Review

Traditional Applications of Tannin Rich Extracts Supported by Scientific Data: Chemical Composition, Bioavailability and Bioaccessibility

Maria Fraga-Corral 1,2, Paz Otero 1,3, Lucia Cassani 1,4, Javier Echave 1, Paula Garcia-Oliveira 1,2, Maria Carpena 1, Franklin Chamorro 1, Catarina Lourenço-Lopes 1, Miguel A. Prieto 1,5 and Jesus Simal-Gandara 1,6

1 Nutrition and Bromatology Group, Analytical and Food Chemistry Department, Faculty of Food Science and Technology, Ourens Campus, University of Vigo, 32004 Ourense, Spain; mfragat@uvigo.es (M.F.-C.); pazotofuertes@gmail.com (P.O.); lucia_cassani@hotmail.com (L.C.); javier.echave@uvigo.es (J.E.); paula.garcia.oliveira@uvigo.es (P.O.); maria.carpena.rodriguez@uvigo.es (M.C.);
chamorro1984@gmail.com (F.C.); clopes@uvigo.es (C.L.-L.)
2 Centro de Investigación de Montanha (CIMO), Campus de Santa Apolonia, Instituto Politécnico de Bragança, 5300-253 Bragança, Portugal
3 Department of Pharmacology, Pharmacy and Pharmaceutical Technology, Faculty of Veterinary, University of Santiago de Compostela, 25002 Lugo, Spain
4 Research Group of Food Engineering, Faculty of Engineering, National University of Mar del Plata, Mar del Plata RA7600, Argentina
* Correspondence: mprieto@uvigo.es (M.A.P.); jsimal@uvigo.es (J.S.-G.)

Abstract: Tannins are polyphenolic compounds historically utilized in textile and adhesive industries, but also in traditional human and animal medicines or foodstuffs. Since 20th-century, advances in analytical chemistry have allowed disclosure of the chemical nature of these molecules. The chemical profile of extracts obtained from previously selected species was investigated to try to establish a bridge between traditional background and scientific data. The study of the chemical composition of these extracts has permitted us to correlate the presence of tannins and other related molecules with the effectiveness of their apparent uses. The revision of traditional knowledge paired with scientific evidence may provide a supporting background on their use and the basis for developing innovative pharmacology and food applications based on formulations using natural sources of tannins. This traditional-scientific approach can result useful due to the raising consumers’ demand for natural products in markets, to which tannin-rich extracts may pose an attractive alternative. Therefore, it is of interest to back traditional applications with accurate data while meeting consumer’s acceptance. In this review, several species known to contain high amounts of tannins have been selected as a starting point to establish a correlation between their alleged traditional use, tannins content and composition and potential bioaccessibility.

Keywords: tannins; pharmacological; medicinal; veterinary; nutritional; traditional application; traditional use; human and animal health

1. Introduction

Tannins have been used throughout history for their pharmacological properties as part of plants and herbs in traditional medicine. Also, they have been extensively used since the 18th Century by leather manufacturers to improve leather resistance in the dyeing or tanning process, as they can precipitate gelatin adhered to animal skin and provide a brownish color. Hence, the name of this group of phytochemicals [1]. Tannins are a heterogeneous group of polyphenols, secondary metabolites in plants synthesized in response to biotic and abiotic stress inducers. The phenolic rings and hydroxyl groups present in their chemical structures confer them antioxidant and protein-binding properties,
as they have a wide range of molecular weight (500–20,000 Da) that it also showed in their broad structure diversity [2]. By their nature and abundance of hydroxyl radicals, tannins are highly hydrophilic molecules, soluble in aqueous solvents as well as exhibiting a high tendency to stably bond with proteins and carbohydrates [3]. This feature is common to all tannins, yet it seems that their link with polysaccharides lowers the probability of bonding and interacting with proteins [4]. They also share other properties, as the precipitation of colored complexes with iron salts or oxidation by potassium permanganate in alkaline media. Tannins are ubiquitously present in barks, seeds or fruit peels of many vegetable species, but also in brown algae [5]. Although several categorizations have been made on tannins regarding their molecular weight, properties and source, tannins are widely accepted to be classified under their functional units. As such, hydrolyzable tannins (HT), proanthocyanidins or condensed tannins (CT) and complex tannins (CoT) can be found on terrestrial plants, while phlorotannins (PT) have only been reported in brown macroalgae [4]. Among tannin diversity, the most abundant are terrestrial tannins, of which CT are generally most common. Even though their concentration and class differ in the different fractions of plants, tannins seem to have similar properties such as antioxidant, antimicrobial or predator-deterrent (i.e., against helminths or herbivores) [6].

Regarding tannins structure, galloyl units are the bricks that form HT, but depending on their chemical unions and radicals, they may be differentiated as gallotannins (GT) or ellagitannins (ET), relying upon the presence of gallic acid (GA) or ellagic acid (EA) subunits on degradation [7]. As such, they are synthesized from the shikimate pathway [2]. In general terms, GT are polymers of galloyl coupled with polyol, catechin or triterpenoid units, frequently found in the form of pentagalloyl glucose (PGG). The complexity of HT grows as more galloyl units are coupled through meta- or para-depside bonding, forming a chained structure of ester (oxidative) bonds [8]. ET are mainly galloyl units organized through C-C bonds such as in hexahydroxydiphenol (HHDP), HHDP-esters or nonahydroxytriphenoyl (NHTP) esters subunits [6]. The hydrolyzation of the HHDP subunit prompts EA subunits. The hydrolyzable label of HT indicates its low resistance to be hydrolyzed by high temperatures, acids, bases and specific enzymes such as tannase, commonly resulting in pyrogallol or GA products [9]. However, many ET are much more resistant to hydrolyzation because of the additional C-C bonding of their polyphenolic residue with the polyol unit [10].

