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Review

Nutraceutical Aspects of Selected Wild Edible Plants of the Italian Central Apennines

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Abstract: All over the world, wild edible plants are an essential source of chemical components that justify their use in folk medicine. The aim of this review is to document and summarize the knowledge of ten wild plants analyzed in a previous study for their ethnomedical significance. *Achillea millefolium*, *Borago officinalis*, *Foeniculum vulgare*, *Gentiana lutea*, *Juniperus communis*, *Laurus nobilis*, *Malva sylvestris*, *Satureja montana*, *Silybum marianum* and *Urtica dioica* were the subjects of our study. They are commonly found in the central Italian Apennines and the Mediterranean basin. Phytochemicals contained in wild plants, such as phenols, polyphenols, flavonoids, condensed tannins, carotenoids, etc., are receiving increasing attention, as they exert a wide range of biological activities with resulting benefits for human health. Based on the 353 studies we reviewed, we focused our study on the following: (a) the ethnobotanical practices and bioactive phytochemicals; (b) the composition of polyphenols and their role as antioxidants; (c) the methodologies commonly used to assess antioxidant activity; (d) the most advanced spectroscopic and spectrometric techniques used to visualize and characterize all components (metabolomic fingerprinting). The potential of pure compounds and extracts to be used as nutraceuticals has also been highlighted through a supposed mechanism of action.

Keywords: wild edible plants; ethnobotany; medicinal food; nutraceuticals; functional foods; Italian Apennines; Mediterranean basin

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1. Introduction

In recent decades, several epidemiological studies have shown a progressive growth in the incidence of chronic degenerative diseases in the population, mainly due to an incorrect diet. The main factors responsible for the pathogenesis of degenerative diseases are believed to be oxidative stress and inflammatory processes, which are involved in cardiovascular diseases, rheumatoid arthritis, and diabetes mellitus [1]. Thus, medicinal plants rich in antioxidants, such as polyphenols, flavonoids, and carotenoids, may contribute to the prevention of chronic diseases [2,3]. Natural products are important therapeutic agents and are becoming an attractive option as they have a lower incidence of adverse reactions and lower costs than synthetic pharmaceuticals [4].

The supplementation of natural products with antioxidant activity into the diet is therefore considered the main solution to reduce the occurrence of many health problems. For this reason, there is a growing interest in unexplored plants or wild plants characterized by bioactive molecules with potential health-beneficial effects [5]. Wild plants have been known for centuries in folk medicine for their therapeutic properties, and many scientific studies have determined the chemical composition of plant extracts and highlighted their side effects. In folk medicine, commonly used extraction procedures include conventional

methods such as maceration, percolation, decoction, and infusion. Most wild plants known for their therapeutic effects are often used as food. They are especially common in salads as green vegetables, but are also cooked, fried, or boiled, used in omelet dishes, etc. [6].

Wild plants may play an essential role in a healthy diet as an alternative source of minerals, vitamins, and phytochemicals with antioxidant capacities, or they can be used as supplements to formulate functional foods. The use of wild plants in popular cuisine is a common practice in Italy [7], but their consumption varies in different regional districts. Generally, all plant organs are consumed, including the leaves, tender stems, bulbs, seeds, and roots [8]. In Italian tradition, as well as in other countries, wild plants are generally eaten in salads or as boiled vegetables in soups, herb omelets or drink preparations [8]. The Central Apennine mountains represent one of the world's biodiversity hotspots, with a rich flora characterized by the presence of numerous endemics [9].

In recent decades, social and economic changes have caused the depopulation of mountain villages in the Apennines; as a result, wild food plants are declining due to the lack of oral transmission of traditional knowledge from generation to generation. Modern lifestyles are quickly transforming traditions, and the consumption of wild foods is not as common as it was in the past [10]. Minerals and the primary metabolites of plants are essential for humans. In contrast, the secondary metabolites of plants are not vital to humans, but experimental research has shown that they promote health and longevity [10].

The ten wild edible plants reported in this analysis are the result of a selection based on these criteria:

(1) An analysis of about 90 wild plants reported for their ethnopharmacological properties by Fortini et al. [11];

(2) The selection of the ten most common wild edible plants identified in the flora of the south–central Apennines that are used as food or beverages without adverse health effects [8,11].

The aim of the present review is as follows:

(a) To provide an overview of wild food plants typical of the Mediterranean basin and traditionally used in the gastronomy of the central Apennine area (Italy), characterized by their high biological diversity and whose cultural heritage is well known;

(b) To summarize the current knowledge on the potential use of edible wild plant extracts in the prevention or treatment of some of the most widespread diseases in developed countries, such as cardiovascular diseases, cancer, neurodegenerative diseases, diabetes, obesity, and liver disease;

(c) To illustrate and discuss the chemical composition of edible wild plants, their nutritional properties, and their relationship with the biological effects reported in the literature for the development of nutraceuticals or functional foods;

(d) To identify the methodologies that are commonly used to assess antioxidant activity in vitro and in vivo, and to highlight widely used advanced spectroscopic and spectrometric methods that are able to identify all primary and secondary metabolites contained in an extract (metabolic fingerprinting).

2. Strategy of Searching Articles

A comprehensive phytochemical analysis of the ethnobotanical literature and a biological activity search on the food plants used in the Apennine and Mediterranean area were carried out using existing online scientific databases, such as Scopus, Web of Science, Wiley Online Library, and Science Direct, as well as Google Scholar keywords. The search was limited from 2000 to November 2023. The information summarized in Tables 1 and 2 was obtained from research articles (in vivo or in vitro studies). A total of 353 studies were selected and included in this review.

3. Role of Nutraceuticals

The term nutraceutical is commonly used in marketing, but there is no regulatory definition. Nutraceuticals are substances that are not recognized as nutrients but that have

positive physiological effects on the human body and possess multiple therapeutic benefits. Epidemiological studies indicate that a diet rich in plant-based foods significantly reduces the risk of chronic-degenerative diseases, suggesting that some natural components found in plants may be effective agents for the prevention of diabetes, hypertension, heart disease, Alzheimer's disease, and arteriosclerosis [12,13].

Some nutrients, herbal products, probiotics, polyunsaturated fatty acids, and phytochemicals are considered nutraceuticals. Since ancient times, many plant extracts, now marketed as herbal products, have provided hundreds of remedies to treat acute and chronic diseases.

Herbal nutraceuticals are foods prepared from plants, and some examples include Yarrow (*Achillea millefolium*), which contains bioactive components useful for treating lack of appetite, gastric disorders, or diarrhea, or Chamomile (*Matricaria recutita*), which is widely used to treat insomnia, gastrointestinal disorders, inflammation, wounds, ulcers, muscle spasms, etc. [14].

The term 'probiotics' refers to live microorganisms that, when administered in sufficient quantities, provide health benefits by regulating the balance of human intestinal microorganisms and inhibiting the colonization of pathogenic bacteria in the gut. In addition, probiotics help the body build a healthy protective layer of the intestinal mucosa, enhancing the intestinal barrier effect and improving immunity [15].

Polyunsaturated fatty acids (PUFAs), mainly omega-3 and omega-6, have been shown to decrease the production of inflammatory eicosanoids, cytokines, and reactive oxygen species (ROS), and to possess immunomodulatory effects. They are, therefore, able to alleviate inflammatory pathologies and are effective in the prevention and treatment of coronary heart disease, hypertension, diabetes, arthritis, and other inflammations [16].

Phytochemicals are non-nutritive bioactive plant components that have attracted interest in human nutrition due to their potential effects as antioxidants, as well as their anti-inflammatory, immunomodulatory, and anticarcinogenic effects. They are naturally occurring secondary metabolites that impart color, taste, odor, and texture to plants [17]. Many vegetables, wild plants, legumes, whole grains, fruit, fruit and vegetable juices, tea/coffee, and spices have nutraceutical properties as they contain compounds with antioxidant activity, such as flavonoids, phenolic acids, anthocyanins, terpenoids, tannins, carotenoids, phenylethanoid glycosides, etc. [18]. Antioxidants used in the diet consist of different phytochemical molecules that are present in low concentrations [18], and their consistent inclusion in the diet has a protective effect against free-radical-related disease [19,20].

Polyphenols are found more abundantly in the edible parts of plants and are considered one of the main classes of plant compounds responsible for antioxidant activity, as they can scavenge free radicals such as reactive oxygen species; thus, they are of particular interest to the food and pharmaceutical industries [21]. Polyphenols are considered the principal agents responsible for several biological [22] and pharmacological functions, as they exhibit anti-inflammatory, antimicrobial, anti-allergic, antiviral, antithrombotic, and hepatoprotective activity, and they are involved as signaling molecules in some biochemical reactions [23], and in modulating a range of cancer signaling pathways [24].

3.1. Antioxidant Activity

In biological systems, oxidative stress is a complex process characterized by an imbalance between the production of free radicals (ROS) and the body's ability to eliminate these reactive species through endogenous and exogenous antioxidants. During metabolic processes, a variety of reactions take place in which the initiators are reactive oxygen species (ROS), such as hydrogen peroxide (H_2O_2), the superoxide radical anion (O_2^-), and many others. Endogenous antioxidants are enzymes, such as superoxide dismutase (SOD), catalase (CAT), and glutathione peroxidase, while examples of non-enzymatic compounds include bilirubin and albumin [25]. When an organism is exposed to a high concentration of ROS, the endogenous antioxidant system fails, and to compensate for this antioxidant

deficit, the body can use exogenous antioxidants provided through food, dietary supplements, or pharmaceuticals. The main characteristic of an antioxidant compound is that it can prevent or break the chain of oxidative propagation by stabilizing the radical that is generated, thus reducing oxidative damage in the human body. Phenolic compounds, through their distinctive chemical structure, reduce or inhibit free radicals by reducing oxidative stress and, thus, inflammatory processes [26].

Data from the literature suggest that plant polyphenols (PPs), especially phenolic acids and flavonoids, can inhibit the inflammation process by regulating the production of pro-inflammatory molecules, such as cytokines like tumor necrosis factor (TNF-α), nitric oxide (NO), and leucocyte adhesion, which are produced during inflammatory reactions. PPs have been shown to play a crucial role in the immune-inflammatory response [27,28]. Hence, inhibition of the production of such pro-inflammatory molecules is expected to have therapeutic value against inflammatory diseases. By blocking reactive oxygen species, flavonoids can mitigate photo-oxidative damage in plants [29,30].

The mechanisms of action of these compounds in the human organism have not been fully elucidated [5]. Studies have indicated that the mechanism underlying the radical-scavenging activity of polyphenols is related to the high reactivity of the phenolic OH-groups through hydrogen atom donation. Radicals can be inactivated through the following equation [26]:

$$PPs(OH) + R^{\bullet} \rightarrow PPs(O^{\bullet}) + RH$$

where $R^{\bullet}$ is a free radical and $O^{\bullet}$ is a reactive oxygen species.

In flavonoids, structure–activity relationship (SAR) studies have shown that to achieve the best antioxidant activity, the following functions are required in the chemical structure: an ortho-hydroxy substitution in the B ring, a C2-C3 double bond, and a carbonyl function at C4 in the C ring (Figure 1) [31,32]. The free hydroxyl groups on the B ring donate hydrogen atoms to a radical to obtain neutral derivatives with stable molecular structures, interrupting the chain reaction. At the same time, a relatively stable flavonoid radical is produced. Flavonoids with the C2-C3 double bond in conjugation with a C4 carbonyl group are planar; this structural feature allows for a charge delocalization from the A ring to the B ring throughout the aromatic system. In flavonoids with the ortho-dihydroxy group (catechol), the formation of flavonoid phenoxy radicals can be stabilized via the mesomeric equilibrium with the ortho-semiquinone structures [33]. Moreover, some flavonoids can chelate transition metal ions (pro-oxidants), which are responsible for the production of reactive oxygen species and inhibit the lipoxygenase reaction [5].

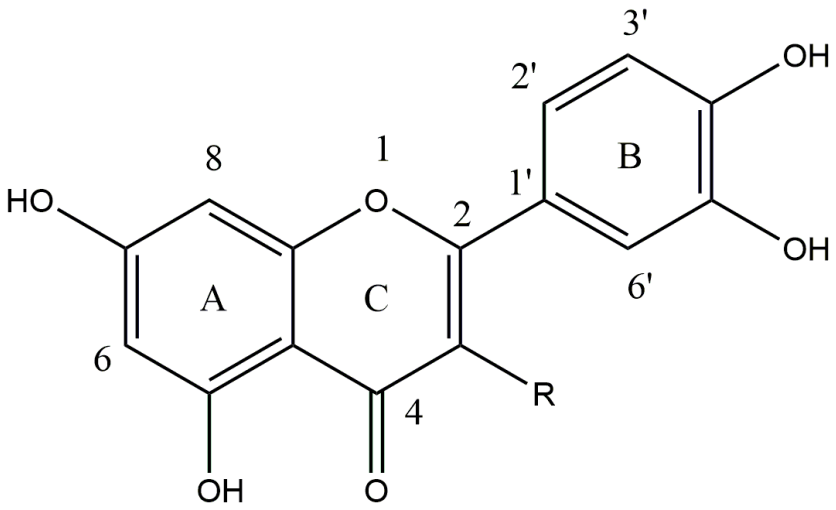

Figure 1. Basic structure of flavonoids. R=OH flavonols; R=H flavones.

Phytoestrogens belong to the class of flavonoids but, due to their structural similarity to estrogens, are able to interact with the estrogen receptor [32,34]. Although polyphenols

and flavonoids are generally associated with health-promoting properties, it has been reported that, when consumed in high doses, flavonoids can act as pro-oxidants and mutagens, and are thus cytotoxic [35].

The method based on the Folin–Ciocalteu reagent is commonly used to determine and quantify total phenols in many matrices. This method evaluates the ability of phenols to react with oxidizing agents, but is not very selective as it reacts with any phenol [36].

3.2. Methods of Estimation of Total Antioxidant Activity (TAC)

The antioxidant activity of an extract can be evaluated in vitro or in vivo by means of simple experiments. Several in vitro methods are proposed and described in the literature to determine the effectiveness of antioxidant compounds in different matrices (plant extracts, blood, etc.) using lipophilic, hydrophilic, and amphiphilic media (emulsions). Because of their mechanism, in vitro methods can be divided into two main groups: (a) hydrogen atom transfer (HAT) reactions and (b) transfer reactions of a single electron (SET) [37].

