequently studied in terms of their biological properties, although there are some research articles from the 90s and the beneficial properties of *C. nobile* on digestive health are generally well known. Their biological (mainly, antiinflammatory,[50] antitumor,[51] and antimicrobial[52]) properties are a consequence of the action of SL and F, as well as tannins and EO.[52] Considering all this information and due to the knowledge gap in some of the abovementioned species, this review is aimed at compiling currently available information of the nutritional and biological properties of this plant and also their current uses in the industry. In this way, it is intended to scientifically justify the traditional use of these plants and highlight the bioactivities and compounds that could be of interest to diversify their food industry applications, thereby revalorizing them (Fig. 2).

2. Plants from Asteraceae family candidates for functional food applications

In this section, scientific studies evaluating the beneficial properties of the selected plants will be explained. In addition, in Table 1, the traditional form of application (oral administration being the most common form) and the diseases treated with these plants are summarized in order to highlight their possible use as food plants. Table 2 lists numerous studies of the bioactivities and bioactive compounds that are considered to play a fundamental role in them. The compiled information may be of reference for its potential application in functional foods.

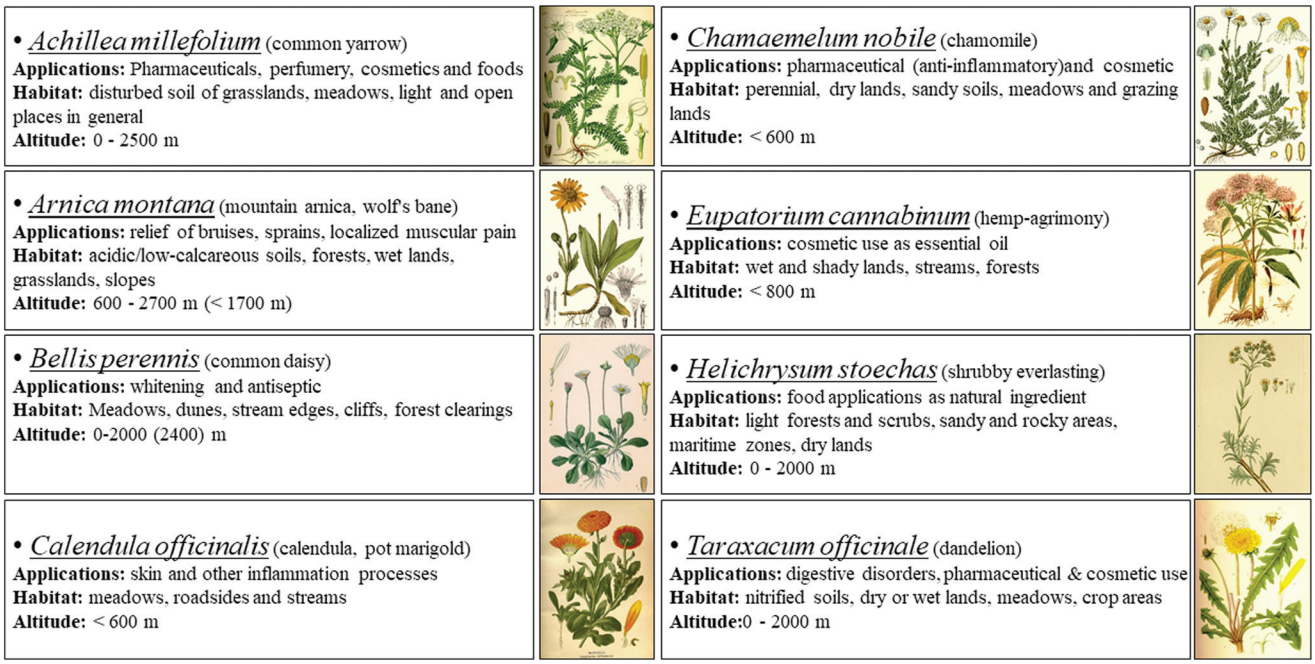

Fig. 1 Identification and characteristics of the different species studied in this review.[178,179]

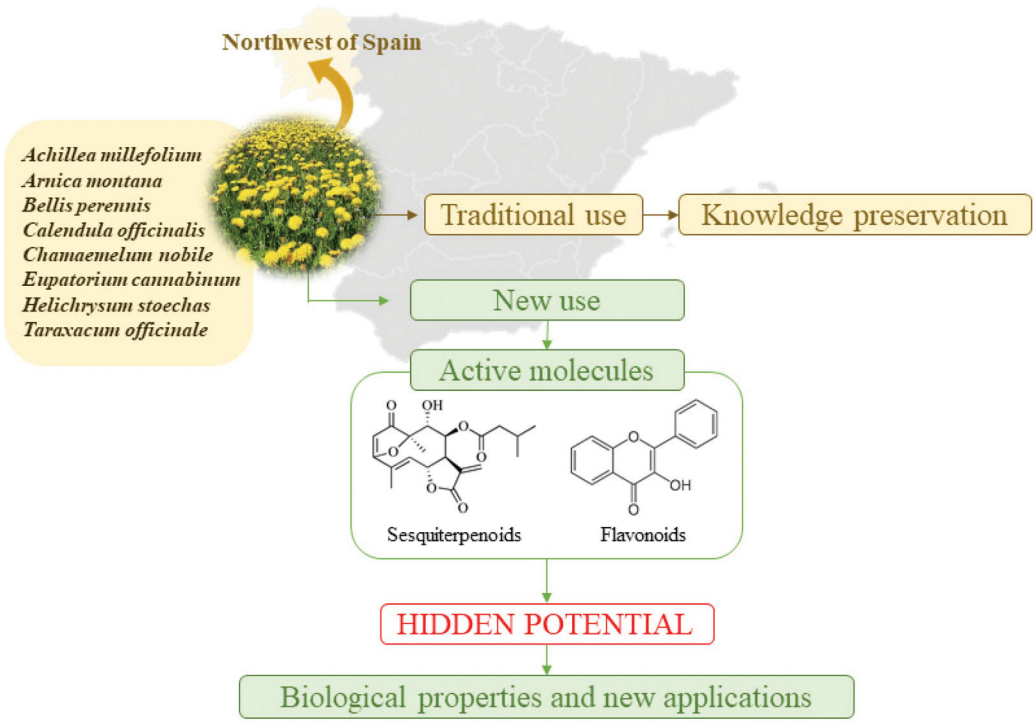

Fig. 2 TP of the Asteraceae family present numerous bioactive compounds, responsible for their biological properties and their use in folk medicine. These plants are currently used in different products, but the understanding of their mechanisms of action and compounds involved in the bioactive properties could prompt the development of new industrial applications.

2.1. *A. millefolium*

This plant—traditionally known as yarrow—grows in Asia, Africa, Europe, and America, and it is very common in folk medicine.[53] Stems, leaves (L), and special flowers (FL) are used to prepare an infusion or decoction for the treatment of diabetes and gastrointestinal, spasmodic, cardiovascular, respiratory, and hepatobiliary disorders, and they have been used as a

Table 1 Asteraceae plants in traditional medicine

Plant	Part used	Mode of application	Properties	Diseases treated	Ref.
Achillea millefolium	AP, L, FL	Infusion, decoction	Analgesic, anti-spasmodic, hemostatic, antioxidant, anti-inflammatory, anti-diabetic, antimicrobial, liver protector	Diabetes/gastrointestinal, respiratory, hepatobiliary and inflammatory disorders/wounds	1–3
Arnica montana	R, FL	Tinctures, ointments	Antioxidant, anti-inflammatory and antimicrobial	Bruises/sprains/rheumatic pain/skin inflammation/wounds	4–6
Bellis perennis	Fresh and dried FL	Infusions, decoction, ointments	Antioxidant, anti-inflammatory, anticancer, antimicrobial, anxiolytic, diuretic, digestive or antipyretic	Bruises/wounds/cold/gastrointestinal problems/headaches/skin disorders	7 and 8
Calendula officinalis	FL	Aqueous extracts, ointments and other remedies	Antioxidant, anti-inflammatory, antibacterial, antiviral, cytotoxic and wound healing, hypotensive	Cuts/wounds/dermatological diseases/skin and oral inflammation/fevers/gastritis/jaundice/hypotension/rheumatism	9–13
Chamaemelum nobile	FL	Decoction, infusions, extracts, lotions	Antibacterial, antifungal, insecticidal, hypotensive, anti-platelet aggregation, anti-inflammatory, hypoglycemic, antioxidant, cytotoxic, bronchodilator, analgesic, emollient	Fever/sun stroke/insomnia/back pain/neuralgia/rheumatism/skin disorders/indigestion/flatulence/diarrhea/headaches/nervousness/gout/eye irritation	14–17
Eupatorium cannabinum	AP	Infusion, decoction	Choleretic, laxative, diuretic and hypocholesterolemic	skin diseases/hepatitis/headache/diarrhea/diabetes/hypertension/respiratory disorders	18–21
Helichrysum stoechas	AP, FL	Infusion	Diuretic, digestive	Cold/fever, nervousness/urinary bladder, gallbladder and pancreas problems/respiratory disorders/nervousness	17, 22 and 23
Taraxacum officinale	L, R, FL	Infusion, decoction	Diuretic expectorant, laxative, liver tonic, wound healing	Digestive problems/liver and gallbladder complains/skin problems/eye inflammation/arthritis and rheumatism	24–27

Abbreviations: AP, aerial parts; R, roots; FL, flowers; L, leaves.

hemostatic and externally applied to heal wound and inflammation.[54,55] The main phytochemical compounds that have been isolated from *A. millefolium* are EO, PC (including PA and F, *e.g.*, apigenin, rutin, or lutein), fatty acids, amino acids, tannins, and Te.[53,54] Different biological properties have been attributed to this plant, such as antioxidant, anti-inflammatory, analgesic, hemostatic, antitumor, antidiabetic, antimicrobial, spasmolytic, liver protector, anti-asthmatic, and anxiolytic,[54,56–58] which could be of interest for food enrichment.