Reducing compounds donate electrons or hydrogen atoms to compounds which have higher reduction/oxidation (redox) potentials. The latter group of compounds includes free radicals and other oxidants occurring in living systems. These methods are widely used due to their high speed and sensitivity. When assessing the antioxidant capacity/activity of a sample, more than one method should be used [37]. Diverse tests have been developed to evaluate the potential antioxidant activity of plant extracts or pure secondary metabolites in vitro. The most popular assay includes 2,20-azinobis (3-ethylbenzothiazoline-6-sulphonic acid (ABTS) [38,39]. The antioxidant activity (colorimetric method) measured by ABTS• reduction is usually referred to as that of Trolox (6-hydroxy-2,5,7,8-tetramethylchroman-2-carboxylic acid), a standard antioxidant. This allows for the results to be expressed in Trolox equivalents (TE).

2,2-diphenyl-1-picrylhydrazyl (DPPH) radical scavenging activity, a colorimetric method, is one of the most stable free radicals and is frequently used in the evaluation of radical scavengers in natural foods. The DPPH assay method is straightforward and can be used to perform a quick manual analysis of antioxidant contents [40]. The ferric reducing antioxidant power assay (FRAP), a colorimetric method, is based on the reduction of the 2,4,6-tripyridyl-s-triazine (TPTZ)–Fe^{3+} to the deep blue TPTZ-Fe^{2+} complex [41,42]. The cupric-reducing antioxidant capacity (CUPRAC) method uses copper 2+-neocuproine (2,9-dimethyl-1,10-phenanthroline), which can be reduced by antioxidants [43]. The oxygen radical absorbance capacity (ORAC) assay is based on the inhibition of the oxidation of a fluorescent substrate (and fluorescence loss) by peroxyl radicals. Commonly used peroxyl radical generators in this assay are represented by azo-compounds that decompose at elevated temperatures [44,45]. Chemiluminescence (CL) assays are based on the reaction of ROS/RNS with detection reagents to generate species in an excited state that emit light upon de-excitation to the ground state [46]. The main chemiluminescence reagents that are used include luminol, lucigenin, and peroxyoxalate [37].

Less popular methods include the potassium ferricyanide reducing power (PFRAP) assay [47], the total reactive antioxidant potential (TRAP) test [48], and the β-carotene-linoleic acid bleaching (BCLB) assay [49].

For all in vivo methods, the samples that are to be tested are usually administered to mice, rats, etc., following methods that ensure strict compliance with recommended doses and administration times. Upon completion, the animal is typically sacrificed, and the blood and/or tissues are used for analysis [50]. The main methods used with plasma are the Ferric-Reducing Ability of Plasma (FRAP) [51] and the measurement of γ-Glutamyl transpeptidase activity (GGT), which is important for glutathione homeostasis [52]. The estimate of reduced glutathione (GSH) is used as an index of cell protection from free radicals, peroxides, and other toxic compounds [53]. Estimating glutathione peroxidase (GSHPx) activity is important; this activity may indicate a disturbance of the prooxidant/antioxidant balance [54]. Glutathione-S-transferase (GST) is believed to play a physiological role in initiating the detoxification of potential alkylating agents, including pharmacologically

active compounds. Under these circumstances, GST is important to carcinogenesis and chemoresistance [55]. Erythrocyte lysate can be used as a substrate for the evaluation of antioxidant enzymes such as SOD and CAT activity [50]. The glutathione reductase (GR) assay is important for maintaining the supply of reduced glutathione [56]. Finally, lipid peroxidation (LPO) is the most important test, which considers the quantity and physiological importance of biological membranes and lipoproteins. LPO is commonly used to estimate the oxidative state of the cell [57].

3.3. Metabolomics Analysis

The phytochemicals contained in plant food sources or non-food plants are an unlimited reservoir of nutraceutical compounds with a broad range of biological activities [58,59]. The plant metabolome consists of primary metabolites, secondary metabolites, vitamins, organic acids, alkaloids, etc.; therefore, the metabolome of plants is the main target in the search for new nutraceuticals at present [60].

Metabolomic analysis allows for the simultaneous detection of all primary and secondary metabolites in a biological system and provides qualitative and quantitative information on its components. Metabolomics is, therefore, a powerful tool for defining the phytochemical profile in an extract and allows several phenomena to be monitored. It can help to understand plant responses to stress, assess changes in natural products in different tissues/organs or during growth or ripening, etc. [61]. Metabolomics can be undertaken using two different approaches: non-targeted and targeted methods.

Currently, the two main analytical techniques used for these purposes are nuclear magnetic resonance (NMR) spectroscopy in both 1D and 2D experiments and mass spectrometry (MS), often coupled with separation techniques such as liquid or gas chromatography (LC or GC) [62–64].

NMR methods provide information on a wide range of compounds present in the plant extract in a single experiment, offering advantages in terms of the simplicity of sample preparation, the time required for analysis, high reproducibility, and the acquisition of a large amount of data in a relatively short time [65]. NMR spectroscopy is a non-destructive technique because the sample can be recovered and used in a further experiment. However, the main drawback of NMR spectroscopy is its relative lack of sensitivity, coupled with the overlapping of signals in the ^{1}H NMR spectrum of biological samples, which limits the identification of metabolites. The acquisition of 2D NMR experiment series (TOCSY, HSQC, HMBC) in metabolomics workflows can reduce the signal overlap and provide crucial information to elucidate the structure of metabolites.

Over the years, efforts have been made to improve sensitivity and resolution in NMR experiments with ultra-high-field magnets [66].

The richness of this information often results in high spectral complexity, so multivariate data analysis is required to study the spectra and extract meaningful information.

NMR is an evolving field, and many new techniques are emerging in NMR-based metabolomics analysis. Among these, high-resolution magic-angle sample spinning (HRMAS) has been increasingly applied in recent years [67] due to its potential in solid-state sample analyses without previous extraction. Other new NMR applications include hyperpolarization methods, ultrafast 2D NMR methods, pure-shift NMR techniques, and hybrid NMR approaches [67].

MS-based techniques are the most widely implemented strategies for metabolomics purposes, especially UPLC-MS with electrospray ionization (ESI), thanks to the greater sensitivity that this technique offers. In recent years, further developments have taken place using high-resolution (HR)-MS techniques, with the possibility of accurately determining the mass of a compound. However, these techniques are less robust than NMR techniques. A difference can be found between targeted and non-targeted methods. The results of the former are generally comparable across studies, whereas non-targeted methods require careful quality-control procedures to assess robustness and repeatability over time [68]. Moreover, the high sensitivity offered by MS, especially HRMS techniques, has disadvan-

tages, such as ion suppression, meaning that other strategies are required to increase the number of metabolites.

Multivariate methods are routinely used to visualize biological data, identify possible clusters, and build predictive models based on the amount of data obtained from previous spectral datasets [69]. Multivariate data analysis (MVA) can be divided into two main categories: unsupervised analyses to explore data without any class membership and supervised analyses to discriminate among known groups of interest. Techniques such as Principal Component Analysis (PCA) and Orthogonal Partial Least Squares Discriminant Analysis (OPLS-DA) provide an essential platform for the rapid interpretation of information-rich spectral datasets to infer biological conclusions. Through the proper application of preprocessing transformations, the optimal choice of analysis algorithms, and the judicious application of validation metrics, MVA can lend a powerful hand in the biological understanding and exploration of complex metabolic systems.

4. Botanical Information, Ethnobotanical Practices, and Bioactive Phytochemicals in Wild Edible Plants

The characteristic botanical information (systematics, etymology, distribution, habitat, etc.) was obtained for each species analyzed in this study. Table 1 provides references showing where the complete information can be obtained.

Table 1. Botanical information, including scientific name and important morphological characteristics, systematics, etymology, distribution, and habitat.

Scientific Name and Important Morphological Characters	Systematics	Etymology	Distribution and Habitat	Ref.
Achillea millefolium L. Perennial herbaceous plant, roots in the rhizome; hairy stem; simple or branched; leafy; ascending; can reach up to 80 cm in height. The hairy leaves have contours, both lanceolate and linear. The flowers are white or pink, whitish achenes. The fruits are achenes.	Domain Eukaryota, Kingdom Plantae, Division Magnolio-phyta, Class Magnoliopsida, Subclass Asteridae, Order Asterales, Family Asteraceae, Subfamily Asteroideae, Tribe Anthemideae, Subtribe Achilleinae, Genus *Achillea*, Species *A. millefolium.*	Tradition (Pliny) states that Achilles healed some wounds of his comrades in arms during the siege of Troy, with the plant, hence the name of the genre. The name (milfoil) is due to its deeply indented leaves; in fact, the epithet refers to the numerous foliar laciniae that characterize this plant.	The *A. millefolium* is native to Europe; it grows in temperate regions all over the world up to 2500 m. It prefers sunny places, meadows, and the edges of paths and railways; it also adapts well to dry, stony, and acidic soils.	[70,71]
Borago officinalis L. is an herbaceous plant; it can reach up to 80 cm. It has elliptic oval leaves and petioles, with rough hair and a dark green color, collected in a basal rosette 10–15 cm long, which are then smaller on the stem. The flowers have five petals arranged in a blue-purple star. The fruits are achenes that contain small seeds.	Domain Eukaryota, Kingdom Plantae, Division Magnolio-phyta, Class Magnoliopsida, Order Solanales, Family Boraginaceae, Genus *Borago* and specie *B. officinalis*.	The etymology of its name is uncertain. Some suppose that it derives from the Arabic "abou" and "rash". Others assume that it comes from the Latin "wad" or from the Celtic "barrach", meaning "brave man". The Italian name Borage comes from the Latin Borago.	This herb is well adapted to the Mediterranean basin and widespread throughout Italy, where it grows spontaneously up to 1800 m above sea level. It prefers a rich soil, without stagnant water.	[72,73]
Foeniculum vulgare Mill is complex and difficult to summarize. It derives from the distinction between the varieties of wild fennel and "sweet" fennel (horticultural production).	Eukaryota Domain, Kingdom Plantae, Division Magnolio-phyta, Class Magnoliopsida, Subclass Rosidae, Order Apiales, Family Apiaceae, *Foeniculum* Genus *and F. vulgare* Specie.	The names comes from foenum, meaning hay, due to the subtlety of the leaves and its intense aromatic odor. Vulgare means that the plant is quite widespread (vulgar = common).	Fennel is a typical Mediterranean plant. It is mainly found in southern regions and islands, from sea level up to about 1000 m altitude. It prefers sunny, unspoilt, dry, and pebbled places.	[74,75]

Table 1. *Cont.*

Scientific Name and Important Morphological Characters	Systematics	Etymology	Distribution and Habitat	Ref.
Juniperus communis L. is an evergreen shrub or tree with a twisted trunk, of 1–10 m tall, with linear, needle-like, pungent leaves, gathered in verticils of 3. Male flowers are yellowish; female flowers are small greenish cones, which produce berries (called cuddles).	Domain Eukaryota, Kingdom Plantae, Subkingdom Tracheobionta, Superdivision Spermatophyta, Division Pinophyta, Class Pinopsida, Order Pinales, Family Cupressaceae, Genus *Juniperus*, Specie *J. Communis*.	The term Juniperus derives from iúnix, heifer, and pário, meaning giving birth. This is due to its presumed properties favoring childbirth. Communis epithet obviously means common, banal.	It is widespread, from marine regions to mountainous areas, and is found in dry pastures, as well as on moors or scrubland. It is a very long-lived species in the temperate regions of the northern hemisphere. It is resistant to low temperatures, and tolerates aridity and strong wind.	[76,77]
Malva sylvestris L. is an annual herbaceous plant that is biennial or perennial. The stem can grow to 60–80 cm. The leaves of palminervia have 5–7 lobes and an irregularly serrated margin. The flowers are grouped axils of leaves. The fruit is a circular poliachenio.	Eukaryota Domain, Kingdom Plantae, Division Magnolio-phyta, Class Magnoliopsida, Order Malvales, Family Malvaceae Genus *Malva* and Specie *M. sylvestris.*	The genus name, the consonant with the greek "Malatto" and "malákhe", means emollient, benevolent, with reference to the soothing properties of these plants.	The plant is native to Europe and temperate Asia; it can be found in fields and uncultivated places.	[78,79]
Gentiana lutea L. is an herbaceous, perennial species with very slow growth. It can reach up to 150 cm, with a single stem that is hollow inside, and green leaves. The flowers are yellow, sometimes punctuated with darker color, star-shaped, and gathered in bundles to the axil of the upper leaves. The fruit is an oblong oval capsule, which opens at maturity in two parts, containing brown oval seeds.	Domain Eukaryota, Kingdom Plantae, Phylum Magnolio-phyta, Class Magnoliopsida, Order Gentianales, Family Gentianaceae, Genus *Gentiana*, Specie *G. lutea*	According to Pliny, Gentiana derives from Gentius (in Greek, , Gentios) Genzio, last king of the Illyrians (II century BC), discoverer of the antimalaric properties of the roots of *G. lutea*. The lutea name derives from lúteus (yellow); that is, the floral color.	Gentian is a plant that grows in meadows and low-humidity pastures, as well as in calcareous soils, rich in organic substances, with heavy sunlight. In Italy, it grows in the central-southern Apennines, at an altitude that varies between 1000 and 2200 m above sea level.	[80,81]
Laurus nobilis L. The laurel often appears in shrubs when pruned. In natural conditions, it becomes a tall tree reaching up to 10 m. It is an evergreen plant. The leaves are ovate, dark green, leathery, glossy on the top, and dull underneath. The fruits of the laurel are black and shiny berries with only one seed.	Domain Eukaryota, Kingdom Plantae, Subkingdom Tracheobionta, Superdivision Spermatophyta, Division Magnoliophyta, Class Magnoliopsida, Subclass Magnoliidae, Order Laurales, Family Lauraceae, Genus *Laurus*, Specie *L. nobilis* L.	The name of this plant comes from the Latin "laus", meaning praise, to highlight the curative properties of the plant, which have been "praised" from ancient times. "Nobilis" stands for illustrious, important, famous. For others, the vulgar name would be derived from the Celtic root "laur", meaning green.	*L. nobilis* is a common species along the northern coastal areas of the Mediterranean basin. In Italy, it grows spontaneously in the central and southern areas along the coast, while in the northern regions it is cultivated.	[82,83]
Satureja montana L. is an herbaceous species which grows to 50 cm. The stems are woody at the base, tetragonal, erect, and have short back hairs when pubescent. They are usually widely branched from the bottom to form a small bush. The leaves are bright green, opposite, and subsessile. The fruit is formed by 4 oval achenes dotted with small grains.	Domain Eukaryota, Kingdom Plantae, Subkingdom-Tracheobionta, Superdivision Spermatophyta, Division Magnoliophyta, Class Magnoliopsida, Subclass Asteridae, Order Lamiales, Family Lamiaceae, Tribe Mentheae, Genus *Satureja*, Specie *S. montana.*	The term Satureja is of uncertain etymology. The specie name "mountain" comes from mons montis, mountain, meaning "of the mountains", because it grows 1000–1400 m above sea level.	Winter savory is a perennial semi-evergreen species native to the mountainous regions of central–southern and western Europe. Its habitat is that of calcareous, rocky, arid lands, at the edge of mountain roads, at up to 1400 m altitude.	[84]

Table 1. *Cont.*

Scientific Name and Important Morphological Characters	Systematics	Etymology	Distribution and Habitat	Ref.
Silybum marianum (L) Gaertn is an herbaceous species with vigorous bearing that can reach up to 150 cm. The plant is completely glabrous and spiny. The scape is robust, streaked, and branched, with erect branches. The plant has hermaphroditic flowers, with a tubular red-purple corolla; these are united in large globular end heads, covered with strong bracts.	Domain Eukaryota, Kingdom Plantae, Subkingdom Tracheobionta, Superdivision Spermatophyta, Division Magnoliophyta, Class Magnoliopsida, Subclass Asteridae, Order Asterales, Family Asteraceae, Subfamily Cichorioideae, Tribe Cardueae, Subtribe Carduinae, Genus *Silybum*, Specie *S. marianum*.	The term Silybum comes from the Greek sílybon/síllybon, the name which Dioscorides called some edible thistles, which was taken over by Pliny to denote sillybus, a type of thistle. The name "marianum" derives from the Virgin Mary.	Milk thistle is a wild species, widespread in all the Mediterranean regions from sea level to submountain areas. Its habitat is in ruins, along roads, and in uncultivated areas, and it is common in desert and sub-desert areas ranging from the Mediterranean basin to Central Asia.	[85,86]
Urtica dioica L. Nettle is a perennial, deciduous herbaceous plant, 30–250 cm tall. It has an erect, densely hairy, striated, and grooved stem. The leaves are large, ovate, and opposite; lanceolate, jagged, and pointed; dark green on the upper side, and lighter and hairier on the lower side. The female flowers are collected in long hanging spikes, while the male flowers are grouped in erect spikes.	Domain Eukaryota, Kingdom Plantae, Division Magnoliophyta, Class Magnoliopsida, Subclass Rosidae, Order Urticales, Family Urticaceae, Genus *Urtica*, Specie *U.dioica*.	The name "nettle" probably derives from the Latin "urere" (Urtica), meaning burn, indicating the effect of the irritating substances contained in stinging hairs.	*U. dioica* is widespread in Europe, most of Asia, North Africa, and North America. In Italy, it is found in all regions: uncultivated land, woods, urbanized areas, roadside, and places in the half-shade of nitrate-rich soil, ranging from the plains to 2300 m above sea level.	[87,88]

Table 2 lists the main ethnobotanical uses, phytochemical constituents, and biological activity of the selected wild edible plants (see also Figure 2).

Table 2. Phytochemical components, ethnobotanical uses, and biological activity of selected wild edible plants.

Scientific Name	Ethnobotanical Uses	Phytochemical Components	Biological Activity	Ref.
A. millefolium L.	Tea for gastrointestinal disorders. Essential oils (from flowers) against influenza. Infusions, decoctions, or fresh juices against hemorrhage, hemorrhoidal, menstrual problems, and dysmenorrhea, toothache, headache, diuretic, wounds, and burns (hemostatic).	Rutin; luteolin 7-O-glucoside; apigenin 4′-O-glucoside; apigenin 7-O-glucoside; luteolin 4′-O-glucoside	Anti-inflammatory activity, treatment of gastrointestinal and hepato-biliary disorder and skin inflammation. The in vitro anti-inflammatory activity was established through the inhibition of matrix metalloproteinases (MMP-2 and -9), which are involved in psoriasis and atopic dermatitis and in inflammatory bowel diseases such as ulcerative colitis and Crohn's disease.	[89–93]
B. officinalis L.	Diuretic; promotes perspiration; emollient; lenitive; mild laxative; diuretic. Decoction of leaves against rheumatism and as a diuretic. Leaf poultice against tooth abscess. Digestive; depurative.	Flavonoids; phenolic acids; rosmarinic acid; syringic; sinapic; chlorogenic acids. β−sitosterol, oleuropein; lithospermic acid (leaves); tocopherols; sterols; squalene.	Anti-inflammatory properties (HaCaT and BJ cell lines) and anti-ageing properties. Weak anti-inflammatory activity in murine RAW 264.7 macrophage cell. Cytotoxic effects of extracts by MTT assay against human liver (HPG2), prostate (LNCaP) and colon (HT-29) cancer.	[11,94–104]
F. vulgare Mill.	Antispasmodic and carminative effects. Promotes intestinal peristalsis. Diuretic action. Cures respiratory diseases as an expectorant.	Cirsiliol, 4-O-caffeoylquinic acid (4-CQA); vanillic acid; O-coumaric acid; rosmarinic acid; kaempferol; resveratrol; rutin; myricetin; catechin; quercetin.	Antioxidant; antimicrobial; anti-inflammatory. Protection against cardiovascular diseases, neurological disorders, and diabetes, and hepatoprotective effects.	[105–120]

Table 2. *Cont.*

Scientific Name	Ethnobotanical Uses	Phytochemical Components	Biological Activity	Ref.
G. lutea L.	In folk medicine, it is known for its digestive and appetite-stimulating effects. Other uses include antipyretic, hepatoprotective, hypoglycemic, antianemic, and cardiotonic activity; for sores and minor wound healing; for stomach ulcers, as an immune stimulant.	Isovitexin, isosaponarin, isoorientin, isoorientin-2′-O-glucoside, and isoorientin-4′-O-glucoside	Anti-inflammatory properties, with the rate of enzyme inhibition increasing with time.	[121–127]
J. communis L.	Urinary antiseptic for acute and chronic cystitis; diuretic; emmenagogue; sudorific; digestive; anti-inflammatory. Used as a stimulant and disinfectant against constipation, chronic Bright's disease, migraine, dropsy, rheumatic swellings, and infantile tuberculosis.	Quercetin, kaempferol, myricetin, isorhamnetin, and patuletin derivatives in their composition. Quinic acids, 5-O-caffeoylquinic, catechin, epicatechin, luteolin, apigenin, naringenin, amentoflavone, and their derivatives.	Antidiabetic, anti-inflammatory, antihypercholesterolemic, antihyperlipidemic, and hepatoprotective effects. Anticancer properties alleviate cardiovascular disorders. Anticataleptic activity alleviates neuropathologies and improves the mental state of individuals.	[128–134]
L. nobilis L.	In cooking recipes, it is used to provide an aroma and a spicy flavour to meat, fish, broths, and vegetables. It is a component of two typical Italian vegetable infusions: one used as a digestive, called "canarino", and one for the treatment of respiratory aliments, called Ricotto or Ricuotto. It is used in treatments for gastro-intestinal disorders, carminative, diarrhea, hemorrhoids, stomach aches, and kidney diseases.	Isoquercitrin, luteolin, rutin, apigenin derivatives, catechin, cinnamtannin B1, epicatechin hexoside, (+)-catechin, (−)-epicatechin, epigallocatechin, and methyl eugenol. Gallic; vanillic; rosmarinic acid; ferulic acid; coumaric acid. Costunolide; santamarine; reynosine.	Anti-inflammatory: reduction in lung inflammation caused by LPS and in skin lesions and inflammation caused by Propionobacterium acnes.	[135–142]
M. sylvestris L.	Used to treat various ailments, such as colds, antiseptic, colic, constipation, cough, cystitis, high fever, migraines, puerperal mastitis, stomachic, wounds, and abscesses. Leaves, flowers, fruits, roots, shoots, and seeds are applied in infusions, decoctions, poultices, liniments, lotions, baths, and gargles.	Gossypetin 3-sulphate-8-O-β-Dglucoside; hypolaetin 3′-sulphate; isoscutellarein 8-O-ß-D-glucuronpyranoside; hypolaetin 8-O-ß-D-glucuronopyranoside; 3-O-β-D-glucopyranosyl-8-O-β-D-glucuronopyranoside; hypolaetin 4′-methyl ether 8-O-β-D-glucuronopyranoside.	Antibacterial, anti-inflammatory, antioxidant, and anti-inflammatory activity on carragenin-induced edema in rats. Antiproliferative activity on cancer cell lines. Reduction in nephrotoxicity induced by gentamicin.	[11,143–155]
S. montana L.	Effective against colds, asthma, antitussive and expectorant, cough, bronchitis, and inflammation of the respiratory tract.	Rosmarinic acid, caffeic acid and its glycoside derivatives. Quercetin, catechin or luteolin derivatives.	High antimicrobial potential, together with antioxidant and anxiolytic capacity. Hepatoprotective effects, protection against cardiovascular ailments, and uses in cancer treatment.	[156–161]
S. marianum (L) Gaertn	Antihypertensive; stimulates milk production in rats and insect (flies) repellents. Used in the treatment of liver dysfunctions and gallbladder disorders, laxatives, and breast cancer treatment.	Flavonoids. Flavonolignan complex composed of isosilychristin, isosilybin A and isosilybin B, silybin A and silybin B, silychristin, silydianin, and taxifolin mariamide A and mariamide B (seeds).	Antidiabetic agent (α-glucosidase and PTP1B inhibitory activities), used in the treatment of chronic hepatitis, cirrhosis, and hepatic toxic lesions, with choleretic and cholagogue effects. Applied in Italy to treat liver and gastrointestinal disorders and as a laxative, with anti-inflammatory, antioxidant, cardiovascular protective, anti-cancer, and neuroprotective effects.	[11,162–168]

Table 2. *Cont.*

Scientific Name	Ethnobotanical Uses	Phytochemical Components	Biological Activity	Ref.
U. dioica L.	In folk medicine, it has been used to treat rheumatism, arthritis, gout, eczema, anemia, urinary tract infections, kidney stones, hay fever, and the early stages of an enlarged prostate.	3-O-caffeoylquinic acid; 4-O-caffeoylquinic acid; 5-O-caffeoylquinic acid; caffeoylmalic acid; *p*-coumaroylmalic acid; quercetin O-rutinoside.	Antiviral, antimicrobial, antioxidant, anti-inflammatory, antiaging, and cytotoxic/anticancer effects, as well as benign prostatic, hyperplasia, antidiabetic, antiendometriosis, and nephroprotective effects.	[169–171]

4.1. Ethnobotanical and Ethnomedicinal Relevance

A. millefolium L. (Asteraceae family) is commonly known as yarrow or milfoil. It is the best-known and most widespread species, and has been one of the most used plants in both folk and conventional medicine for over 3000 years [172]. *A. millefolium* is native to Europe and western Asia, widespread in most temperate regions, and represented by about 85 species, which are mostly found in Europe, Asia, and North America [173]. In Bosnia–Herzegovina, the flowers are used as vegetables or in the preparation of liqueurs [129]. The leaves can be eaten cooked or raw. As they have a slightly bitter taste and a strong licorice-like scent, they can be added to mixed salads [6,11]. The plant is used in traditional medicine against wounds, burns, and internal and external bleeding due to its hemostatic properties. Almost all the pharmacological activities are attributed to the flowering tops and leaves [174]. Several cultures use this plant for different treatments. In Italy, it is mainly used against gastrointestinal problems but is also used also for urinary problems such as diuretics, menstrual problems, toothache, and sedatives [89]. These properties are attributed to the essential oils, sesquiterpenes, and phenolic compounds [92,93]. The recipe states that three cup of *Achillea* tea a day, prepared with 1.5 g crude drug, equal to a 900 mg extract, would cause an anti-inflammatory effect [90].

The *Borago* genus belongs to the Boraginaceae family. It comprises only five species, *B. officinalis*, *B. trabutii*, *B. longifolia*, *B. pygmaea*, and *B. morisiana*, all of them native to the Mediterranean basin. In folk medicine, most medicinal plants are used as aqueous extracts, which provide raw materials for different medicinal purposes. *B. officinalis* seeds and the aerial parts are traditionally used to treat respiratory, cardiovascular, and gastrointestinal diseases [103]; borage juice and tea are used to treat flu, colds, injuries, and ulcers. Borage is generally cultivated for its culinary and medicinal uses; currently, the preferentially consumed parts are the seeds, which are marketed for their oil. Therefore, borage is considered an oilseed crop [104]. As a vegetable, borage is included in many recipes from different countries: in Germany, it is used for the preparation of green sauce; in the Italian region, Liguria is an ingredient in the famous "Preboggion"; in Crete, in France, in Great Britain, and in Spain, it is boiled and sautéed with garlic. *Borago* flowers are used as snacks, salads, vinegar aromatizers, fritters, and soups in Italy, Libya, and Spain [175].