Starting with the antioxidant activity, numerous studies have evaluated the antioxidant activity of different extracts, formulations, and compounds of *A. millefolium*. For example, the methanolic extract, infusion, and decoction of wild and commercial yarrow were compared in terms of their antioxidant activity *in vitro*, using 2,2-diphenyl-1-picrylhydrazyl (DPPH) assay, ferric reducing/antioxidant power assay (FRAP), β-carotene/linoleate assay (inhibition of β-carotene bleaching), and the inhibition of lipid peroxidation in porcine brain, using thiobarbituric-acid-reactive substances (commonly known as the TBARS assay). The results showed that commercial yarrow presented a higher antioxidant activity compared with the wild samples. Decoctions presented greater DPPH scavenging activity (EC_{50}: 0.20 mg mL^{-1}), inhibition of β-carotene bleaching (EC_{50}: 0.22 mg mL^{-1}), and TBARS inhibition (EC_{50}: 0.08 mg mL^{-1}), whereas infusions showed the greatest reducing power (EC_{50}: 0.13 mg mL^{-1}) using a FRAP test.[59] A recent study evaluated the radical scavenging activity of different extracts of *A. millefolium* by DPPH and 2,2′-azinobis(3-ethylbenzothiazoline-6-sulfonic) acid (ABTS) scavenging assays. According to the results, the water extract exhibited the greatest antioxidant activity and a correlation between the PC content and results was observed.[60] EO from this plant have been also found to present antioxidant properties and could scavenge DPPH radicals.[61] The antioxidant effects of this plant have been also corroborated using *in vivo* models, increasing the antioxidant defenses and reducing lipid peroxidation in different models, such as acetic-acid-induced gastric ulcers[62] and cyclophosphamide-[63] and nicotine-induced toxicity in rats.[64]

Regarding antiinflammatory properties, EO seem to be responsible for this activity. For example, EO of yarrow significantly repressed the production of nitric oxide (NO) in macrophages stimulated by lipopolysaccharide (LPS).[65] A later study reported that different *A. millefolium* fractions reduced the production of tumor necrosis factor alpha (TNF-α), interleukin 8 (IL8), and IL6 in LPS-activated macrophages. In particular, the chemical composition of the most active fractions revealed a higher content in the EO components.[66] Antiinflammatory effects have been also observed *in vivo*. Traditional oil yarrow extracts were used in the treatment of the irritated skin of volunteers. The results showed that the extracts improved the erythema index, as well as skin capacitance and its pH, demonstrating significant antiinflammatory

Table 2 Studies on *A. millefolium*, *A. montana*, *B. perennis*, *C. officinalis*, *C. nobile*, *E. cannabinum*, *H. stoechas*, and *T. officinale* bioactivities and their related compounds

Effects	Effects observed	Compounds	Ref.
Achillea millefolium			
Antioxidant	*In vitro*: Positive results in DPPH, ABTS, FRAP, β-carotene bleaching, TBARS assays *In vivo*: Increase antioxidant defense, reduction of lipid peroxidation	PC, EO	28–34
Anti-inflammatory	Inhibition of pro-inflammatory cytokines in LPS-stimulated macrophages	EO	35–37
Antitumor	Cell cycle arrest & apoptosis of HCT-15, NCI-H460, HeLa, K562, MiaPaca-2, MCF, HepG2 cells	PC, F	28, 29 and 38–40
Antimicrobial	Inhibition of bacteria *S. aureus, S. typhimurium, S. mutans, B. cereus, E. coli, P. aeruginosa, P. mirabilis* and fungi *C. albicans, B. cinerea, R. stolonifera, V. dahliae, A. niger* and *C. gloeosporioides*	EO	41 and 42
Other activities	Relax the airways of rat trachea. Anxiolytic effects on mice. Improvement of skin hydration and appearance	NA	1, 43 and 44
Arnica montana			
Antioxidant	*In vitro*: Positive results in DPPH, ABTS, inhibition of linoleic acid peroxidation, FRAP and chelating power. Inhibition of lipoxygenase and xanthine oxidase. Reduction of oxidative stress in mouse fibroblast L929 cells. *In vivo*: Antioxidant defense, reduction of lipid and protein oxidative damage	PC, F, SL, Ps	4 and 45–48
Anti-inflammatory	*In vitro* and *In vivo*: Inhibition of NF-κB pathway, reduction of pro-inflammatory cytokines	SL, F, PC, PS	45–49
Antitumor	Cytotoxic effect against anaplastic astrocytoma and glioblastoma multiform cells	EO	50
Bellis perennis			
Antioxidant	Positive results in DPPH, ABTS, FRAP, ORAC and β-carotene bleaching assays	PC, F	7 and 51–53
Anti-inflammatory	Inhibition of NO production in LPS-stimulated RAW 264.7 cells	PC, Te	52 and 53
Antitumor	Inhibition of HL-60, MCF-7, HepG2/C3A, A-549 and DLD-1 cancer lines	Sa, NA	53 and 54
Antibacterial	Inhibitory activity against *S. pyogenes*, *S. aureus* and *S. epidermis*	NA	53
Other properties	Accelerated wound healing, hematoprotective and nephroprotective activities, hypolipidemic effects	NA	52, 55 and 56
Calendula officinalis			
Antioxidant	*In vitro*: Positive results in DPPH, ABTS, FRAP, chelating power, β-carotene bleaching, TBARS, scavenging of NO, hydroxyl radical and lipid peroxyl radicals. *In vivo*: Increase antioxidant defense, reduction of lipid peroxidation	PC, F	9–12, 57 and 58
Anti-inflammatory	*In vitro*: Inhibition of TNF-α in LPS-stimulated macrophages *In vivo*: Inhibition of pro-inflammatory cytokines and the expression of Cox-2. Reduction inflammation of different disease-model animals	F, Tt	59–61
Wound healing	Activation of NF-κB pathway, stimulation of re-epithelization	Tt, Ca, EO	13
Antitumor	Cytotoxic effects against HeLa, HepG2, K562, colon, melanoma and leukemia cancer cells	Tt, F	9, 59 and 62
Antimicrobial	Inhibitory effects on *E. coli, P. aeruginosa, B. subtilis*, *S. aureus, L. monocytogenes, S. typhimurium*, *C. albicans*, *C. parapsilosis* and *A. niger.* Inhibition of promastigotes and amastigotes of *L. major*	NA	12, 63 and 64
Chamaemelum nobile			
Antioxidant	Positive results in DPPH, FRAP, inhibition of lipid peroxidation	PC, OA, EO	16 and 65
Anti-inflammatory	*In vitro*: Inhibition of inflammatory pathways *In vivo*: Inhibitory and analgesic effects on paw edema	PC, Ps	15, 66 and 67
Antitumor	Cytotoxic effects MCF-7, NCI-H460, HCT-15, HeLa, HepG2, K562, SKMEL-3 cancer cell lines	PC	14 and 16
Antimicrobial	*In vitro*: Inhibitory activity against *S. aureus*, *Bacillus* sp., *P. aeruginosa* and *E. coli.* *In vivo*: Inhibition of *P. aeruginosa* in wounds	PC, EO	65, 68 and 69
Eupatorium cannabinum			
Antioxidant	Positive results in DPPH assay and electrochemical potential sweep technique.	PC, EO	18 and 19
Anti-inflammatory	*In vitro*: Modulation of pro-inflammatory factors *In vivo*: Reduction of pro-inflammatory cytokines in mice models	SL	21 and 70
Antitumor	Cytotoxic effects against Jurkat, CCRF-CEM, HL-60, BT-20, HepG2, Caco-2 cell lines	NA	21, 70 and 71
Antimicrobial	Inhibition of *E. coli*, *B. cereus*, *S. aureus*, *E. faecalis, S. faecalis, B. subtilis, P. mirabilis, E. coli, S. typhi, P. aeruginosa* and *C. albicans, B. theobromae, C. gloeosporioides*	EO	72–74
Helichrysum stoechas			
Antioxidant	Positive results in DPPH, ABTS, FRAP, CUPRAC, β-carotene bleaching and TBARS assays	PC	23 and 75–77
Anti-inflammatory	Inhibition of NF-κB and TNF-α	NA	78
Antitumor	Inhibit the proliferation of HeLa cells	NA	23
Antimicrobial	Inhibitory effects against *E. coli*, *P. aeruginosa*, *P. mirabilis*, *K. pneumoniae*, A. *baumannii, E. faecalis*, *S. aureus, M. phlei, C. albicans* and *C. parapsilosis*	NA	75 and 79
Neuroprotective	Inhibition of enzymes related to central nervous system and neurotransmitter metabolism	NA	23 and 75
Taraxacum officinale			
Antioxidant	*In vitro*: Scavenging activity against DPPH, OH^- and O_2^-, inhibition of lipid peroxidation. Induction of antioxidant defense-related genes in RAW 264.7 cells. Blocks H_2O_2-induced toxicity in L02 cells *In vivo*: Increase O_2^- scavenging activity, reduced lipid peroxidation and protein oxidative damage	SL, PIEs, Ps, HA	26, 80 and 81
Anti-inflammatory	*In vitro*: Inhibition of NF-κB inflammatory pathway, reduction of pro-inflammatory cytokines *In vivo*: Inhibition of pro-inflammatory compounds and genes related with inflammation	PC, Ps	82–85
Antitumor	Induces apoptosis in HepG2, MCF7 and HCT116 cell lines	Ps	86 and 87