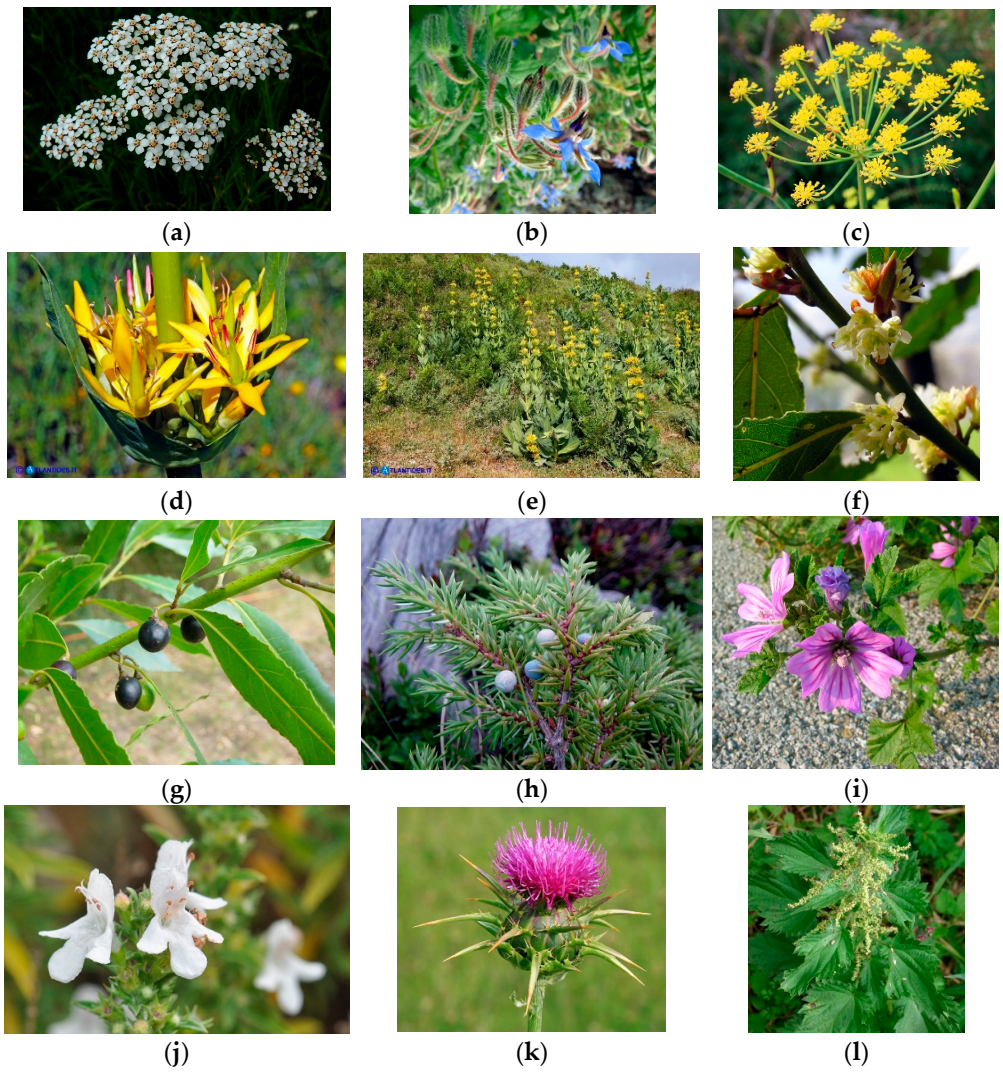

Figure 2. Some examples of plant wild species traditionally used in the central Apennines as food and/or medicine: (**a**) *A. millefolium* [70]; (**b**) *B. officinalis* [72]; (**c**) *F. vulgare* [74]; (**d**,**e**) *G. lutea* L. subsp. *Lutea*, reprinted with permission from Ref. [176]; copyright 2008–2024, Giuliano Mereu, (**f**,**g**) *L. nobilis*, reprinted with permission from Ref. [177]; copyright 2008, Marinella Zepigi (**h**) *J. communis*, reprinted with permission from Ref. [177]; copyright 2008, Marinella Zepigi (**i**) *M. sylvestris*, reprinted with permission from Ref. [177]; copyright 2008, Marinella Zepigi (**j**) *S. montana*, reprinted with permission from Ref. [178]; copyright 2024, Enzo de Santis (**k**) *S. marianum*; [179] (**l**) *U. dioica* [180].

Fennel (*Foeniculum vulgare* Mill.) is a plant belonging to the Apiaceae family and represents one of the most used plants in traditional medicine. It is a plant that grows spontaneously as a native aromatic plant in the large area around the Mediterranean basin, particularly in Israel, Egypt, and Tunisia, and on both coasts of the Adriatic Sea: Montenegro, Croatia, and Italy [108,112–116,181,182]. Alcoholic beverages are often enriched with aromatic components, such as herbs (leaves, roots, seeds, and flowers), fruits (whole fruit, peel, and hazel) and natural sweetening agents [117,183]. The preparation of these drinks dates to ancient Mediterranean history, and aromatic plants and essential oils are still used today [118]. In popular Italian cuisine [159], fennel liqueur, reaching 30% alcohol content, called "Finocchietto", is produced by macerating the fruits of *F. vulgare* in alcohol [119]. The characteristic flavor of fennel essential oil is related to the presence of anethole, fenchone, and estragole, which are the main chemical components. Anethole has a sweet, anise-like note, while estragole has a bitter flavor. The composition and concentration of the individual components depend on the geographical origin of the plant. Generally,

southern European plants produce sweeter-tasting extracts, while plants from central and northern Europe have more bitter flavors [112]. Fennel can also be used as an herbal tea for stomach aches due to its antispasmodic and carminative effects, aids intestinal peristalsis, has a diuretic effect, acts as an expectorant, and is also recommended for respiratory diseases [120].

Gentiana lutea L. is also known as yellow gentian, bitter root, and bitter herb. Belonging to the Gentianaceae family, it grows wild in hilly areas of Europe as far as Japan and is present in the traditional medicine of many countries [184], especially due to its antiseptic and anti-inflammatory properties [185]. The roots are the most widely used part of the plant as they are rich in bitter-tasting molecules such as amarogentin and gentiopicroside, and they have been known for their medicinal properties since antiquity. *G. lutea* L. radix is often used in the preparation of bitter liqueurs to stimulate the appetite and improve digestion. "Amaro di genziana" is a typical liqueur produced in the Abruzzo region of Italy. The quality of the gentian root is assessed by evaluating the main bitter principle, gentiopicroside [186].

Gentiana is considered a pleiotropic drug as it has multiple properties, such as antimicrobial, antioxidant, anti-inflammatory, anti-atherosclerotic, antihypertensive, hepatoprotective, and antidepressant activity [125–127]. *Gentiana* is a plant included in the "Regional Red Lists of the Plants" of Italy and is a protected plant (L.R. 11.9.1979 no. 45).

The *Juniperus* genus is a member of the Cupressaceae family [187] and has about 68 species and 36 variants of the same species. The *J. communis*, also called Zimbro, is the only species of *Juniperus* that has been documented as existing in both hemispheres, and has been found in the arctic regions of both Asia and North America. The Alps, Scandinavia, Poland, northwest European lowlands, and the mountainous regions of the Mediterranean in Europe are home to more varieties [188,189]. The considerable variety in the morphological traits and chemical composition of secondary metabolites can be traced to the vast geographical dispersion of the species [187]. Berries have a fragrant, spicy aroma and a slightly bittersweet flavor. Mature, dark berries are used in cuisine to season sauces and stuffing, and in pickling meats, and are also used to flavor spirits like gin or grappa. *Juniperus* has been traditionally used in many countries as a diuretic, antiseptic, and digestive [131].

Laurus nobilis L. is a member of the family Lauraceae, which comprises 32 genera and about 2000–2500 species [141]. It is cultivated in temperate areas of the world, mainly in south Europe and the Mediterranean basin [190,191]. It is also known as laurel, bay laurel, or sweet bay, and is the laurel tree featured Greek and Roman mythology [142], where it was considered a symbol of peace and a sign of victory in both military and sports competitions. Laurel is used in cooking as a flavoring and provides a spicy taste for meat, fish, broths, and vegetables. It is a component of a typical Italian plant infusion used as a digestive, named "canarino" [135]. Based on the classifications of diseases and remedies in ethnomedicine and ethnopharmacology suggested by Staub et al. [136], the major uses of *L. nobilis* include treatments for gastro-intestinal complaints, including indigestion, constipation, and flatulence; it is also used for diarrhea, hemorrhoids, and stomach aches. The leaves are traditionally used to reduce blood glucose levels and for fungal and bacterial infections [136]. This species is also reported to treat kidney diseases and coughs, colds, flu, and sore throats. Laurel leaves are one of the main ingredients of a preparation used for the treatment of respiratory ailments that are often called "Ricotto" or "Ricuotto". They still used in this way today and can be found in the traditional phytotherapy of central and southern Italian regions [135]. Essential oils or fumigations with bay leaves are also used as repellents and insecticides against home insects and crop pests [138].

Malva sylvestris L. is a flowering plant belonging to the Malvaceae family. It is native to north Africa, southwest Asia and southern Europe (Mediterranean area), although it is widespread worldwide as a weed [192]. Its edible uses are found in popular gastronomy; the young leaves are eaten raw in salads or, together with the sprouts, are used in soups and as boiled vegetables [143]. Traditionally, the plant has been used to treat various ailments,

such as coughs, colds, diarrhea, dysentery, hypertension, and skin diseases [11]. The Greeks and Romans noted its emollient and laxative properties, and several ethnobotanical surveys conducted in Europe highlight the potential of this neglected local resource, whose use is now on the brink of disappearance [143]. Roots, shoots, leaves, flowers, fruits, and seeds are applied in infusions, decoctions, poultices, liniments, lotions, baths, and gargles [98,149–155]. Also known as mallow, it is considered to have spasmolytic, lenitive, and choleretic effects. It is also used as a bronchondilator, an expectorant, in acne and skin care, and as an antiseptic, emollient, and demulcent [153–155].

Satureja montana L., known as winter savory, is a plant belonging to the Lamiaceae family. This family includes approximately 236 genera and more than 6000 species, some of them important medicinal plants [193]. The *Satureja* genus is mainly distributed in the Mediterranean area. Reports have been registered in Italy [194–196], Spain [197], France [198], Montenegro [199], Slovenia [200], Croatia [201], Serbia [202], Bosnia, and Herzegovina [203]. Winter savory is often used in Mediterranean recipes, and, recently, the use of its essential oil as a natural antibacterial agent in food packaging has been reported. [204,205]. The enrichment of olive oil with winter savory essential oil (EO) has led to low values of lipid oxidation and a higher concentration of antioxidants (total phenols and pigments) [206]. Winter savory dried leaf is used as an herbal tea [207]; this is an aqueous preparation that is extemporaneously prepared for oral administration for therapeutic purposes. In some regions of Italy, it is used for nervous gastric pains, bloating, and vomiting [161].

Silybum marianum L. Gaertn. (milk thistle) is a medicinal plant widespread in southern Europe, northern Africa, and parts of southern Russia, and found in North and South America and southern Australia. The aerial parts of the plant are edible and are cooked like the artichoke [208]. In Italy, its use has been reported in the treatment of liver and gastrointestinal disorders and as a laxative [168]. The leaves, unripe fruits, roots, and the bark are used in the treatment of gastroenteritis, diarrhea, and dysentery, while the leaves are applied on sores and for hemorrhoidal pains [11]. The leaves also act as a choleretic and cholagogue [74] and the Greeks have suggested that *S. marianum* could be used to treat gallstones and allergic coughs, and for "blood purification" [164].

Urtica dioica L. (stinging nettle) is an herbaceous perennial flowering plant growing in temperate and tropical wasteland areas around the world. It grows 1–2 m high and produces pointed leaves and white to yellowish flowers. Nettle has a well-known reputation for giving a savage sting when the skin touches the hairs and bristles on the leaves and stems [169]. *U. dioica* is certainly one a primitive vegetables that has been consumed since time immemorial. For a long time, in folkloric medicine, it has been used to treat rheumatism, arthritis, gout, eczema, anemia, urinary tract infections, kidney stones, hay fever, and the early stages of an enlarged prostate [169,209].

4.2. Bioactive Phytochemicals

Many secondary metabolites were isolated from each plant; Figures 3 and 4 show some of the most significant natural products from the polar, apolar, and essential oil (EO) extracts.

The MeOH extract of Italian *A. millefolium* (Vercelli, Italy) was shown to contain chlorogenic acid, 1,3-dicaffeoylquinic acid, 1,4-dicaffeoylquinic acid, 3,4-dicaffeoylquinic acid, 3,5-dicaffeoylquinic acid, and phenolic compounds like rutin, luteolin 7-O-glucoside, apigenin 4′-O-glucoside, apigenin 7-O-glucoside, and luteolin 4′-O-glucoside [91]. Major volatile compounds found in the Italian *A. millefolium* include the following: α-pinene, 17.2%; sabinene, 3.9%; β-pinene, 2.1%; (E)-methyl isoeugenol, 8.8%; β-bisabolene, 16.6%. *Achillea* oils were shown to have antifungal activity [210] and cytotoxicity activity against cancer cells [211]. Other compounds, like alkaloids, choline, achillinin A, azulene, chamazulene, salicylic acid, artemetin, lignans, tannins, and flavonoids, were found in this plant [172,174].