Table 2 *(Contd.)*

Effects	Effects observed	Compounds	Ref.
Antimicrobial	Inhibition of *S. aureus, E. coli, K. pneumonia, P. mirabilis, Micrococcus luteus, Vibrio cholera, P. aeruginosa, B. cereus, Shigella sonnei, C. albicans, C. neoformans, A. niger* and B. *cinerea*. Inhibition of influenza and hepatitis C viruses	NA	27 and 88–90
Other properties	Anticoagulant, α-glucosidase inhibitory activity, immunostimulant or neuroprotective	NA	80 and 91–94

Compounds: NA, not analyzed; PC, phenolic compounds; F, flavonoids; Ps, polysaccharides; Te, terpenoids; Tt, triterpenoids; EO, essential oil; SL: sesquiterpene lactones; Sa: saponins; Ca: carotenoids; OA, organic acids; PIEs, 4-hydroxyphenylacetate inositol esters; HA, hydroxycinnamic acids.

properties, thereby justifying the traditional uses of *A. millefolium.*[67] It is also beneficial as a therapy in the case of patients with multiple sclerosis. For its evaluation, a placebo-controlled clinical trial was carried out over a year with different amounts of *A. millefolium* extract (0.2 and 0.5 g day^{-1}), which significantly reduced the relapse rate and prevented progression in multiple sclerosis associated with relieving inflammation. Thus, this plant may become complementary treatment for multiple sclerosis[68] and also toward the relief of pain from diseases such as primary dysmenorrhea; this has been corroborated in a trial carried out with 50 women in western Iran.[69]

This plant has also been reported for presenting antitumor properties, inducing cell-lifecycle arrest, and apoptosis of different cancer lines. PC have been reported to play an important role in these cases. For example, casticin—F isolated from yarrow—induced the apoptosis and cell-lifecycle arrest at the G2/M stage for different cancer cell lines.[70] A later study reported that the hydroethanolic extracts of yarrow displayed inhibitory effects on small-cell lung cancer (NCI-H460) and colorectal adenocarcinoma (HCT-15) cell lines (with GI_{50} values of 187.3 and 70.8 μg mL^{-1}, respectively) by altering the cell lifecycle and induction of apoptosis. The authors suggested that PC could be the bioactive compounds responsible for the antitumor activity.[71] A study by Abou Baker (2020), as mentioned earlier, also determined the cytotoxicity of different extracts against several cancer cell lines. Ethyl acetate extracts showed the greatest cytotoxic effects against cervical carcinoma (HeLa) and chronic myelogenous leukemia (K562) cancer cells, with IC_{50} values of 0.58 and 0.73 μg mL^{-1}, respectively. Similar to the previous example, the antitumor activity may be related to the high amount of PC present in the extracts.[60] Other cancer cell lines that have been inhibited by *A. millefolium* include breast adenocarcinoma (MCF-7), hepatocellular carcinoma (HepG2), and pancreatic human tumor cell line (MiaPaca-2).[59,72]

Several studies have demonstrated the antibacterial and antifungal activities of *A. millefolium*. For instance, EO extracted from this plant showed *in vitro* antibacterial activity against different bacteria and fungi. Regarding bacteria, *Staphylococcus aureus*, *Salmonella typhimurium* (minimal inhibitory concentration (MIC) of 125 μg mL^{-1}), and *Streptococcus mutans* (MIC of 250 μg mL^{-1}) were the most affected, while *Candida albicans* strains were the most susceptible fungi species (MIC: 125–250 μg mL^{-1}).[45] In the study by Kazemi (2015), *Bacillus cereus*, *Escherichia coli*, *Pseudomonas aeruginosa*, and *Proteus mirabilis* were the most affected bacterial species by the EO (MIC: 2.5 μg mL^{-1}). With regard to the *C. albicans* and *Aspergillus fumigatus* fungi, the MIC values were 1 and 2 μg mL^{-1}, respectively.[65] Yarrow EO have been reported to inhibit other fungi, namely, *Botrytis cinerea*, *Rhizopus stolonifera*, *Verticillium dahliae*, *A. niger*, and *Colletotrichum gloeosporioides.*[73] In an *in vivo* study involving cancer patients, a trial was performed using *A. millefolium* distillate as a mouthwash to reduce oral mucositis. This solution could be given to all patients during chemotherapy and had no side-effects.[74]

Other activities have been attributed to *A. millefolium*, such as anti-asthmatic and anxiolytic. It facilitated wound healing in a study conducted with first-time pregnant women with episiotomy wounds[75] Organic and hydroalcoholic extracts have demonstrated the relaxation of airways in the rings of isolated rat trachea in a dose-dependent manner. Hexanic extracts were the most efficient ones, which acted through the blockage of calcium channels and NO release.[54] Regarding anxiolytic activity, the oral administration of yarrow hydroalcoholic extracts produced anxiolytic effects in mice, with a behavior similar of that caused by diazepam.[57]

2.2. *A. montana*

Commonly known as arnica, *A. montana* is native to the central mountains in Europe. R and FL extracts have been externally applied as tinctures or ointments to alleviate different problems such as bruises, sprains, rheumatic pain, or skin inflammation; it is even used in veterinary treatment for joint inflammations as well as for cleaning and treating wounds in the skin.[76,77] Among the phytochemical compounds present in this plant, PA, F, EO, Te, and SL could be highlighted. Some studies have attributed arnica to have antioxidant and antiinflammatory properties.[77,78] However, despite being a plant widely used in traditional medicine and currently employed in commercial products, there are a few studies that support their properties, compared with other plants of the Asteraceae family. Other less studied bioactivities of *A. montana* include anticancer, antimicrobial, immunomodulation, hepatoprotective, analgesic, or anticough properties[79,80]

The antioxidant properties of this plant have been briefly studied, but it has been described that F and SL are the primary causes of this action.[81] The antioxidant activity of tinc-

tures from different parts (FL, herb, and rhizome) of *A. montana* was assessed by DPPH assay, inhibition of linoleic acid peroxidation, FRAP, and chelating power assays. Except for the case of linoleic acid peroxidation, a correlation was observed between the antioxidant activity with the PC content of each part of the plant. In addition, tinctures displayed high *in vitro* inhibitory activity in a dose-dependent manner against lipoxygenase and xanthine oxidase—two enzymes that produce reactive oxygen species (ROS).[81] The ability to scavenge free radicals of arnica PC and polysaccharides (Ps)-rich extracts has been assessed by the DPPH assay. The results showed that the inhibition of DPPH was augmented in a dose-dependent manner, the PC-rich extract being the most efficient (IC_{50}: 0.66 mg mL^{-1}). In addition, the extracts and also their liposomal formulations significantly reduced the oxidative stress caused by H_2O_2 in mouse fibroblast L929 cell culture.[82] The EO of *A. montana* have also demonstrated antioxidant properties. DPPH and ABTS assays conducted with EO showed IC_{50} values of 4.79 and 0.35 mg mL^{-1}, respectively. The results of FRAP (IC_{50}: 31.15 mg mL^{-1}) and phosphomolybdenum assays (55.69 mg ascorbic acid equivalents per g) also demonstrated the antioxidant effects of arnica EOs.[76] Several *in vivo* studies have corroborated the antioxidant properties of arnica. For example, methanol extracts of arnica FL were orally administered to collagen-induced arthritis rats; a significant improvement in the antioxidant defense was observed in the joints, spleen, and plasma of the treated animals (reduced lipid peroxidation and protein oxidative modification) compared with the control.[83] Thus, the traditional use of this plant in treating rheumatoid arthritis is scientifically justified. Recently, the topical application of an ointment containing *A. montana* tincture has been demonstrated to reduce the oxidative stress produced by UVB radiation in mice ears, reducing carbonylated proteins and lipid peroxidation and improving antioxidant defense.[84]

Several studies have evaluated the antiinflammatory properties, explaining the use of this plant in inflammatory disorders. It has been described that SL and F, in a lesser extent, act through the inhibition of nuclear factor kappa-light-chain enhancer of activated B cells (NF-κB), which regulates the transcription of genes involved in inflammation.[81,82] Extracts of *A. montana* have been reported to exert potent inhibitory effects against human neutrophil elastase (released by neutrophils during inflammation) and NF-κB, attributed to the high content of SL.[85] A further study demonstrated that *A. montana* tinctures suppressed the transcription of interstitial collagenase-3 and collagenase-1 in bovine and human articular chondrocytes due to the inhibition of the DNA binding of NF-κB and activator protein-1. In the previous study of Gaspar *et al.* (2014), PC and Ps extracts and their liposomal formulations exerted antiinflammatory effects in H_2O_2-treated L929 cell culture by reducing the production of IL-6, IL-8, and TNF-α.[82] Antiinflammatory properties have also been evaluated in collagen-induced arthritis rats and UVB-radiated mice. In both cases, *A. montana* reduced the levels of proinflammatory cytokines, such as NO, NF-κB, IL-1β, IL-6, and TNF-α.[83,84]

2.3. *B. perennis*

Traditionally known as the common daisy, this plant is native to western, central, and Northern Europe and Middle Asia. Usually, fresh or dried FL are prepared in infusions, decoctions, and ointments. They have been used to treat bruises, wounds, cold, gastrointestinal problems, headaches, and skin disorders, among other diseases; they also have been consumed as diuretic, digestive, or antipyretic.[86,87] In their phytochemical composition, PA, F, EO, and Tt Sa are the major components described[88,89] and the bioactivities reported include antioxidant, antiinflammatory, anticancer, antimicrobial, anxiolytic, anti-hyperlipidemic, or wound healing.[87,89,90]

Several studies have evaluated the antioxidant properties of *B. perennis*, which have been attributed to PC. For example, a significant correlation between PC and F contents and the results of DPPH and oxygen radical absorbance capacity (ORAC) assay has been observed in several studies.[88,91] Recently, the antioxidant activity of methanolic *B. perennis* extracts, among other plants, has been evaluated using DPPH, ABTS, β-carotene bleaching method, and FRAP assays. In this case, the IC_{50} value for DPPH was 168.4 μg mL^{-1} while that for the ABTS assay was 74.69 μg mL^{-1}. Further, β-carotene bleaching afforded an IC_{50} value of 78.45 μg mL^{-1} after 30 min and 85.28 μg mL^{-1} after 60 min. Finally, for the FRAP assay, the IC_{50} value was 557.89 μg mL^{-1}.[90]

The antiinflammatory properties of the common daisy have been evaluated *in vitro*. *B. perennis* extracts were evaluated for studying the inhibition of NO production in murine macrophage LPS-stimulated RAW 264.7 cells, where methanolic and dichloromethane extracts were found to be the most effective. The authors considered that PC and Te were the bioactive compounds responsible for this action.[91] Similarly, in a further study, methanolic *B. perennis* extract has demonstrated to reduce NO production in a dose-dependent manner in LPS-stimulated RAW 264.7 cells, without affecting the cell viability. The results of this study showed that the extract reduced NO production in all the tested concentrations (25–1000 mg mL^{-1}), causing a 71.7% inhibition at the maximum concentration.[90] Although more studies are necessary to elucidate the mechanisms of action of the antiinflammatory effects of *B. perennis* and corroborate their effects using *in vivo* models, these studies support its traditional use in various diseases such as eczema or rheumatism.

To our knowledge, few studies have reported the anticancer properties of *B. perennis*. Sa isolated from R exhibited cytotoxic effects against human promyelocytic leukemia (HL-60) cells. In another study, methanol extracts presented a modest anticancer effect against MCF-7 and HepG2/C3A cell line. Recently, it has been shown that daisy extracts had cytotoxic effects against human lung carcinoma (A-549) and human colon adenocarcinoma (DLD-1) cell lines.[91] This study also evaluated the antibacterial properties of the extracts. In particular, ethyl acetate fraction was the one that inhibited the most species of microorganisms, namely, *Streptococcus pyogenes*, *S. aureus*, *S. epidermis*, and *Enterococcus cloacae*, with inhibitory zones of

12.4, 10.7, 12.9, and 15.9 mm. In general, the extracts were more effective against Gram-positive species.[91]

2.4. *C. officinalis*

This plant, commonly known as pot marigold, is widely distributed and extends throughout Europe and Asia and can be also found in Australia.[92,93] Traditionally, *C. officinalis* has provided different uses, including the elaboration of food, dyes, cosmetics, and traditional remedies.[92,94] FL were used to prepare aqueous extracts, ointments, and other remedies, particularly for the treatment of cuts, wounds, dermatological diseases, and skin and oral inflammation, as well as other disorders such as fever, gastritis, jaundice, hypotension, or rheumatism.[47,95,96] Numerous phytochemicals have been identified in *C. officinalis*, such as PC (including PA, F, coumarins, *etc*.), Te, and Ca.[95,97] Its reported bioactive properties include antioxidant, antiinflammatory, antibacterial, antiviral, cytotoxic, and wound healing.[97,98]

Several studies have demonstrated the antioxidant properties of *C. officinalis*. For example, the water extracts of *C. officinalis* have shown to scavenge DPPH, hydroxyl radical, and lipid peroxyl radicals in a dose-dependent manner, showing a clear correlation with the PC content of the extract.[99] Similarly, infusion and hydromethanolic extracts were evaluated using DPPH, FRAP, β-carotene bleaching inhibition, and TBARS assays. In all the cases, an antioxidant effect was observed, which could be attributed to the presence of F, demonstrating that these compounds are involved in the antioxidant properties of the plant.[95] A recent study revealed that the lyophilized extracts of marigold inhibited the lipid peroxidation of *in vitro* brain tissues of Wistar rats.[97] Antioxidant effects have also been reported *in vivo.* Wistar rats subjected to burn injury fed with *C. officinalis* aqueous extracts showed a better antioxidant defense system than the control animals. Lipid peroxidation and tissue damage markers were significantly lower in a dose-dependent manner.[98] Hydroalcoholic extracts of *C. officinalis* also reduced lipid peroxidation when administered to male Sprague-Dawley rats.[100] In hairless mice irradiated with UVB, a topical formulation containing *C. officinalis* effectively protected the skin against oxidative damage, maintaining reduced glutathione levels close to nontreated animals and reducing the histological changes.[101]

Several studies have evaluated the antiinflammatory properties of *C. officinalis*, mainly *in vivo*. In LPS-stimulated macrophages, an FL extract significantly reduced the production of TNF-α. The same extract also inhibited paw edema induced by carrageenan, dextran, and formalin in mice when administered orally. The results showed that *C. officinalis* modified the activity of proinflammatory cytokines, such as IL-1β, IL-6, TNF-α, and interferon-γ, and it also inhibited the expression of cyclooxygenase-2 (COX-2).[102] Different Tt isolated from the FL of *C. officinalis* showed strong antiinflammatory activity on 12-O-tetradecanoylphorbol-13-acetate-induced inflammation in mice.[103] More recently, the hydroalcoholic extracts of marigold inhibited acute inflammation caused by ulcerative colitis effects on rats, which could be attributed to the presence of bioactive compounds in the extracts, including F and Tt.[100]

The most popularly reported properties of marigold, *i.e.*, the wound healing ones, have been corroborated. Scratch assays showed that compounds from *C. officinalis* accelerated wound closure in NIH-3T3 fibroblasts human dermal fibroblast. In human keratinocytes, *n*-hexane and ethanol extracts modulated the initial phase of wound healing, which is temporal inflammation necessary in the beginning of the process. The application of extracts led to the activation of NF-κB and the production of IL-8. This proinflammatory cytokine is involved in the proliferation and migration of keratinocytes, which facilitates re-epithelization and wound healing. Although the compounds involved in this action were not analyzed, Tt and Ca are considered to play a role in it.[47]

Other properties such as antitumor or antimicrobial have been attributed to this plant. With regard to its antitumor effects, it has been demonstrated that the hydromethanolic extracts of *C. officinalis* exhibited a cytotoxic effect against HeLa and HepG2 cancer cell lines, while no cytotoxic effect was observed in nontumor cells.[95] Marigold tea showed a strong cytotoxic effect against different cancer cell lines, particularly toward Fem-x cells, followed by HeLa and human erythroleukemia (K562) cells. The authors considered that F-glycosides were involved in the observed effects.[104] Other compounds, such as Tt extracted from *C. officinalis*, displayed cytotoxic effects against colon, melanoma, and leukemia cancer cells.[103] In the case of antimicrobial activity, *C. officinalis* exhibited inhibitory effects against bacterial species such as *E. coli*, *P. aeruginosa*, *B. subtilis*, *S. aureus*, *L. monocytogenes*, and *S. typhimurium*, as well as fungi species such as *C. albicans*, *C. parapsilosis*, and *A. niger*.[92,97,105] Finally, *C. officinalis* has also shown anti-leishmania effects, inhibiting the growth of promastigotes and amastigotes of *Leishmania major.*[105]

2.5. *C. nobile*

C. nobile, called Roman chamomile, is a perennial herb found in wild and cultivated habitats in Western Europe, North America, and Northern Africa.[106,107] This plant has a long tradition and has been used to alleviate fever and sun stroke, insomnia, back pain, neuralgia, rheumatism, skin conditions, indigestion, flatulence, headaches, and gout.[108,109] Bioactive compounds identified in Roman chamomile include Te, F, and coumarins, as well as other components such as angelic and tiglic acid esters, anthemic acid, fatty acids, and choline.[107] Numerous biological properties have been documented for *C. nobile*, such as antioxidant, antibacterial, antifungal, insecticidal, hypotensive, anti-platelet aggregation, antiinflammatory, hypoglycemic, cytotoxic, bronchodilator, and endocrine.[110]

The antioxidant properties of this plant have been evaluated in several studies. For example, methanolic extract, decoction, and infusion of *C. nobile* were evaluated in terms of composition and antioxidant potential using DDPH, FRAP, and

inhibition of lipid peroxidation assays using β-carotene model system in liposomes and TBARS assay in brain homogenates. According to the results, methanolic extract presented a better β-carotene bleaching activity and TBARS inhibition (EC_{50} values of 443.32 and 82.33 μg mL^{-1}, respectively), while infusion achieved better DPPH scavenging results (EC_{50}: 408.46 μg mL^{-1}). These results may be related to the high PC content of methanolic extracts and organic acids (OA) in the case of infusion.[106] The EO of *C. nobile* also present antioxidant properties, as showed by the DPPH radical scavenging and FRAP assays (602.73 and 0.13 μg mL^{-1}, respectively).[111]

As evident in the literature, the antiinflammatory properties of *C. nobile* are one of the most studied and described. Six octulosonic acid derivatives were isolated from FL and were evaluated using different assays directing nonsteroidal antiinflammatory drugs-activated gene-1 (NAG-1), NF-κB, inducible nitric oxide synthase (iNOS), and ROS. In addition, the effects on peroxisome proliferator-activated receptors (PPARα and PPARγ) and liver X receptor, as well as factors related to the inflammation process and metabolic disorder, were evaluated. All the compounds increased the NAG-1 activity, which is involved in the antiinflammatory process, and inhibited ROS production, reducing the cellular oxidative stress. Some compounds also activated PPARγ and PPARα, resulting in the suppression of the inflammatory process. Considering these results, these compounds may partially explain the antiinflammatory properties of *C. nobile.*[112] Recently, the oral administration of EO from Roman chamomile reduced paw inflammation and exerted analgesic effects against thermal pain, corroborating the use of *C. nobile* in the treatment of inflammatory disorders.[113] Ps and EOs of Roman chamomile have been also reported to possess *in vivo* antiinflammatory effects.[110]