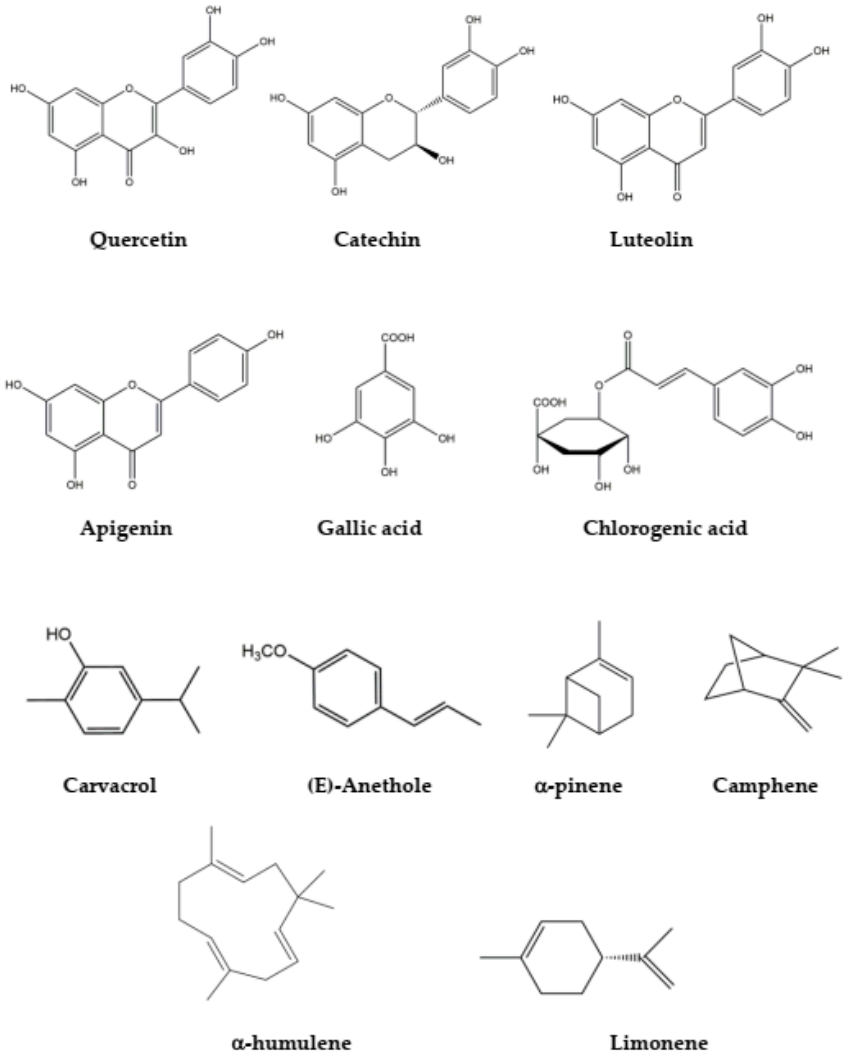

Figure 3. Common plant phenolic components and some volatile essential oil components (carvacrol; (*E*)-anethole; α-pinene; camphene; α-humulene; limonene).

An analysis of the aerial parts (methanolic extracts) of *B. officinalis* from Algeria revealed the presence of many flavonoids, rosmarinic acid, gallic acid, and chlorogenic acid, while, in the essential oil, spathulenol was the main component [212]. A lignane derivative, officinalioside, was isolated from the polar extract of borage's aerial parts from Egypt, along with megastigmane derivatives (actinidioionoside, (6S,9R)-roseoside, crotalionoside C), and kaempferol 3-O-β-D-galactopyranoside [213]. The RP-HPLC analyses of the methanolic, ethanolic, and aqueous extracts of Borage flowers from Iran confirmed the presence of phenolics (gallic acid; pyrogallol; salicylic acid; caffeic acid), flavonoids (myricetin; rutin), and isoflavonoid (daidzein). The EO from borage flowers was also prepared, and the major individual fatty acids were α-linolenic, stearidonic, palmitic, linoleic, and γ-linolenic acids [214]. As a member of the Boraginaceae family, *B. officinalis* is also known for its pyrrolizidine alkaloid content and its toxic properties [215]; oleuropein and litospermic acid were also identified in the aqueous extract of the plant [101]. The seed oil of *B. officinalis* is considered one of the richest natural sources of γ-linolenic acid (GLA, 18:3 n-6), ranging from 20 to 23% of the total fatty acid composition. GLA displays interesting medicinal properties, such as anti-inflammatory and anti-cancer properties, and can be used as an emollient of the skin and mucous membranes [104]. The main polyunsaturated fatty acids that were identified were linoleic acid (18:2 n-6), α-linolenic acid (18:3 n-3), γ-linolenic acid

(18:3 n-6, GLA), and stearidonic acid (SDA, 18:4, n-3), which account for approximately 70% of the polyunsaturated fatty acids [216].

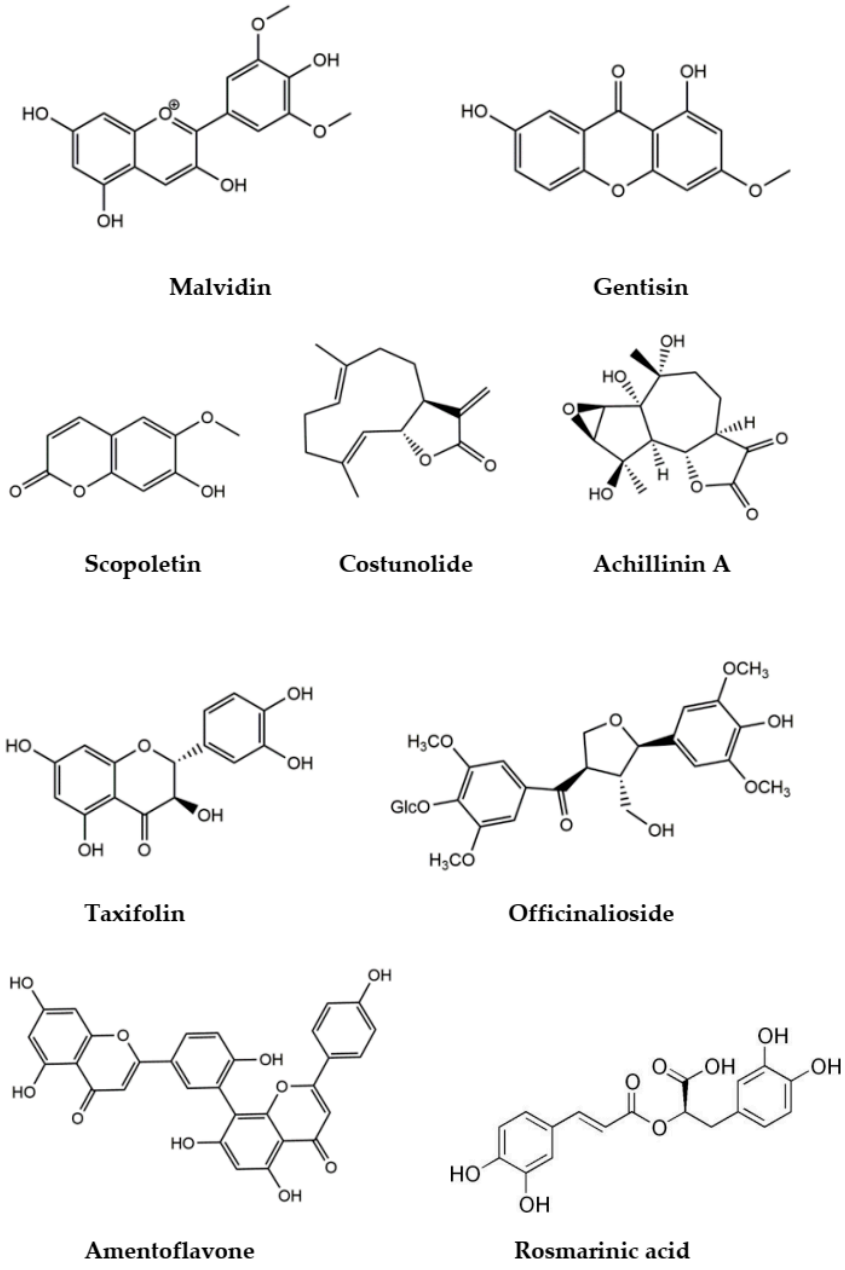

Figure 4. Some natural products from wild plants: malvidin from *M. sylvestris*; gentisin from *G. lutea*; scopoletin from *U. dioica*; costunolide from *L. nobilis*; achillinin A from *A. millefolium*; taxifolin from *S. marianum*; officinalioside from *B. officinalis*; amentoflavone from *J. communis*; rosmarinic acid from *F. vulgare*.

In general, the main ingredients of *F. vulgare* EOs are anethole (40–70%), fenchone (1–20%), and estragole (2–9%). *Trans*-anethole is also a common main component of fennel populations, especially cultivated populations. Alpha-pinene, camphene, methyl chavicole, and limonene are also presented in essential oils [112,115,217,218]. Differences in the quality of the essential oils' composition have been observed. These differences may be caused by different chemotypes, phenological stages, drying conditions, distillation modes, and geographic and climatic factors [115,181]. The main composition of fennel essential oil from mid–southern Italy includes α-pinene (33.75%), β-pinene (5.13%), myrcene (5.25%), 3-carene (6.12%), γ-terpinene-like (9.45%), estragole (25.06%), and (*E*)-

anethole (5.30%) [113]. Flavonoids and some important hydroxycinnamic acids are the most abundant polyphenols in fennel waste. Methanolic fennel seed extracts from Saudi Arabia were shown to contain vanillic acid, o-coumaric acid, and rosmarinic acid. Among the flavonoids, kaempferol, resveratrol, and rutin were found in higher concentrations, followed by myricetin, catechin, and quercetin [111]. In an aqueous extract of *F. vulgare* waste, 24 phenolic compounds were found, and 4-O-caffeoylquinic acid (4CQA) had the highest concentration of 1949 mg/g and 5824 mg/g of total polyphenols [110]. These exert evident antioxidant activity and other important biological properties, such as anti-inflammatory and anti-tumor activities, as well as the ability to modulate cell signaling and gene expression in different experimental models [5], making them good candidates for nutraceutical applications [219]. Complex trimers of stilbenes diglucosides were isolated from polar extracts of the fruit of *F. vulgare,* which were tested for their in vitro antioxidant activity [142].

Several secondary metabolites have been identified from *G. lutea*, such as iridoids, secoiridoids, xanthones, and flavones, which are distributed in different concentrations between the aerial parts and rhizomes. Gentiopicroside and stemoside were found to be abundant in the roots; iso-vitexin predominated in the leaves, and the amount of isogentisin was found to be ten times higher in the flowers than in the leaves. [220–223]. Iridoids and secoiridoids are a broad group of cyclopentane [c] pyran monoterpenoids found in the *Gentiana* genus, particularly in the leaves of *G. lutea*. Loganic acid, sweroside, amarogentin, gentiopicroside, swertiamarin, and their derivatives belong to these classes of compounds. They have been shown to have a large variety of pharmacological properties, including hepatoprotective, antitumor, and anti-inflammatory effects. Isovitexin, isosaponarin, isoorientin, and its glycosides are the main flavonoids isolated from *Gentiana* and known for their antioxidant and anti-inflammatory activities [224]. Xanthones such as isogentisin, gentisin, mangiferin, and gentiol are compounds of great interest due to their antibacterial, antifungal, hepatoprotective, and antioxidant activity. They have mainly been isolated in roots as mono- or polymethyl ethers or as glycosides. [225–228].

J. communis species contain a complex mixture of secondary metabolites that are responsible for both organoleptic characteristics, such as aroma and color, and beneficial health effects. These metabolites can be divided into several major categories, such as carotenoids and chlorophylls, phenolic compounds, and Volatile Organic Compounds (VOC's) [229]. Generally, most phenols reported in the *Juniperus* plant include caffeoylquinic acids with their corresponding derivatives, amentoflavone, catechin, epicatechin, quercetin, and their derivatives (see Table 2) [132]. Flavonols and flavones have been shown to act as radical scavengers and are associated with anti-inflammatory, antimicrobial, anti-proliferative, and pro-apoptotic properties. Furthermore, flavanones acting in synergy with flavones can inhibit the development of estrogen-dependent colon tumors. [133]. Several anthocyanins have also been isolated in juniper berries and, generally, occur in the form of cyanidin, delphinidin, peonidin, and pelargonidin glycosides. Anthocyanins also act as radical scavengers and exhibit anti-inflammatory activity, interacting with related pathways, increasing antioxidant defenses, and diminishing proinflammatory biomarkers, thus preventing the occurrence of many oxidative-stress-related disorders [130]. The chemical composition of the essential oil of *J. communis* differs according to the part of the plant that is extracted (berries, leaves, flowers) and the berries' stage of ripening [134].

L. nobilis leaves contain flavonoids such as isoquercitrin, luteolin, and rutin, and apigenin derivatives and flavonols such as catechin, cinnamtannin B1, epicatechin hexoside, (+)-catechin, (−)-epicatechin, epigallocatechin, and methyl eugenol. Many phenolic acids have been detected: rosmarinic acid, caffeic acid, 3,4-dihydroxybenzoic acid, 2-hydroxycinnamic acid, and others (see Table 2). Several cyclic terpenoids were found in *L. nobilis*, such as gazaniolide, spirafolide, reynosin, costunolide, santamarine, and lauroxepine [139]. The chemical composition of the EO from laurel leaves has been analyzed in different studies, and 1,8-cineole was found to be the major component [139]. Other compounds were present in appreciable amounts, such as camphene (0.05–13.4%),

linalool (0.37–47.21%), methyl eugenol (3.3–7.8%), D- limonene (21.6–32.4%), sabinene (0.34–14.05%), neoiso-isopulegol (2.5%), eugenol (0.22–2.47%), γ-terpinene (0.23–3.48%), α-pinene (1.39–8.92%), β-pinene (3.0–6.22%), and terpinen-4-ol (1.21–5.2%). α-terpinyl acetate (5.9–15.33%) and α-humulene (0.51–8.58%) were major constituents [141,230–233]. Anthocyanins were found in berries from *L. nobilis* with cyanidin 3-O-glucoside (41%) and cyanidin 3-O-rutinoside (53%) [139]. The main compounds of berries' EO were 1,8-cineole, α-phellandrene, β-pinene, α-pinene, α-terpinyl acetate, sabinene, camphene, germacrene D, and β-caryophyllene [139,141]. Several megastigmane and phenolic components were also isolated from polar extracts of *L. nobilis* leaves that exhibited anti-inflammatory activity [142,234].

Many phenolic compounds were detected in extracts from various parts of *M. sylvestris*. Total phenolic compounds were identified in leaves (386.5 mg g^{-1}), flowering stems (317.0 mg g^{-1}), flowers (258.7 mg g^{-1}), and immature fruits (56.8 mg g^{-1}) [143]. The primary components of the leaves were identified as gossypetin 3-sulphate-8-O-β-D-glucoside (gossypin) and hypolaetin 3′-sulphate, followed by isoscutellarein 8-O-β-D-glucuronpyranoside, hypolaetin 8-O-β-D-glucuronopyranoside, 3-O-β-D-glucopyranosyl-8-O-β-D-glucuronopyranoside, and hypolaetin 4′-methyl ether 8-O-β-D-glucuronopyranoside [145,235,236]. Anthocyanins like malvin (malvidin 3,5-glucoside), found only in flavylium cationic form, were mostly identified in flowers [237–240]. Oenin (malvidin 3-O-glucoside), malvidin, delphinidin, delphinidin-3-O-glucoside, kaempferol derivatives, quercetin, apigenin, myricetin, and genistein were detected in the flowers, and the total anthocyanin content was found to be 0.42–7.3% of the dry weight [239,241,242]. The leaves of *M. sylvestris* contain γ-sitosterol, stigmasterol, and campesterol [243]. Vernolic acid, linoleic acid, palmitoleic acid, sterculic acid, myristic acid, lauric acid, malvalic acid, oleic acid, and palmitic acid are the primary fatty acids found in seed oil [244,245]. Sesquiterpenes, nor-terpenes, monoterpenes, and diterpenes were also found in *M. sylvestris* [246]. Linalool, linalool-1-oic acid, and linalool-2-oic acid were detected in aqueous extracts from fresh leaves, along with several megastigmane derivatives [247].

S. montana (winter savory) is used in cooking due to its distinctive aroma, which is related to the presence of essential oils. The EO yield from the fresh plant can vary between 0.12 and 0.7% [197,203,248,249], with the volatile fraction mainly being characterized by thymol and carvacrol (oxygenated monoterpenes), indicators of antimicrobial activity [250,251], associated with open-chain and/or monocyclic monoterpenes that exhibit an allelopathic effect [252]. Carvacrol has been classified as Generally Recognized As Safe (GRAS) and approved for use in food [253], while linalool and p-cymene (non-oxygenated monoterpenes) have been shown to have analgesic effects [204]. Polar extracts contain variable amounts of secondary metabolites, such as phenolic acids, phenylpropanoids, fatty acids, tannins, and tocopherols [254,255]. The main constituents of the phenolic acid components were caffeic acid (78.17 μg g^{-1}) and gallic acid (15.36 μg g^{-1}). Quercetin, p-coumaric acid, chlorogenic acid, and ferulic acid were represented at concentrations of 2.36, 1.59, 1.36, and 0.50 μg g^{-1}, respectively [255].

From *S. marianum*, a typical extract, namely silymarin, is used. This is a mixture of different flavonolignans, and, at present, the term "silymarin" is indicative of an extract of *S. marianum* that is rich in these compounds. It is composed of silicristin, isosilybin A and B, dehydroxylysilybin and silybin, and flavonoids such as taxifolin, with silybinin being the most active. Silybinin consists of two diastereoisomers: silybin A and silybin B [256]. Flavonolignans have been isolated from the seeds and fruits and are the biologically active constituents of the plant; to date, 23 compounds have been identified from this species [163]. Several other minor flavonolignans have also been found: silychristin, isosilychristin, and silydianin, with several flavonoids, such as taxifolin [167], and 3′-O-methyltaxifolin and dihydrokaempferol from plant seeds [257]. Polyphenolic compounds such as hydroxycinnamic acids (caffeic, chlorogenic, ferulic, and cynarinic acids) and flavonoids (apigenin; catechin; luteolin; luteolin-7-O-glucoside; quercetin) have also been identified [257]. The oil fraction is known to be rich in fatty acids, palmitic (C16:0), oleic

(C18:1) and linoleic (C18:2) organic acids, sterols (cholesterol, campesterol, and stigmasterol) and tocopherol (vitamin E), triacylglycerols, and phospholipids.

The active chemical part of *U. dioica* includes several compounds from the lipophilic and hydrophilic extracts of different parts of the plant [170]. In particular, the commonly known phytochemical components from *U. dioica* are flavonoids, tannins, volatile compounds, and sterols [171,258,259]. Hexahydrofarnesyl acetone, carvacrol, carvone, naphthalene, copaene-8-ol, anethol, geranyl acetone, β-ionone, α-ionone, and phytol are characterized as the main components of *U. dioica* essential oil [260,261]. Rhizomes of *U. dioica* contain other biologically active compounds, such as scopoletin, sterols, fatty acids, polysaccharides, and isolectins [262]. Extracts of *U. dioica* have been studied for their various potential therapeutic applications: antitumor, antimicrobial, analgesic, and anti-inflammatory activity has been evidenced. Extracts showed antioxidant properties, and experimental tests proved that the constituents of *U. dioica* may have neuroprotective effects [263].

4.3. Evaluation of In Vitro Antioxidant Activity of Selected Edible Wild Plants

The antioxidant activity of *A. millefolium* was tested by different assays. DPPH scavenging test of MeOH extract showed an IC_{50} = 1.18 mg mL^{-1}; total antioxidant capacity (TAC) based on Cu (II) reduction and lipid peroxidation measurements (TBARS/LDL) were also calculated [91]. In the same study, Total Polyphenol Content (TPC) for the Italian plant was determined by Folin–Ciocalteau assay, with a result of 281.7 mg g^{-1} reported as mEq of Gallic acid [91]. Dias et al., in 2013, reported the results of DPPH, TBARS, and inhibition of β-carotene bleaching tests [264]. Mohammed et al., in 2023, described the antioxidant activity of the essential oils using TAA, DPPH, FRAP, and Metal Chelating Assay (MCA) [211], and the Total Flavonoid Content (TFC) of the Iranian plant was measured using the standard curves of Rutin and reported as mg per g dry weight [265].

B. officinalis seed extracts from Poland were assessed for their total polyphenol content using the Folin–Ciocalteau method, followed by an evaluation of antioxidant potential using the FRAP assay and the free radical method with the DPPH reagent. The flavonoid content in borage seeds was much lower than that observed in borage flower and leaf oil; however, the antioxidant activity of the seed meal infusion was high [266].

The antioxidant activity of essential oil extracted from different parts of *F. vulgare* was evaluated, showing that the leaves have a better EC_{50} (12.37 mg mL^{-1} at 60 min incubation) than seeds and umbels [267]. A similar study conducted on Tunisian EOs from fennel, characterized by their richness in estragole, revealed an important antioxidant activity [182], while the antioxidant activity of Tajikistan fennel EO was moderate. EC_{50} values were between 30 and 210 mg L^{-1} [268]. Finally, the Italian wild cultivar of fennel has a better antioxidant activity in essential oil when compared to cultivated fennel [269]. The total phenolic content (TPC) of the methanolic fennel seed extract (FS) was 70.42 mg gallic acid equivalent (GAE) g^{-1}; Total Flavonoids (TFC) and Total Flavonols (TFL) were 4.83 and 4.93 mg quercetin equivalent (QE) g^{-1}, respectively. Antioxidant activity was 9.36 µmol of Trolox equivalent (TE) g^{-1} [111].

The most studied part of *G. lutea* is the roots due to the presence of characteristic secoiridoid glucosides. *G. lutea* root's antioxidant activity was evaluated through various assays, including total phenolic content (TPC), DPPH, ferric-reducing antioxidant power (FRAP), and oxygen radical absorbance capacity (ORAC). Both methanol and ethanol produced the extracts with the highest activity, but methanol is toxic and not suitable for human use. Ethanol is safe and environmentally friendly and should be the first choice when producing extracts from natural resources. pH also plays a significant role in antioxidant activity, with higher activity observed under acidic conditions while increased pro-oxidant action was observed under alkaline conditions [125]. Gentiopicroside and stemoside were not directly involved in antioxidant activity, but mass spectrometry data indicated that antiradical scavenging activity is probably associated with xanthones' glycosides [226].

Furthermore, in vivo studies have evaluated the antioxidant activity of *G. lutea* root extract against ketoconazole-induced testicular damage in rat models [270].

In vitro tests showed that the *J. communis* ethanolic extract of berries showed a half-maximal inhibitory concentration (IC_{50}) of 1.42 μg mL^{-1}. Berries' methanolic extracts and essential oils also exhibited the capacity to scavenge DPPH•, ferric species, and β-carotene species. Ethanolic extracts of *J. communis* berries also showed the ability to scavenge peroxyl radicals and reduce power potential [271]. The remarkable antioxidant capacities displayed by *J. communis* extracts are indeed linked to their phenol and terpenoid content, in particular, quercetin, which contains the flavan-3-ol system, with hydroxyl groups in the 'key positions' of its structure (see Section 3.1), making it a potent radical scavenger. Regarding the antioxidant activity of terpenes, it has already been reported that α-pinene, p-cymene, limonene, and linalool possess notable capacities to block lipid peroxidation and to avoid deoxyribose degradation [272].

L. nobilis L. is a source of monoterpenes and other antioxidant compounds, such as tocopherol. The ultrasound-assisted extract (UAE) of dried laurel leaves from Brazil presented total phenolic compounds (TPC) of 47 mg GAE g^{-1} per extract, and the hydrodistillation extract (HD) shows a TPC of 22 mg GAE g^{-1} extract and EC_{50} (35 ± 1 μg mL^{-1}). Although phenolic compounds are the primary natural antioxidants, they are not the only class of substances that contribute to the antioxidant performance of natural products, which explains the good EC_{50} results obtained for the HD extract, since this extract does not possess α-tocopherol [230]. A potent suppression of lipid peroxidation was observed in aqueous and ethanolic extracts, with 96.8% and 98.6% inhibition rates, respectively, when using a linoleic acid emulsion at a concentration of 60 μg mL^{-1} [139].

M. sylvestris contains phenolic compounds in its leaves and flowers, which may be responsible for the plant's antioxidant activity [273]. Several tests have also determined the antioxidant properties of the plant. In the DPPH test, the aqueous extract at concentrations of 20 g mL^{-1} and 100 g mL^{-1} showed scavenging activity by decreasing the DPPH radical by 24% and 30%, respectively. The 0.1 mg mL^{-1} aqueous extract demonstrated 87% antioxidant activity when tested using the ß-carotene-linoleic acid assay. Antioxidant activity was also found in the EO of *M. sylvestris* (77% antioxidant activity) [151,274]. Overall, the antioxidant activity in the seed extracts was moderate to poor [275–277].

Due to the presence of polyphenolic compounds, ethyl acetate fractions of *S. montana* from MeOH extract and the total EO demonstrated radical scavenging activity via DPPH and ABTS assays. A spray-dried hydroalcoholic extract of winter savory, in combination with 10% maltodextrin as a carrier and drying agent, also showed the same activity [278]. EOs show less antioxidant activity than aqueous or ethanol extracts; this is due to the presence of carvacrol and sesquiterpenes that do not give rise to antioxidant activity [279].

Several studies on antioxidant activity were carried out on methanol, ethanol, and aqueous extracts and EO. However, many papers agree that the remarkable antioxidant properties of *S. marianum* are significantly related to its flavonolignan content [165].

The aqueous extract of *U. dioica* leaves exhibited antioxidant activity, achieved by the DPPH radical scavenging (IC_{50} = 16.93 ug mL^{-1}), reducing power (EC_{50} = 30.07 ug mL^{-1}), and polarographic (HPMC = 243.2% mL^{-1}) assays [259]. Based on these results, *U dioica* extracts have been proposed as an antioxidant and as a source of anti-ageing phytochemicals for cosmetic applications [280]. A comparative study by Carvalho et al. demonstrated that the antioxidant properties of *U. dioica* are greater than those observed for the aerial parts of other nettle species [171].

5. Therapeutic Potential of Selected Edible Wild Plants

5.1. Anti-Inflammatory Activity

A. millefolium has shown anti-inflammatory activity. It is used in the treatment of gastrointestinal and hepato-biliary disorders and to treat skin inflammation. This activity is probably due to the presence of sesquiterpenes, known for their anti-inflammatory activity through the inhibition of arachidonic acid metabolism. Antiphlogistic activities

have been observed in Yarrow fractions enriched with flavonoids and di-caffeoylquinic acids. The anti-inflammatory activity of this extract is ascribable to the inhibition of human neutrophil elastase, which is known to be associated with the inflammatory process. The in vitro anti-inflammatory activity was also established through the inhibition of matrix metalloproteinases (MMP-2 and -9). These proteases are involved in psoriasis, atopic dermatitis, and inflammatory bowel diseases such as ulcerative colitis and Crohn's disease. Azulenes, which make up about half of the chemical compounds in yarrow, are a potent anti-inflammatory agent [90].

The seed oil of *B. officinalis* has shown powerful anti-inflammatory and analgesic effects. Seed oil was tested against carrageenan-induced inflammation and compared with indomethacin, a known anti-inflammatory drug. The analgesic effect of *Borago* seed oil was tested in mice using two assays: the tail immersion test, which is used to determine the central analgesic effect, and the writhing test, which is used to determine the peripheral analgesic effect in mice [94]. Borage extracts have exhibited anti-inflammatory properties, as observed in the methanolic extracts, which result in a potent inhibition of collagenase and elastase activity. This characteristic underlines the anti-ageing properties, meaning that borage extracts are a source of valuable bioactive compounds with protective effects on skin cells [97].

The oral administration (200 mg kg^{-1}) of *F. vulgare* fruit methanolic extract exhibited inhibitory effects against acute and subacute inflammatory diseases and type IV allergic reactions and showed a central analgesic effect. At the same time, the administration of methanolic extracts of *F. vulgare* led to an increase in plasma SOD and catalase while MDA decreased. These data seem to demonstrate that the use of methanolic extracts from fennel seeds is effective in relieving inflammation [281]. Extracts and pure compounds from *F. vulgare* fruits showed antioxidant activity in vitro (DPPH, TBARS); the antioxidant activity was higher in the pure compounds than the crude extracts but was weaker than the reference compound, i.e., quercetin [282].

G. lutea L. has been used to prevent or treat inflammatory disorders for centuries. In vitro studies have shown that *G. lutea* root extracts have anti-inflammatory properties, with the rate of enzyme inhibition increasing with time. In vivo studies have also demonstrated that apolar and alcoholic extracts of *G. lutea* rhizomes have anti-inflammatory activity in different animal models [127].

The anti-inflammatory effects of *J. communis* have already been evaluated by in vitro and in vivo studies. The anti-inflammatory activity is closely associated with the presence of phenolic compounds and terpenes, such as amentoflavone, α-pinene, 1-octanol, and linalool. These compounds have been shown to inhibit inflammatory cytokine and prostaglandin expression [125]. Recently, loganic acid and gentiopicroside were tested in silico using an innovative technique named Inverse Virtual Screening (IVS) to highlight putative partners among a panel of proteins involved in inflammation and cancer events [283].