C. nobile has been described to present cytotoxic effects against several cancer cell lines. In the study of Guimarães *et al.* (2013), the effects of methanolic extracts, infusions, and decoctions in MCF-7, NCI-H460, HCT-15, HeLa, and HepG2 were evaluated. Methanolic extracts presented the best cytotoxic activity, with GI_{50} values ranging between 82.52 μg mL^{-1} for MCF-7 and 168.40 μg mL^{-1} for HepG2. These results were attributed to the high content of PC.[106] Similarly, Kandelous *et al.* (2016) investigated the anticancer as well as apoptotic activity of ethyl acetate fraction of *C. nobile* on different cancerous cell lines. The obtained results showed that the ethyl acetate fraction of *C. nobile* exhibited antiproliferative activity on MCF-7, K562, and human melanoma (SKMEL-3) cell lines, causing cell apoptosis, while minimal growth inhibitory response in normal cells.[108]

Regarding antimicrobial properties, several studies have evaluated the extracts and compounds of *C. nobile*, both *in vitro* and *in vivo*. The water extracts of Roman chamomile, rich in PC, showed inhibitory activity against *S. aureus*, *Bacillus* sp., *P. aeruginosa*, and *E. coli*, with inhibition zones ranging between 12.66 and 10 mm.[114] The EO of *C. nobile* have been reported to present relatively low *in vitro* antifungal properties against *A. fumigatus*, *A. flavus*, *A. ochraceus*, and *Penicillium citrinum.*[111] In another study, the authors investigated the antimicrobial and wound healing properties of *C. nobile* against *P. aeruginosa* in rats. An ointment was prepared with the ethanolic extract of Roman chamomile and applied in previously infected wounds. The results showed that the *C. nobile* ointment significantly inhibited *P. aeruginosa* and also stimulated wound healing compared with the control.[115]

2.6. *E. cannabinum*

E. cannabinum, commonly known as hemp-agrimony, is a herbaceous plant common in Europe, North America, Central Asia, and Northern Africa. It has been used in traditional medicine as a good choleretic, laxative, diuretic, and hypocholesterolemic, as well as to treat skin diseases (*e.g.*, psoriasis, eczema, and boils), hepatitis, headache, diarrhea, diabetes mellitus, and hypertension.[116,117] The presence of F, Ps, nontoxic alkaloids, SL, and EO is related to some biological properties, such as antioxidant, cytostatic, antibacterial, or immunological properties.[117–119] Pyrrolizidine alkaloids of *E. cannabinum* comprise echinatine isomers, lycopsamine, and intermedine, as well as a number of their beta-acetyl, beta-angelyl/tiglyl, and beta-(iso)valeryl esters. From the alkaline aqueous extract of *E. cannabinum*, polysaccharides were isolated and identified as 4-*O*-methylglucuronoxylans. Finally, flavones and flavonol glycosides were identified in the aerial parts (AP) of *E. cannabinum*, comprising 6-methoxyflavones hispidulin and eupafolin, flavonol glycosides astragalin, kaempferol-3-rutinoside, hyperoxide, isoquercitin, and rutin.[120] This is a plant with a long history in traditional medicine and some studies have been conducted to analyze its properties.

Regarding the antioxidant properties, hydroalcoholic extracts rich in PC such as caffeic acids and methoxylated flavones—eupatorin and eupatilin B—showed a DPPH scavenging activity of 59% at 3 mg mL^{-1}.[117] The antioxidant potential of hemp-agrimony EO was assessed by the electrochemical potential sweep technique, showing higher antioxidant activity than quercetin.[119] In the case of antiinflammatory activity, more studies have been conducted. Ethanolic extracts modulated the inflammatory signals of stimulated neutrophils, like ROS, IL-8, production and release of TNF-α, and expression of adhesion molecules. Eupatoriopicrin, the major SL found in *E. cannabinum*, has shown inhibitory effects on the release of IL-8 and TNF-α by activated human neutrophils.[121] In mice models subjected to LPS-induced damage, it has been observed that the injection of *E. cannabinum* extracts reduced the levels of proinflammatory cytokines TNF-α, IL-1β, and IL-6.[118] In thioglycolate-induced peritonitis mice models, eupatoriopicrin suppressed the inflammatory response.[121]

E. cannabinum has been reported to have cytotoxic effects against different cancer cell lines. For example, hydroalcoholic extracts exerted a dose–response cytotoxic effect against leukemia peripheral blood lymphocytes (Jurkat cells) at concentrations ranging between 7 and 500 μg mL^{-1}.[117] Ethanolic extract also showed anticancer effects against the HT29 colon cancer line, reducing cell viability and producing mitotic and nuclear disruption and nonapoptotic cell death. In addition,

the extract enhanced the effects of two compounds (bisphenol A and doxorubicin) used as chemotherapeutic agents, suggesting that *E. cannabinum* can be used as an adjuvant in cancer treatment.[122] Thymol derivatives, isolated from the R *of E. cannabinum*, displayed cytotoxic effects against DLD-1, human lymphoblastic leukemia cell line (CCRF-CEM), and HL-60 cell lines.[116] A recent study evaluated the antiproliferative effects of chloroform and water extracts of hemp-agrimony against *in vitro* human mammary gland/breast carcinoma (BT-20), HepG2, human colorectal adenocarcinoma (Caco-2), and Jurkat cells. Chloroform extract was effective against all the cell lines, with IC_{50} of 7.35 μg mL^{-1} for Jurkat cells and over 100 μg mL^{-1} for HepG2 and BT-20. In the case of water extracts, only Jurkat cells were affected, with IC_{50} of 13.77 μg mL^{-1}. These results suggest that the active compounds may have a nonpolar character.[118]

Regarding the antimicrobial properties, different *E. cannabinum* extracts have shown inhibitory effects against *E. coli*, *B. cereus*, *S. aureus*, *E. faecalis*, and *C. albicans.*[123] EO inhibited the growth of *S. aureus*, *Streptococcus faecalis*, *B. subtilis*, *B. cereus*, *P. mirabilis*, *E. coli*, *S. typhi*, and *P. aeruginosa*, but Gram-positive bacteria were found to be the most sensitive.[124] EO have also demonstrated antifungal activity against fungi such as *Botryodiplodia theobromae* and *Colletotrichum gloeosporioides.*[125] Finally, the acetylcholinesterase inhibitory activity of *n*-hexane, ethyl acetate, and methanol extracts of the Iranian *E. cannabinum* have been investigated.[126]

2.7. *H. stoechas*

H. stoechas is the scientific name of an everlasting FL, which grows in the Iberian Peninsula. Traditionally, an infusion of FL and AP of this plant has been used to treat disorders such as influenza and cold, fever, and nervousness, as well as a diuretic and to treat gallbladder, urinary bladder, digestive, and pancreatic problems.[50,127,128] Regarding the chemical composition, some compounds have been identified in this plant, including F, chalcones, phloroglucinol derivatives, EO, α-pyrones, and Te.[129] Several biological studies have described that *H. stoechas* possess antimicrobial, antiinflammatory, antioxidant, anti-α-glucosidase, anti-tyrosinase, anti-acetylcholinesterase, and anti-dipeptidyl peptidase-4 properties.[50,127]

Among the reported bioactivities of *H. stoechas*, the antioxidant property is the most analyzed. For example, methanolic extracts of *H. stoechas* FL and leafy stems were evaluated by means of the total antioxidant capacity, DPPH and ABTS radical scavenging assays, FRAP and chelating power, and inhibition of β-carotene bleaching. The results showed that, in general, the FL extracts had a higher antioxidant activity. It is worth highlighting the fact that the correlation analysis demonstrated a significant relationship between the results of the antioxidant analysis with the PC present in the samples, except the β-carotene bleaching assay.[129] Another study analyzed the antioxidant activity of the hydroalcoholic extract and decoction of *H. stoechas* and corroborated their antioxidant properties by means of the DPPH scavenging, FRAP, inhibition of β-carotene bleaching, and TBARS assays. Hydroalcoholic extract showed a greater antioxidant activity in all the assays (EC_{50} values between 79.84 and 36.62 μg mL^{-1}) compared with decoction due to the higher content of PC in the first preparation (135.61 mg g^{-1}).[128] Recently, different extraction techniques were employed to extract *H. stoechas* and their antioxidant activity was evaluated. Extracts obtained with accelerated solvent extraction showed antioxidant effects in DPPH, ABTS, FRAP, and cupric reducing antioxidant capacity (CUPRAC) assays. As reported in other studies, these results were correlated to the PC and F content, corroborating that these compounds are involved in this bioactivity. However, ultrasound-assisted extracts were the most active metal chelator. In this case, the compounds involved are believed to be thermolabile, which are degraded in other extractive techniques, but not by ultrasonication-assisted extraction (UAE).[50]