L. nobilis extracts have shown the ability to reduce edema caused by chemicals in the ears and paws and lung inflammation caused by LPS. Bay leaf extracts also induced a reduction in skin injuries and inflammation caused by *Propionobacterium acnes* [140]. Megastigmane and phenolic components able to inhibit nitric oxide production were isolated from polar extracts of *L. nobilis* leaves [142], and it has been proven that lauroside B induces apoptosis in human melanoma cell lines by inhibiting NF-κB activation [234].

Numerous studies have investigated the anti-inflammatory properties of *M. sylvestris* [284]. Their results claim that malvidin 3-glucoside, isolated from *M. sylvestris* leaves, is mainly responsible for the anti-inflammatory action on the skin. In carrageenan-induced oedema in rats, the anti-inflammatory properties of creams with various concentrations of mallow extract were evaluated. A 5% malva cream effectively reduced carrageenan-induced edema when compared to placebo therapy. This effect was greater than that of a cream containing 2% indomethacin, used as a positive control and a potent non-selective inhibitor of cyclo-oxygenase-2 (COX-2) [148]. The beneficial component rutin was isolated in a chemical investigation of *M. sylvestris* extract. This flavonoid is widely used in plant-based beverages, cuisine, and folk medicine [285]. Rutin

has been shown to be an anti-inflammatory therapeutic candidate, with a novel mechanism for selective COX-2 inhibition [286].

Methanolic extracts from *S. montana* were evaluated for their anti-inflammatory activity using COX-1, COX-2, 5-LOX, and MPO inhibition assays. The alcoholic extract showed both a powerful anti-inflammatory activity and a strong antioxidant activity [287].

Silymarin extract from *S. marianum* showed an important anti-inflammatory effect in carrageenan-induced rat paw oedema, inhibiting the release of elastase proteinases from neutrophils as a response to normal and chronic inflammation [165]. The common molecular targets of *S. marianum* are the multiple signaling pathways associated with oxidative stress and inflammation. In addition, flavonolignans are potential PPARγ and ABCA1 agonists, PTP1B inhibitors, and metal chelators [288].

5.2. Anti-Microbial Activity

A. millefolium extracts show antimicrobial activity. They are used as an infusion for respiratory tract infection [172], against flu as an antiseptic [174], to treat gastrointestinal infections, and as an anti-acne [90]. Many papers reported the antifungal activity of the essential oils on various fungal strains, with an MIC ranging from 0.32 to 1.25 μL mL^{-1} against dermatophyte strains [210]. Vitalini et al. 2011 reported luteolin 7-O-glucoside and apigenin 7-O-glucoside as the most active compounds against the *Plasmodium falciparum* chloroquine-resistant strain (IC_{50} of MeOH extract = 44.6 μg mL^{-1}) [91].

In *B. officinalis* flower extracts, high (methanolic extract), moderate (ethanolic extract), and weak (aqueous extract) antimicrobial activity was reported [214]. Flavonoid-rich extracts and EO *Borago* aerial parts were tested on bacteria isolated from respiratory infections of clinical patients. Multiresistant hospital isolates were found to be sensitive to the flavonoid extracts and to the essential oil; interestingly, *Escherichia coli* (resistant), *Streptococcus pneumoniae* (sensitive to amoxicillin), and *Klebsiella pneumoniae* (sensitive to Imipeneme) were sensitive to flavonoids [289].

Fennel essential oils showed extensive antibacterial activity against Gram-positive bacteria and fungi such as *Aspergillus niger*. Gram-negative bacteria, particularly *E. coli*, are less sensitive to fennel essential oils, as well as *Listeria innocua* CECT910 and *Pseudomonas fluorescens* [290–292]. An antimicrobial role against *Giarda duodenalis* has been described by the *trans*-2,4-undecadienal (IC_{50} 72.1 μg mL^{-1}). However, it was not active as the positive control metronidazole (IC_{50} 0.5 μg mL^{-1}) against the parasite [293]. The activity of the essential oil of *F. vulgare* also varied considerably between Gram-negative and Gram-positive bacteria. This low antimicrobial activity also seems to be related to strain susceptibility and the essential oil's composition, which is poor in components such as carvacrol and thymol, which are usually associated with higher antimicrobial activity [294]. Other authors specifically describe controversial antimicrobial properties obtained using different extraction methods [295].

Interestingly, the experiment was designed to evaluate the effectiveness of fennel essential oil in controlling *Fusarium solani* infections on *Vicia faba* L. The growth of *F. solani* was inhibited both in vitro and in vivo, allowing for a reduction in disease incidence by 50%. The essential oil acted on both the fungus and the plant as an enhancer of defense reactions [296].

In vitro studies have shown that *Pseudomonas aeruginosa*, *Bacillus subtilis*, *Proteus mirabilis*, *Staphylococcus epidermidis*, and *Candida albicans* were the most sensitive to Gentiana leaf extract, with MIC values between 0.12 and 0.31 mg mL^{-1} [220,297,298]. The flower extract was not very active against the tested microorganisms, with the most sensitive being *Salmonella enteritidis* (MIC 0.15 mg mL^{-1}). Both leaf and flower extracts showed an antitubercular effect against *Mycobacterium bovis*. Tests performed on isolated pure compounds showed a broader spectrum of activity; gentiopicrin was active against *E. coli* (0.12 mg mL^{-1}), while it had a moderate effect against *Staphylococcus aureus* and *Salmonella typhimurium* (0.15 mg mL^{-1}). Xanthone isogentisin was particularly active against *M. bovis*,

while moderate activity was observed against the gram-negative *E. coli* and *P. aeruginosa* (0.15 mg mL^{-1}) and the gram-positive *Micrococcus luteus* (0.15 mg mL^{-1}).

A different biological activity was observed in *J. communis* extracts. In phenol-rich extracts, antiparasitic action dominates, whereas essential oils exhibit antimicrobial effects. [129]. Generally, extracts with a more balanced composition in their components showed greater antibiotic effects against multiresistant hospital isolates belonging to the species *S. aureus*, *Serratia marcescens*, *Enterobacter cloacae*, *K. pneumoniae*, *P. aeruginosa*, *Acinetobacter baumanii*, and *Listeria monocytogenes*, as well as *C. albicans*. The use of essential oils obtained from *J. communis* biomass, without differentiating each of its parts, showed remarkable inhibitory activity against *E. coli* at concentrations between 1.25 and 2.5 mg mL^{-1} [299]. Notable inhibitory activities were observed against other Gram-negative bacteria, such as *P. mirabilis*, *K. pneumoniae*, *P. aeruginosa*, and *Morganella morganii*; however, only slight activity against *L. monocytogenes* and methicillin-resistant *S. aureus* was observed [130]. The different effects against various pathogenic fungi obtained using the EOs of *Juniperus* are believed to be related to the composition of the EOs, particularly the ratio of sesquiterpene hydrocarbons and oxygenated aromatic hydrocarbons [300].

Since ancient times, *L. nobilis* has been an important ingredient in traditional medicine for the treatment of different infectious diseases [301]. *L. nobilis* EO, seed oil, and a methanolic extract of seed oil showed antibacterial activity in vitro. However, the methanolic extract of the seed oil has higher antibacterial activity than the EO. *L. nobilis* was detected to have EO activity against *S. aureus*, *B. subtilis*, and *Staphylococcus intermedius*. One of the main constituents of bay leaf is 1,8 cineole, which may be responsible for its antibacterial activity. The antifungal activity of EO from leaves was examined on seven strains of plant pathogenic fungi in vitro at different concentrations. The highest antifungal activity was obtained against the fungus *Botrytis cinerea* at a concentration of 250 mg mL^{-1} [302]. Bay leaf EO has shown efficacy against a large panel of Gram-negative and Gram-positive bacteria and three fungi [303].

M. sylvestris exhibited moderate activity against selected microorganisms associated with typical antibiotics [304]. De Souza et al. showed the antimicrobial activity of *M. sylvestris* aerial part extracts against *C. albicans*, *S. aureus*, *M. luteus*, *B. subtilis*, *S. epidermidis*, *E. coli*, and *Saccharomyces cerevisiae*. Their study reported that ethanol extracts of *M. sylvestris* were active against *P. aeruginosa*, *B. subtilis*, and *E. coli*, whereas methanol extracts only showed activity against *S. cerevisiae* [305]. The antimicrobial activity of ethanolic extracts of the leaves and flowers against *Helicobacter pylori* strains ranged from moderate to low [306]. Other studies showed that the seed oil inhibited the growth of all tested microorganisms except the Gram-negative bacteria [307]. The only preparation of *M. sylvestris* that demonstrated substantial antimicrobial activity against fungi was an aqueous extract of the leaves. The aqueous extract prevented the growth of colonies of the *Fusarium culmorum*, *Aspergillus candidus*, *A. niger,* and *Penicillium* species [308].

S. montana EO (SEO) was demonstrated to have antimicrobial activity in several application fields, ranging from veterinary medicine [309,310] to plant pathology, with phytogenic bacteria such as *Xanthomonas euvesicatoria* [311]. In general, gram-positive bacteria proved to be more sensitive to EO treatment, while gram-negative bacteria were less sensitive—even more resistant yeasts and fungi [312,313]. The impact of SEO is certainly effective and important, but the disposal problem must be taken into consideration, as this can cause problems and modify the microbial communities of soil and water [314]. Encouraging results were obtained from a combined therapy of SEO and antibiotics. For example, associations between SEO and erythromycin and gentamicin have been described. This association improves the effectiveness of monotherapeutic treatments, reduces adverse effects by reducing the dose of the drug, and combats antibiotic-resistant bacteria [253,315]. Antiphytoviral activity was also described [316].

S. marianum extracts were tested against several pathogenic strains, such as *P. aeruginosa*, *E. coli*, *Salmonella typhi*, *S. epidermidis,* and *K. pneumoniae* [317]. In a recent study, Rakelly de Oliveira et al. [318] demonstrated an interesting antibacterial effect of silymarin and its

major compound, silibinin. Indeed, silymarin inhibited *E. coli* at MIC = 512 μg mL^{-1}, while silibinin inhibited 64 μg/mL (MIC = 64 μg mL^{-1}), *P. aeruginosa* (MIC = 1024 μg mL^{-1}), and *S. aureus* (MIC = 1025 μg mL^{-1}). An important effect against *C. albicans* was also observed by Yun e Lee et al. Their results revealed that a possible mechanism of action of silymarin as an antifungal agent may involve an increase in the membrane permeability of *C. albicans* [319].

The antibacterial activity of ethanol and aqueous extracts of *U. dioica* has been demonstrated against both Gram-positive and Gram-negative bacteria and yeasts, including *Proteus mirabilis*, *P. aeruginosa*, *Enterobacter aerogenes*, *E. coli*, *Citrobacter koseri*, *S. pneumonia*, *S. aureus*, *M. luteus*, *S. epidermidis*, and *C. albicans*. The extracts were also active against *Mycobacterium tuberculosis* in cases of multiple drug resistance [170,320]. Notably, the aqueous (microwave-assisted, ultrasound-assisted, and subcritical water extraction) and ethanol extracts of *U. dioica* leaves also confirmed the antibacterial activity, with a minimal inhibitory concentration (MIC) of 9.76 ug mL^{-1} and 0.0625–0.500 mg mL^{-1} against methicillin-resistant (MRSA) and methicillin-sensitive (MSSA) *S. aureus* strains [259]; these observed effects are assumed to be due to the high content of hydroxycinnamic acids (chlorogenic, caffeic, and rosmarinic acids) and flavonoids (quercetin) [321].

5.3. Protection against Cardiovascular Diseases

The hydroalcoholic extract of *B. officinalis* leaves, rich in polyphenols and sterols, produced a concentration-dependent relaxation of spontaneous and K^+-induced contractions (80 mM) in isolated rabbit jejunum preparations, suggestive of a Ca^{++} antagonistic effect. In rabbit aorta preparations, *Borago* showed a vasodilator effect against phenylephrine- and K^+-induced contractions. When tested in guinea pig atria, *B. officinalis* inhibited the force and speed of atrial contractions. These results suggest the spasmolytic effects of *Borago* extracts [103].

Recent experiments in rats suggest that the inhalation of *F. vulgare* essential oil by experimental animals could lead to a reduction in blood pressure [322].

G. lutea root extracts may also have promising activity in the prevention and treatment of cardiovascular disease, particularly thromboembolic disorders, attributable to their bitter constituents, such as amarogentin and isovitexin [125].

L. nobilis decoction is utilized to reduce blood pressure and treat cardio-vascular illnesses [140]. The powdered leaves of *L. nobilis* have positive effects on lipid and blood sugar dysregulation. After treatment, there was a reduction in plasma glucose levels, a decrease in overall cholesterol levels, a significant decrease in low-density lipoprotein (LDL) levels, an increase in high-density lipoprotein (HDL) levels, and a decrease in triglyceride levels [323]. Extracts of *L. nobilis* leaves showed a vascular protective effect and angioprotective activity on rat liver capillaries, and they prevented the progression of necroinflammation. These results could be explained by the presence of flavonoids, terpenes, and terpenoids with antioxidant and antimicrobial properties [139].

The main components of the EO of *S. montana*, such as carvacrol and thymol, have been found to be responsible for reducing serum cholesterol levels. Carvacrol and other monoterpene hydrocarbons, flavonoids such as apigenin, and phenolic acids such as labiatic acid could contribute to the antiplatelet properties [324]. *Satureja* flavonoids also have antioxidant and anti-hyperlipidemic properties [325].

The various traditional uses of *S. marianum* have motivated several experimental investigations into the pharmacological properties of the plant. Antihypertensive and cardioprotective activities have been documented, which seem to be linked to the presence of taxifolin [165].

U. dioica (leaves extracts) and isolated flavonoids were active against thrombin-induced platelet aggregation (IC50 values of 0.25 ± 0.05 and 0.40 ± 0.04 mg/mL) [326].

5.4. Role of Wild Plants in Cancer Prevention and Treatment

Due to the considerable number of different secondary metabolites, the tested species exhibit toxic activity against the growth of tumor cell lines, and several experiments were

conducted both in vivo and in vitro. *A. millefolium* showed activity on human cancer cell lines (MCF-7, NCI-H460, HCT-15, HeLa, and HepG2) with low toxicity to primary non-cancerous liver cells (PLP2) [264].