Other biological activities have been attributed to this everlasting plant. Extracts of *H. stoechas* have shown antimicrobial effects against different bacteria and fungi. For example, ethanolic and water extracts of this everlasting plant displayed inhibitory effects against *E. coli*, *P. aeruginosa*, *P. mirabilis*, *Klebsiella pneumoniae*, *Acinetobacter baumannii*, *E. faecalis*, *S. aureus*, *C. albicans*, and *C. parapsilosis.*[130] Dichloromethane extract of *H. stoechas* AP has also demonstrated antimicrobial effects against *S. aureus* and *Mycobacterium phlei* as well as the fungi *C. albicans.*[50] Regarding antiinflammatory and antitumor activities, fewer studies have been performed. It has been described that *H. stoechas* presents potent antiinflammatory effects *via* the inhibition of NF-κB and TNF-α.[131] With regard to antitumor activity, a methanolic extract of this plant inhibits the proliferation of HeLa cells *in vitro* in a dose-dependent manner.[127] Finally, *H. stoechas* inhibited enzymes related to the central nervous system and neurotransmitter metabolism, such as acetylcholinesterase, monoamine oxidase, and tyrosinase, suggesting that *H. stoechas* exhibits a neuroprotective action.[50,127]

2.8. *T. officinale*

T. officinale is a herbaceous perennial flowering plant, native to Eurasia and North and South Americas, although it is found as a weed in all parts of the world.[132] Traditionally, the FL, L, and R of this plant have been used to treat digestive problems, liver and gallbladder complaints, skin inflammation, and arthritic and rheumatic diseases, as well as a diuretic, expectorant, and laxative.[132–134] Among the selected plants of the Asteraceae family, *T. officinale* is the most studied; numerous authors have reported its biological activities, such as antioxidant, antiinflammatory, antidiabetic, antimicrobial, and anticancer activities, which have been related to several bioactive compounds such as hydroxycinnamic acids (HA), F, coumarins, SL, and Ps.[46,135]

The antioxidant properties of *T. officinale* extracts and compounds have been extensively studied, both *in vitro* and *in vivo*. Some of the most recent ones will be explained below. For example, different extracts have been demonstrated to scavenge several radicals, including DPPH, hydroxyl- and peroxyl-

radical-induced intracellular oxidation, and suppressed lipid oxidation. In particular, these effects were attributed to the abundant presence of PC.[46] Recently, the antioxidant effect of different R fractions was evaluated by DPPH assay and also assessing the effect on the oxidation markers on human plasma. The HA-rich fractions showed the best results in DPPH assays, but the fractions richer in SL and 4-hydroxyphenylacetate inositol esters (PIEs) exhibited the greatest antioxidant effect in plasma.[133] Water and ethanol extracts of *T. officinale* displayed antioxidant effects on RAW 264.7 cells by inducing heme oxygenase-1, an antioxidant enzyme.[136] Ps extracted from dandelion R also show antioxidant properties, which have been evaluated by radical scavenging assays (DPPH, hydroxyl radical, and superoxide anion) and also in hepatic L02 cells subjected to H_2O_2-induced damage. The obtained results showed that Ps had the ability to scavenge all the radicals in a dose-dependent manner. In the cell culture, the Ps significantly reduced the toxicity associated with H_2O_2, exerting a protective effect without any cytotoxic effect.[134] Regarding *in vivo* studies, the oral administration of dandelion formulations displayed antioxidant effects in obese rats,[137] rabbits with a high-cholesterol diet, or alcohol-induced liver damage in mice.[46,138,139]

Several studies have analyzed the antiinflammatory properties of this plant. Methanol and water extracts of dandelion significantly reduced the inflammatory process caused by LPS in RAW 264.7 cells; this was induced by inhibiting the activation of NF-κB, thereby preventing its translocation to the nucleus. Subsequently, the expressions of iNOS and NO were reduced, attenuating the inflammatory response. The authors considered that these effects could be associated with the high content of PC.[140] More recently, L extracts suppressed inflammation in cultured human colonic cells through the inhibition of NF-κB activation and the consequent reduction in the transcription of proinflammatory genes. Similar to the previous study, PC are considered to play a fundamental role in antiinflammatory activities.[141] In mice subjected to acetaminophen-induced hepatotoxicity, the administration of PC from dandelion lead to a reduction in the serum levels of TNF-α and IL-1β and the inhibition of iNOS and COX-2 expression.[142] Ps also have been reported to present antiinflammatory effects. In CCl_4-induced oxidative stress and inflammation-based rat models, the administration of dandelion Ps suppressed the activation of NF-κB and reduced the expression levels of proinflammatory factors such as iNOS, COX-2, TNF-α, and IL-1β.[143] The proven antiinflammatory effects corroborate the traditional use of this plant to treat disorders such as arthritis, rheumatism, and other inflammatory-related disorders.[144,145]

Numerous studies have demonstrated the anticancer property. An aqueous extract of dandelion R has been shown to induce apoptosis in colon cancer cells, but not in normal cells. In addition, the extract inhibited the migration and invasion of cancer cells in a scratch wound healing assay, suggesting anti-metastasis activity. The effect of *T. officinale* extract was also evaluated in xenograft mice. The obtained results demonstrated that the oral intake of the extract retarded the growth of cancerous cells.[146] R methanolic extracts of dandelion reduced—in a dose-dependent manner—the viability and triggered the apoptosis of HepG2, MCF7, and human colon HCT116 cancer cell lines.[147] A recent study demonstrated that dandelion Ps inhibited the proliferation of hepatocellular carcinoma cell *in vitro*, inducing cell apoptosis and cell-lifecycle arrest.[148]

T. officinale has shown antimicrobial properties against different bacteria such as *S. aureus*, *E. coli*, *K. pneumonia*, *P. mirabilis*, *Micrococcus luteus*, *Vibrio cholera*, *P. aeruginosa*, *B. cereus*, and *Shigella sonnei*, as well as fungi species such as *C. albicans*, *C. neoformans*, *A. niger*, and *B. cinerea.*[135,149] This plant also presents antiviral effects against influenza and hepatitis C viruses by the inhibition of replication.[150,151] Finally, other properties have been attributed to *T. officinale*, such as anticoagulant,[133,152] α-glucosidase inhibitory activity,[153] immunostimulant,[46] and neuroprotective activity.[154]

3. Current applications of TP from Asteraceae family

As shown in the previous sections, different studies have been developed to disclose the chemical profile of many TP and relate their composition and biological properties with their potential applications. Few representatives of the Asteraceae family have been used as natural ingredients in pharmacological, medicinal, and cosmetic products, and they have also been found in food products. In fact, some of these species are sold in different formats, such as teas, capsules, powders, *etc.*, which are considered to be "primary shelf-care products". The multiple properties of the compounds present in some of these plants have prompted the development of patents, as listed in Table 3. Some of the patents shown in the table relate to products that are orally administered, suggesting that the extracts and compounds of the selected plants could be used for the development of functional foods.

A. millefolium has been tested in clinical trials with different target diseases or affections but with inflammation processes associated as the common point. *A. millefolium* was demonstrated to ameliorate pain symptoms after episiotomies or during dysmenorrhea periods; further, it reduced the severity of oral mucositis and decreased biomarkers or scores/ascites when applied for chronic kidney disease or cirrhosis, respectively.[55] In a vulvovaginal candidiasis clinical trial, the results were not conclusive. Even though the vulvar erythema improved after the application of *A. millefolium*, the culture was still positive in nearly 50% subjects.[155] In 2011, the European Medicines Agency (EMA) published the final adopted community herbal monograph on *A. millefolium.* In this report, the therapeutic indications included the treatment of symptoms of some diseases or affections evaluated through the abovementioned clinical trials. The EMA indicated the use of *A. millefolium* as a temporary treatment for the loss of appetite; for mild, spasmodic gastrointestinal complaints (bloating and flatulence); minor spasm associated with menstrual

Table 3 Asteraceae-based current applications. Different species belonging to the Asteraceae family have been used for obtaining extracts from different plant parts in order include them as a part of different topical products that permit the exploitation of their properties and creating innovative applications and patented them

Species	Plant parts	Properties	Application	Patent no.
A. millefolium	FL	Antiseptic and anti-inflammatory	Treatment of oily hair	LU85863A1, US4948583A, CA1269937A
	AP	*Malassezia* yeast inhibitor	Dandruff	DE3300491A1, FR2993455B1, US20150086498A1, WO2013160066A1
	AP	—	Deodorant and antiperspirant	US20150086498A1, WO2013160066A1
	Any	Anti-metastatic	Treatment and/or prevention of neoplastic disorders	WO2001013929A1
A. montana	—	Antiseptic, lubricating and vasoconstrictive	Ocular improvement of the vascular permeability, histamine modulation and inflammatory reduction	MX2017001879A
	—	Anti-inflammatory, analgesic and antimicrobial	Treatment of spinal cross-sectional syndrome	DE202007013655U1
	FL	Anti-inflammatory and analgesic	Treatment of contusions by long-acting slow-release	CN105412191A
	FL/R	Anti-inflammatory	Acne dispelling and skin-care	CN106214538A
	FL	Analgesic	Pain relief	US20200163910A1
	—	Vasodilatator	Treatment of shingles	US20160106797A1
	FL	Plumping	Temporal lip volume increase	US20200170925A1
	—	—	Bruises heal, analgesic, anti-inflammatory	US20180050076A1
	—	—	Wound healing and its prevention post-surgery, post-laser or post-traumatic bruising	WO2009055433A1
B. perennis	Any	Lightening	Treatment of undesired skin pigmentation	AU2008364312B2
	FL/L	Lightening	Dermatosis with cutaneous pigmentation	CN101917965B
	FL	Antioxidant, anti-inflammatory, and lightening	Treatment of hyperpigmentation	CA2550863C
	FL	Neuroprotective	Treatment of hypoxia, especially that caused by ischemia	DE4206233C1
	L	Nutritional	Detoxification, diuresis, reduction of edema, heat regulation, and appetite promoter.	CN105941724A
		Hygroscopicity, anti-bacterial, odorizing	Improve cat litter properties (density, hygroscopicity, bacterial repealing and fragrance)	CN106069818A
C. officinalis	FL	Antioxidant, anti-inflammatory, antibacterial, and healing	Treatment of cutaneous manifestations due to epigenomic imbalance in skin cells	US20160074455A1
	Any	Anti-inflammatory and dermis cells hyperproliferation	Treatment of psoriasis	US6225342B1, WO1998032761A1
	—	Anti-inflammatory	Pain alleviation, calming nerves, endocrine adjustment, digestion promotion, treat dermal treatment	CN106619363A
	—	Moisturizing	Skin moistening, moisturizing, calming and improving sensitive skin	CN103520038A
	—	Epithelizing, bactericidal and bacteriostatic	Treatment of postoperative, post-traumatic wounds, grade I to III A burns, diaper irritations of newborns and infants, and ladders	RO128266B1
	FL/L	Anti-inflammatory, flavoring and preserving	Prevention of gingival disorder	KR20110067358A
	FL	Anti-anaphylaxis and moisture retention water	Relieving and allergy-preventing	CN105581940A
	FL	Anti-proteolytic and cell growth inhibition	Inhibition of skin inflammation and normalization of cell disorders	US20140295004A1
C. nobile	—	Antioxidant	Food preservation	CN102638993B, WO2011045757A1
	FL	Aromatic	Increasing aroma richness, sweet rhyme sense and improvement of cigarettes aftertaste	CN102687904A
	FL/L/S/St	Maintenance or increment of stem cells pigmentation	Preventive agent for canities apparition	JP2012025736A
	FL	Antioxidant, anti-inflammatory, and immunostimulant	Skin sebum dissolving agent, anti-aging, slimming, and whitening	JP2011207819A
	FL/L/St	Taste improver	Taste and aftertaste improvement for high sweetness sweetener	JP2018191582A