B. officinalis EO contains a high concentration of γ-linolenic acid, with several anti-cancer activities, inhibiting the p38 MAPK-dependent activator protein and the mitochondria-mediated apoptosis pathway [327].

The ethanolic extract of *F. vulgare* seeds significantly reduced the growth of lung cancer cells both in vitro and in vivo. The alcoholic extract reduced viability and triggered apoptosis in lung cancer cell lines NCI-H446 and NCI-H661 by targeting the Bcl-2 protein, which may suggest that it has potential as a therapeutic drug for lung cancer [328]. The role of anethole, found in fennel extracts, in anti-cancer activity was demonstrated in albino mice [329].

In vitro studies have investigated the cytotoxic effect of the *G. lutea* leaf extract on various cell lines, including human cervix adenocarcinoma (HeLa), breast cancer (MCF7), prostate cancer (PC3), and colon cancer (LS174). The Gentian methanolic leaf extract demonstrated a moderate cytotoxic effect against HeLa cells, with an IC50 value of 41.1 ± 1.5 μg mL^{-1}, compared to cisplatin, used as a control [125].

Methanolic extracts of *J. communis* leaves have been found to block the growth and development of C6 rat-brain tumor and HeLa human-cervix carcinoma cells, PC3 human-prostate cancer cells, HCT 116 human-colon cancer cells, and MCF7 breast cancer cells. Essential oil and extracts from *J. communis* berries have also been found to suppress A549 human lung adenocarcinoma epithelial cells' growth and development, as well as suppress the development of SH-SY5Y human neuroblastoma cells [330,331].

L. nobilis seed extract was suitable for eliminating multidrug-resistant P-glycoprotein-expressing tumor cells [139]; fresh EO exhibited growth-inhibitory effects on the breast cell line, lung cell line, and brain cancer cell line. The cervix cell line exhibited the lowest sensitivity to essential oil (IC_{50} value of 1.8 μg mL^{-1}) [141].

The study of Alesiani et al. [332] demonstrated the cytotoxic activity of *M. sylvestris* leaf extracts on murine using an MTT assay and human cancer cell lines.

Studies have been conducted on the antiproliferative activity of *S. montana* extracts on "mice's model of induced Ehrlich ascites carcinoma (EAC)". The results show that the extracts had a positive role in inducing oxidative stress in malignant cells [279]. Carvacrol is confirmed to have an antitumor effect on liver cancer [333], as well as apoptosis [334], metastatic breast cancer cells (MDA-MB 231) [335], and on human colon adenocarcinoma (HT-29) and human breast adenocarcinoma (MVF-7) [160].

Silibinin, silymarin, and silybin A and B from *S. marianum* possess anticancer activity on several tumor cell lines [165].

U. dioica aqueous extracts have responded positively in studies on prostate and breast cancer [336,337].

5.5. Neurological Disorders and Wild Plants

The various metabolites may play an important role in neurological disorders. *A. millefolium* is used as a sedative and analgesic against pain (headache, toothache, menstrual pain, and dysmenorrhea) [338,339].

The analgesic effect of *B. officinalis* seed oil was tested in mice using two assays: a tail immersion test to determine the central analgesic effect, and a writhing test, used to establish the peripheral analgesic effect in mice [94].

Inran et al. investigated the role of fennel seed extracts in promoting functional recovery following a mechanical insult to the sciatic nerve of mice, concluding that *F. vulgare* may be a potential therapeutic candidate to accelerate functional recovery after peripheral nerve injury [340,341]. In both studies, the authors considered fennel extracts and *trans*-anethole to be suitable candidates for the prevention and treatment of stress-induced neurological disorders [342].

G. lutea extract and its compounds exert effects on the central nervous system (CNS). Iridoids such as geniposide have been found to exert beneficial effects on neuronal cell cultures due to their ability to activate protein kinase, leading to neuronal cell differentiation [343]. The same plant extracts also enhanced neurite outgrowth [344]. *G. lutea* extract significantly enhanced the viability of cells treated with vinblastine and prevented Bcl-2 phosphorylation induced by the antimitotic drug vinblastine. These results suggested that *G. lutea* may be a potential vegetable resource for preventing and treating Parkinson's and Alzheimer's disease thanks to its MAO-B inhibition activities [345].

A neuroprotective effect was observed in the n-hexane fraction of *L. nobilis*. Indeed, in an in vivo study using rodents with Parkinson's disease, the fraction exhibited a marked inhibition of 6-hydroxydopamine (6-OHDA)-induced cell loss of tyrosine hydroxylase (TH)-positive cells in the substantia nigra [139]. Additionally, bay leaf extracts showed promising results in reducing neuronophagia, localized gliosis, and neural necrosis in the rat brain, helping to resolve the lead-induced imbalance in brain acetylcholinesterase (AcChE) activity [140,346].

The dried methanolic extract from *S. montana* leaves was demonstrated to have significant anxiolytic activity in rats. Carvacrol and rosmarinic acid, used as controls, only showed a moderate anxiolytic effect in some tests [347]. *Satureja* genera essential oil may act as a neuroprotective agent in the early stage of Alzheimer's disease [348], as well as *S. marianum* extracts [165].

5.6. Diabetes and Hepatoprotective Effects of Edible Wild Plants

Recently, *A. millefolium* ethanolic extract was tested for its in vivo antidiabetic effects. The hydroalcoholic extract possesses an anti-diabetic effect in vivo through a multitarget activity involving α-glucosidase inhibition, insulin secretion, and potential insulin-sensitizing actions [165].

B. officinalis was shown to have relevant hypoglycemic activity in rat models [349].

Essential oil and aqueous extracts of *F. vulgare* were administered to rats with streptozotocin-induced diabetes, with hyperglycemia corrected from (162.5 + 3.19 mg dL^{-1}) to (81.97 + 1.97 mg dL^{-1}), and reducing the pathological abnormalities in diabetic-induced rats [350] A similar study showed that fennel seed extract and its active ingredient *trans*-anethole can protect the liver from diabetes-induced liver damage in rats, probably through its hypoglycemic and antioxidant effects [351]. Experimental treatments with the 80% methanolic extract of the wild and cultivated fennel showed hepatoprotective effects at a concentration of 12.5 μg mL^{-1} and hepatotoxic effects at a concentration of 1000 μg mL^{-1} [352]. In a further study, oxidative stress and the complications of hepatotoxicity caused by CCl_4 injection in rats were reversed by the administration of fennel seed extracts at 300 or 600 mg kg^{-1}. The improvement in liver function was monitored by following the attenuation values of the enzymes ALT, AST, and ALP [111].

Gentiana roots have been widely used in folk medicine, so scientific studies have focused on their choleretic and hepatoprotective properties, which make them a good remedy for stomach and liver inflammations. In pylorus-ligated mice treated with methanolic extract of gentian root in the duodenum, there was a decrease in gastric juice secretion and total acid production, with a noticeable dose-dependent effect at doses of 500 and 1000 mg kg^{-1}. The hepatoprotective activity of gentian root may be due to gentiopicroside, which has been reported in previous studies to resolve cholestasis [353,354]. As the incidence of liver problems has increased in recent years, the use of gentian root extracts may provide an alternative to synthetic drugs due to their hepatoprotective activity [354,355].

Ethyl acetate fractions of *J. communis* leaf extracts have been shown to be hepatoprotective agents, promoting favorable portal triads and central-vein arrangements [356].

Extracts of *L. nobilis* have been used in folk medicine due to their anti-diabetic effect. Diabetic rats treated with *L. nobilis* extracts showed a significant decrease in glucose concentration compared to untreated diabetic rats. A beneficial effect on pancreatic islet regeneration was also observed, and levels of liver enzymes, total protein, creatine ki-

nase, calcium, urea, and ferritin returned to near-normal levels. The EO of *L. nobilis* also suggested the inhibition of alpha-glucosidase, which is an indication of its in vitro antidiabetic activity [139,140]. An extract of *L. nobilis* leaves proved to be a powerful free radical scavenger in vivo, preventing carbon tetrachloride-induced hepatotoxic effects in rats.

The methanolic extract of *M. sylvestris* protected liver tissue from the harmful effects of paracetamol in a dose-dependent manner by lowering the blood levels of liver enzyme markers. In animals treated with mallow, the dramatic lowering of the blood levels of liver enzyme markers was complemented by the regeneration of liver tissue, demonstrating the hepatoprotective properties. The traditional use of mallow in liver problems has been scientifically validated through the hepatoprotective activity of *M. sylvestris* [147,357].

The EO of savory products, through experiments on rats, induces a hepatoprotective effect and a decrease in inflammatory processes in the organs of the gastrointestinal tract [358].

The silymarin extract from *S. marianum* was found to promote hepatocyte regeneration and inhibit liver fibrosis by significantly increasing the survival time of rats with paracetamol-induced liver injury [359]. In addition to the hepatoprotective action, scientific evidence suggests that silibin exerts its activity by interacting with various tissues through the modulation of inflammation and apoptosis, which, together with its antioxidant power, are the key points that have led to its use in various diseases [360]. Oral administration of silymarin extract was able to generate a significant decrease in ALP, ALT, and AST in the liver tissue of rats with lead-induced liver toxicity [361].

U. dioica showed a hepatoprotective effect by increasing the activity of some liver enzymes (paraoxonase, arylesterase, and catalase). Treatment with *U. dioica* reduced oxidative stress, with a decrease in ceruloplasmin levels. Also, treatment with *U. dioica* extracts generated an antioxidant effect, preventing the formation of some oxidant agents such as LOOH and showing a protective effect on the liver in rats damaged by hepatic ischaemia-reperfusion [355]. *U. dioica* can prevent liver fibrosis and cirrhosis, suggesting that this plant probably protects the liver through immunomodulatory and antioxidant activities [362].

5.7. Other Biological Activity

The results of in vitro tests on human keratinocytes (HaCaT) and fibroblasts (BJ) showed that methanol and methanol/water extracts of *B. officinalis* can reduce the intracellular level of reactive oxygen species in skin cells. It has been proposed that oral or topical borage oil may be effective for the treatment of atopic dermatitis. Atopic dermatitis is believed to be associated with an abnormality in the metabolism of essential fatty acids (EFAs), particularly the altered production of gamma-linolenic acid (GLA), so nutritional supplementation with omega-6 essential fatty acids (ω-6 EFAs) is of potential interest for the treatment of atopic dermatitis. Borage oil is of interest because it contains two to three times more GLA than evening primrose oil (*Oenothera biennis* L.). Borage oil is well tolerated in the short term, but no long-term tolerability data are available [363].

In human studies, *G. lutea* extracts were effective in reducing increased intestinal permeability, a problem that causes a more significant absorption of endotoxins due to the loss of integrity of the epithelial cells of the intestine tenuous. In Complementary and Integrative Medicine (CIM), *G. lutea* reduced the time needed to resolve the alterations in intestinal permeability to 4–5 months compared to the expected 6 months [364]. The Committee on Herbal Medicinal Products approved the use of *G. lutea* for mild stomach and gut complaints. Still, they limited their approval to their traditional use and not long-term use, as there is poor evidence from clinical trials [125]. Gentian root and its hydroalcoholic extracts have shown potential in treating skin disorders, including atopic dermatitis and psoriasis. Further research is needed to understand the mechanisms behind these effects and their potential applications in various skin conditions.

Hydroethanolic extracts (90% ethanol, *v*/*v*) of *J. communis* berries displayed antiprogestational and antifertility activity at doses ranging from 50 to 450 mg/kg on female

rats, without estrogenic or antiestrogenic effects. Moreover, the oral administration of hydroethanolic extracts (50% ethanol, *v*/*v*) from *J. communis* berries at doses of 300 and 500 mg/kg in albino female rats from day 1 to day 7 of pregnancy exhibited dose-dependent anti-implantation activity. Furthermore, these extracts, at the same concentrations, generated abortions when administered on days 14, 15, and 16 of pregnancy. No teratogenic effects were detected. [365].

M. sylvestris (aqueous or hydroalcoholic extract) increases skin hydration and prevents or alleviates skin dryness when used as a cream, lotion, serum, patch, emulsion, hydrogel, mask, etc. [2,143]. The extracts of mixed *Mentha piperita* and *M. sylvestris* have a substantial skin-whitening effect. Cosmetics made from the leaves and flowers of *M. sylvestris* and other plant extracts inhibit melanogenesis and tyrosinase activity, improving skin color and reducing pigmentation [2].

Silymarin from *S. marianum* protects the kidneys against renal ischemia/reperfusion injury in Wistar rats. The protective effect is associated with its antioxidant properties, as it possibly acts as a free-radical-scavenger and lipid peroxidation inhibitor. Thus, new therapeutic strategies, such as antioxidant supplementation with flavonoid silymarin, could be explored for protection against damage caused by ischemia and reperfusion [366]. Studies have shown that *S. marianum* extracts have an immunomodulatory effect in vitro and are able to increase lymphocyte proliferation. These properties were strongly associated with the increase in IF-γ, IL-4, and IL-10 [367]. In addition, extracts of *S. marianum* fruits have shown hyperprolactinemic activity, which exerts a stimulating effect on milk production in the mother [162]. An antiulcerogenic effect of *S. marianum* extract has been reported in rats. This activity involves a reduction in acid production and increase in mucin secretion, and the release of prostaglandin E_2 with a decrease in leukotrienes [368].

6. Conclusions

This review has gathered all the basic information on the phytochemical, nutritional, and pharmacological profile of the active ingredients known to date, as published in various books and journals on the wild plants under study from 2000 to November 2023. Most of the ailments treated with wild plants are common: digestive disorders, colds, coughs, circulatory problems, diarrhea, etc. However, there are some examples of treatments for more specific diseases, such as hypertension, hypercholesterolemia, hyperglycaemia, and others. Their use in folk medicine is supported by scientific investigations and, together with the knowledge of their side effects, makes these plants potential sources for nutraceutical purposes. Wild plants are often identified as functional foods because of their higher content of vitamins, antioxidants, trace elements and fibers compared to cultivated crops. The richness of natural antioxidants, mainly phenolic compounds with nutraceutical properties, is crucial in preventing acute and chronic diseases induced by improper nutrition, so wild plants lend themselves to the formulation of dietary supplements with benefits for human health and longevity, allowing for an improved quality of life.

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