Table 3 *(Contd.)*

Species	Plant parts	Properties	Application	Patent no.
E. cannabium	—	Dyer	Natural and environmental-friendly dye that provides excellent color and fastness	CN106118126A
	AP	Anti-inflammatory, cough relieving, expectorant	Veterinary treatment of respiratory diseases such as cough, phlegm, influenza, or bronchitis	CN102048785B
	—	Antiparasitic	Treatment of chicken coccidiosis	CN104758516A
	—	Antibiotic or antiviral	Bacteria or virus inhibitor for medical use or feed additive	CN101422481A
	—	Deodorant and antibiotic	Deodorant	CN101947327B
H. stoechas	AP/FL	Periostin synthesis	Regeneration of cutaneous tissues and skin anti-aging	FR3040625A1
	—	Collagen and periostin synthesis	Stimulation of vaginal collagen generation and periostin reparation for wrinkle resistance	CN106038385A
T. officinale	—	Aromatic and functional	Functional beverage: coffee improved with dandelion properties (immunostimulant)	CN100376168C
	L/R	Health protective	Tea for the prevention of female mammary gland proliferation, detoxification, and immunostimulant	CN101297557B
	R	Dietotherapeutic	Honey-processed dandelion instant coffee	CN101766248A
	L	Antioxidant	Functional food: chocolate with antioxidant properties	KR101032937B1
	FL/P/R	Jelly matrix	Functional food: jellying agent that improve nutritional/functional properties of bread, biscuits, cakes, *etc*.	KR101445678B1
	R	Anti-inflammatory and detoxifying	Dandelion juice with black garlic for preventing colds and other diseases	KR20100028190A
	—	Hepatoprotective	Mixture of fermented dandelion and thistles for improving hepatic functions and protect hepatocytes	KR20140093437A
	R	Flavoring and preservative	Flavored cereals- and dandelion-based coffee substitute	RU2407376C1
	—	Stimulant of dehydroepiandrosterone synthesis	Prevention or improvement of male climacteric	US20150335694A1
	R	Latex rubber matrix	Extraction of latex rubber to apply to rubber, sugar syrups, soluble fiber, food, or beverages	US9611363B2
A. millefolium + *A. montana*	—	Anti-inflammatory	Cosmetic or dermatological treatment of the skin, hair, mucosa	US20040170670A1
A. montana + *C. officinalis*	FL	Analgesic	Relief of painful skin ailments	US20170071874A1
A. montana + *C. officinalis*	FL	Emollient	Reduction of cellulite or fat build-ups	US4795638A
A. montana + *C. officinalis*	—	Anti-viral	Treatment against *Herpes simplex* virus	US20200230187A1
A. millefolium + *C. officinalis* + *T. officinale*	—	Anti-inflammatory, and healing	Treatment of psoriasis	US5165932A
A. millefolium + *A. montana* + *C. officinalis*	FL	Anti-inflammatory	Treatment of inflammation, pain, or swelling	US20170056465A1
A. millefolium + *B. perennis* + *C. officinalis* + *C. nobile* + *elichrysum* sp. + *T. officinale*	—	—	Extracellular protease inhibitors	US20040175439A1
A. millefolium + *A. montana* + *B. perennis* + *C. officinalis*+	Any	Astringent, anti-inflammatory, antiseptic, cicatrizer, tonic, and emollient	Skin treatment	US4933177A
A. millefolium + *A. montana* + *B. perennis* + *C. officinalis*	R/FL	Anti-inflammatory	Treatment of musculoskeletal inflammations (arthrosis, osteoarthritis, rheum, joint stiffness, *etc*.)	US9687518B2
A. montana + *C. officinalis*	FL	Skin-protecting, regenerating, anti-inflammatory and antimicrobial	Treatment of hard-healing wounds	DE202006010673U1
C. officinalis + *Cannabis sativa*	FL	Anti-inflammatory	Reduction of skin lesions (atopic dermatitis, urticaria, radiotherapy or UV-burn, acne)	WO2017175126A1
C. officinalis + *Hypericum perforatum*	—	Anti-inflammatory, regenerative and bactericide	Treatment of dermatosis using low-molecular peptides and free amino acids	WO2005063266A1, EP1708725A1
C. offininalis + *T. officinale* + *Euphrasia officinalis*	—	Anti-inflammatory	Eye-drops, eye-rising solution for treating tired or dry eyes, conjunctivitis or blepharitis	HRP20120273A2

Abbreviations: AP, aerial parts; R, roots; FL, flowers; L, leaves.

periods; or as a healing agent for small superficial wounds. The established posology depends on the administration and the type of extract. Gastrointestinal affections can be treated with different herbal preparations to consume orally: infusion (2–4 g in 250 mL of boiling water, 3–4 times per day), expressed juice (5–10 mL, 2–3 times per day), liquid extract (2–4 mL, 3 times per day), and tincture (ethanol 45% 2–4 mL, 3 times per day or ethanol 31.5% 4.3 mL, 4 times per day). For menstruation pain, the EMA suggested the preparation of a herbal tea (1–2 g in 250 mL boiling water, 2–3 times per day).[156]

A study based on 443 patients analyzed the potential of *A. montana* for causing allergic reactions. The obtained results showed that *A. montana* produces very scarce contact sensitization processes quantified with a total percentage of 1% (5 patients) and mostly associated with the presence of nickel.[157] In fact, the EMA considers the therapeutic use of *A. montana* to be safe for adolescents, adults, and elderly people for the following dosages: 20–25% using tincture or 50% liquid extract in a base for creating a semisolid presentation that can be applied as a thin layer on the affected area up to a maximum of three or four times per day, respectively; and 2.5 mL as an impregnated dressing liquid for its application on the affected area, three to four times daily. Therapeutic indications provided by the EMA for *A. montana* include its application for the relief of bruises, sprains, and localized muscular pain.[158] However, in the literature, many alternatives for *A. montana* applications have been suggested. Fresh *A. montana* plant gel (100 g containing 50 g fresh plant tincture extracted at a ratio of 1 : 20) administrated twice a day for a month and a half was useful for the treatment of mild-to-moderate knee osteoarthritis. This treatment showed a reduction in the Western Ontario and McMaster Universities Osteoarthritis Index, with lower score for pain and stiffness and more than 75% patients would apply it again.[159] This is just one example of the multiple clinical studies that have been developed to reveal the alternative applications of *A. montana*. These works utilized *A. montana* for the potential treatment of very different diseases such as stroke, venous insufficiency, post-surgery treatments, articulation diseases or pain, muscle soreness, dental issues, *etc*.[79] The results demonstrated very variable data due to the different approaches of each work. Different *A. montana* concentrations, extracts, and presentations were used to treat diverse kinds of diseases or pains; the number of subjects varied from one study to another. This variability in the experimental conditions hinders a comparison of the obtained results.

To our knowledge, the human use of *B. perennis* has not been reported by the EMA so far. However, as stated before, different studies have demonstrated its efficacy as antiinflammatory and anti-arthritic[90,91] and antidiabetic and antiobesity[90,160] agents, hematoprotective and nephroprotective[161] agents, and promoter of collagen synthesis.[49]

The EMA indicates the use of *C. officinalis* for the symptomatic treatment of minor skin inflammations (sunburn) or minor wounds but also for treating mouth or throat inflammations. The dosage for skin treatment in children, adolescents, adults, and elderly includes infusions for impregnated dressings prepared with 1–2 g in 150 mL warm water or in boiled water but diluted at the 1 : 3 ratio (2–4 times per day), as well as for semisolid dosage, it should contain from 2 to 20% of *C. officinalis* extract, which can be administrated as a thin layer to the affected area (2–4 times per day). For treating minor inflammations in adolescents, adults, and elderly, it can be used as an infusion (1–2 g per 150 mL water) or a 2% solution for rinsing or gargling 2–4 times per day.[158] As an example for throat treatment, a study used *C. officinalis* together with two other plants to treat gingivitis from a mouthwash that contained hydroalcoholic extracts (5% v/p) of these plants resulting in an effective treatment.[162]

Similar to *A. montana*, *C. officinalis* was demonstrated to rarely provoke allergic reactions (in only 2% cases) that were also related with the presence of nickel. Hence, most clinical trials performed with *C. officinalis* have focused on the treatment of skin affections such as burns, dermatitis, wounds, ulcers, or episiotomies. In all these clinical trials, the application of *C. officinalis* was demonstrated to be safe and resulted in an improvement in the healing capacity of medical treatment when used as a co-adjuvant or even equalize the healing capacity of the medical treatment when used in comparative studies.[163,164] Additionally, *C. officinalis* has been tested for the treatment of other diseases, for instance, as an alternative to the use of clotrimazole for treating vaginal candidiasis or as a cost-effective treatment for tobacco-induced leukoplakia, instead of lycopene. For candidiasis, *C. officinalis* acts more slowly than clotrimazole but it had a long-term effect.[165] For leukoplakia, *C. officinalis* showed an equivalent efficacy as that of lycopene.[166] However, as it happens in clinical trials performed with other TP, the experimental design and outcome measures are very variable between different studies; therefore, well-designed and validated protocols are required to determine the efficacy of calendula.[163]

The EMA considers the use of *C. nobile* as a therapeutic for mild, spasmodic gastrointestinal complaints (bloating and flatulence) or for treating minor mouth or throat inflammations. The posology for these affections are—for oral use—1–4 g as an infusion or 1–4 mL of liquid extract thrice per day and for oromucosal use as an infusion with 2–3 g applied 3–4 per day to wash the mouth or throat.[167] *C. nobile* clinical trials are scarce since most of them named after chamomile have been developed with *Matricaria chamomilla*. Among the available studies in the literature, two randomized double–blind studies have suggested that the application of 2% *C. nobile* gel stabilizes or even improves the symptoms caused by the oral lichen planus disease.[168,169] However, the administration of the same gel for treating the burning mouth syndrome does not appear to have a positive effect.[170] Other works have evaluated the cosmetic potential capacity of *C. nobile.* This cosmetic application includes the oral administration of *C. nobile*, *Crataegus laevigata*, *Houttuynia cordata*, and *Vitis vinifera*. A 12-week treatment was able to suppress yellow and brown spots on the skin.[171]

For *E. cannabinum* and *H. stoechas*, no EMA report or clinical trials for its single administration were found in the scientific literature. *E. cannabinum* was described to be contained in a commercial cream together with other natural components (coconut oil, palm oil, castor oil, olive oil, beeswax, wheat oil, and canola seed oil) and to be effective for minimizing post-burn itch.[172] Similarly, *H. stoechas* was one of the extracts used as an ingredient of syrup based on acacia honey and on moieties derived from *Malva sylvestris*, *Inula helenium*, and *Plantago major* extracts. A clinical trial using this syrup was performed in a subject population of 106 children with persistent cough. The administration of the syrup reduced the severity and shortened the cough duration (preprint work).[173]

The therapeutic use of *T. officinale* reported by the EMA includes its application for relieving mild digestive disorders (abdominal fullness, flatulence, and slow digestion) and even for temporary loss of appetite. It is also considered to be a diuretic and acts as an adjuvant in minor urinary complaints. For digestive affections, it can be consumed as a decoction (3–4 g), as an infusion (4–10 g), as a dry extract (150 mg), as a liquid extract (1–3.31 g equivalents), or as a fresh juice (10 mL), with a frequency of 3 times per day. For urinary disorders, it can be ingested as a decoction or infusion, similar to that in digestive cases.[174] Clinical trials for *T. officinale* are also scarce for single-plant administration. In a study with a small population (17 subjects), a hydroethanolic extract of *T. officinale* fresh leaves was administrated. The urinary volume and frequency were determined before and after *T. officinale* administration. Both volume and frequency were increased with the treatment, which suggested its diuretic capacity.[175] Another work evaluated the efficacy of doing gargles with a *T. officinale* extract for improving the oral hygiene status of 11 subjects with orthodontic appliances. The orthodontic plaque index and the salivary *S. mutans* count were determined three weeks after the collocation of the orthodontic appliances. Both parameters were decreased after one week of treatment, suggesting that *T. officinale* may be incorporated as a natural ingredient for the development of innovative mouthwashes and other dental supplies aimed to preserve oral hygiene.[176] Other clinical trials involve a complex of herbal extracts apart from *T. officinale*, as in the case of a commercial cream that has been described to contain extracts of *Achilleae herba*, *Allium sativum*, *Calendulae flos*, *Urtica folium*, and *Veronica officinalis* herbs. This cream was evaluated in 19 patients from a total of 42 subjects for 12 weeks. Some treated patients reported positive clinical response in the treatment of psoriatic scalp lesions; in all of them, the symptoms were less severe than those in the placebo group.[177]

Many published works have investigated the use of homeopathic concentrations of herbal extracts, which hinder their real effect when compared with a placebo or other chemical compounds. Besides, the use of TP has an inherent variability due to the geographical distribution, the collection season, the plant part used for the extraction protocol, the extraction protocol itself, the final concentration applied, *etc*. Thus, to obtain comparable results, a chemical profile identification should be performed, major biomolecules involved in the mechanism of action disclosed, and their concentration and administration to be specified. Therefore, more scientific works must be developed to determine the actual application of TP-based extracts or molecules.

4. Conclusions and perspectives

In the last few years, a growing interest in the bioactivities and compounds from TP has been observed, both to preserve traditional knowledge and to recover bioactive compounds for industrial applications, including the food industry. In fact, numerous scientific studies have evaluated the action mechanisms behind their beneficial properties in health, justifying its use in traditional medicine. Considering the scientific works compiled in this study, they confirm that the eight selected plants of the Asteraceae family present health benefits and their bioactivities and chemical composition are related to the current patents in which they are applied. In addition, these plants contain diverse bioactive compounds, particularly PC, Eos, and SL, whose recovery could be of interest for the development of new applications in the food industry, such as enrichment of the food matrix to enhance their beneficial properties and also the substitution of synthetic antioxidants, antimicrobials, or colorants. To favor its application in the food industry, more studies and clinical trials are still needed, particularly in the case of *B. perennis*, *C. nobile*, *E. cannabinum*, and *H. stoechas*, so that the knowledge gap between the traditional and scientific approach can be plugged.

Abbreviations

Generic	
AP	Aerial parts
EMA	European medicines agency
FL	Flowers
L	Leaves
NA	Not analyzed
R	Roots
TP	Traditional plants
Compounds	
Ca	Carotenoids
EO	Essential oil
F	Flavonoids
HA	Hydroxycinnamic acids
OA	Organic acids
PA	Phenolic acids
PC	Phenolic compounds
PIEs	4-Hydroxyphenylacetate inositol esters
Ps	Polysaccharides
Sa	Saponins
SL	Sesquiterpene lactones
Te	Terpenoids
Tt	Triterpenoids

Antioxidant assays	
BHT	Butylated hydroxytoluene
DPPH	2,2-Diphenyl-1-picrylhydrazyl
ORAC	Oxygen radical absorbance capacity
FRAP	Ferric reducing/antioxidant power
TBARS	Thiobarbituric-acid-reactive substances
ABTS	2,2′-Azino-bis(3-ethylbenzothiazoline-6-sulfonic) acid
Cell lines	
A-549	Human lung carcinoma
BT-20	Human mammary gland/breast carcinoma
Caco-2	Heterogeneous human epithelial colorectal adenocarcinoma
CCRF-CEM	Human lymphoblastic leukemia cell line
DLD-1	Human colon adenocarcinoma
HaCaT	Human aneuploid immortal keratinocyte
HCT-15	Colorectal adenocarcinoma
HeLa	Cervical carcinoma
HepG2	Hepatocellular carcinoma
HL-60	Human promyelocytic leukemia
HT29	Human colon cancer
K562	Human erythroleukemia
MCF-7	Breast adenocarcinoma
MiaPaca-2	Pancreatic human tumor
MRC-5	Human fetal lung
NCI-H460	Non-small-cell lung cancer
SKMEL-3	Human melanoma
SMMC-7221	Human hepatoma
Inflammation related molecules	
COX-2	Cyclooxygenase-2
IL-1β	Interleukin 1 beta
IL-6	Interleukin 6
iNOS	Inducible nitric oxide synthase
LPS	Lipopolysaccharide
NAG-1	Nonsteroidal antiinflammatory drugs-activated gene-1
NF-κB	Nuclear factor kappa-light-chain enhancer of activated B cells
NO	Nitric oxide
PPARs	Peroxisome proliferator-activated receptors
ROS	Reactive oxygen species
TNF-α	Tumor necrosis factor alpha

Conflicts of interest

There are no conflicts to declare.

Acknowledgements

The research leading to these results received institutioanl and financial support from the: Programa de Cooperación Interreg V-A España—Portugal (POCTEP) 2014–2020 (Projects Ref.: 0181_NANOEATERS_01_E and 0377_IBERPHENOL_6_E); MICINN supporting the Ramón&Cajal grant for M. A. Prieto (RYC-2017-22891); Xunta de Galicia and University of Vigo for supporting the post-doctoral grant of María Fraga Corral (ED481B-2019/096) and the pre-doctoral grant of P. García-Oliveira (ED481A-2019/295); to Xunta de Galicia for the program EXCELENCIA-ED431F 2020/12; to Ibero-American Program on Science and Technology (CYTED – AQUA-CIBUS, P317RT0003); by EcoChestnut Project (Erasmus+ KA202) that supports the work of M. Carpena; by the Bio Based Industries Joint Undertaking (JU) under grant agreement no. 888003 UP4HEALTH Project (H2020-BBI-JTI-2019), the JU receives support from the European Union's Horizon 2020 Research and Innovation Program and the Bio Based Industries Consortium.

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