The CT structure is regularly built upon catechins or epicatechins, the most common being (2,3-trans)-(±)-catechin and (2,3-cis)-(±)-epicatechin, which are flavan-3-ols moieties [11]. They are thus originated on the flavonol pathway [12]. The polymerization of CT is usually formed by bonding other catechins through C4-C8 bonds, but C4-C6 bonds may also be created, albeit less frequently [5]. The position of hydroxyl groups gives away a variation on their hydroxylation pattern in the A and B ring of the flavanol-3-ol unit, which in turn provides the classification of several groups of CT such as procyanidins (3,5,7,3′,4′-OH), prodelphidins (3,5,7,3′,4′,5′-OH), propelargonidins (3,5,7,4′-OH), profisetidins (3,7,3′,4′-OH), prorobinetinidins (3,7,3′,4′,5′-OH) or proteracacinidins (3,7,8,4′-OH) among others. Among these groups, procyanidins are the most abundant in nature, which can be sorted on the linkage between flavanyl units in A (double), B or C (single) class [13,14].

On the other hand, CoT are tannins of high molecular weight resulting from the bonding of flavan-3-ols with either GT or ET via a C–C bond. Some examples of CoT are acutissimin A and B, which can be isolated from Quercus sp. and Castanea sativa or cameliiatannin A from Camellia japonica [3].

PT are common tannins present in algae and constituted upon molecules of phloroglucinol (PG, aromatic ring with 1,3,5 hydroxyl groups) that polymerize with ease between C1-C3. They are grouped into three distinctive classes based on the coupling between subunits: fucols (C–C), phloroetols (C-O-C) and fucophloroetols (C–C and C-O-C). Increasing complexity in their structure is correlated to a higher presence of PG subunits (3 to 7 subunits) [15]. As well as terrestrial tannins, PT exert, in some cases, antimicrobial
protection while their potent antioxidant properties confer protection against UV-A and UV-B radiation [6]. A general perspective of tannin classification attending to their structure is presented in Figure 1.

Figure 1. Classification and general representative structures of tannins. Functional groups are circled. Rings in catechin molecule are labeled as A, B and C. R = radical, H, OH; GT = gallotannins; ET = ellagitannins; HHDP = hexahydroxydiphenol.

Generally, tannins are accumulated in vegetable cells in a special vacuole of recent discovery called tannosome, from which they are secreted to tissues. The inclusion of tannins in this vacuole avoids a disruptive binding of tannins with metabolic proteins or polysaccharides [13]. In the case of ET, it is worth noting that they show much lower protein binding activity at low/neutral pH, in contrast with the rest of the tannin groups [6]. Yet, this is not always the case, as they may also be embedded in cell walls. This is most prominent in the case of PT since they are integrated into the cell wall and bound to algal polysaccharides like alginate, laminarin or fucoidan [16]. Correlating to their biosynthesis pathways, different classes of tannins do not tend to accumulate simultaneously in the same tissue, as their concentrations may change with environmental conditions (i.e., seasonal changes) and plant tissue structural characteristics [17].

Tannins have rather undesirable organoleptic properties, as they are bitter and give a brownish color to foods. Nevertheless, they show remarkable antioxidant properties that justify their use as food additives to improve food-shelf life and safety, an issue that has made several tannins undergo trials for their legal approval as such additives. Furthermore, their precipitation properties are accounted for their decades-long use as clarification agents in the beverage industry (i.e., in beer, juices and wines) [18]. For instance, in the case of wines, ET from oak or chestnut are transferred to the wine during barrel aging, which is an appreciated feature in aged wines. As another example, tannic acid, a common GT found in many species, is approved as a flavoring agent in the EU [19]. However, it has also been reported alongside many other tannins to provide further oxidative and antimicrobial protection when added to foods [4]. In the same sense, several in vitro, in vivo and clinical studies researching the bioactive properties of tannins have been developed throughout the years [20]. Thus, it is evidenced by their polyvalent potential, whether as additives, nutraceuticals or pharmaceutics. The mentioned findings are paired with increased consumer demand for natural products, with a preference to avoid or replace synthetic compounds in food, for example [21]. Furthermore, the feasibility of tannin
extraction and acquisition proves that it is affordable and may be carried out with little difficulties even from by-products of the agri-food industry, such as barks, leaves, peels or seeds that are not exploitable for other uses, since these fractions are accounted for the highest tannin concentrations. Among these plant tissues, some remarkable examples involve peels and/or seeds from several fruits (i.e., grape, pomegranate), citrus, nuts (i.e., chestnut, walnut), herbs (i.e., tea, basil, cinnamon), legumes and barks of trees (i.e., Acacia spp., Castanea spp., Quercus spp.) [17,22–24]. Some common sources of currently commercialized tannin extracts are trees such as chestnut (C. sativa) for HT and quebracho (Schinopsis balansae & Schinopsis lorentzii) for CT [25]. In the case of these woody trees, tannin content in barks may be as high as 38% of dry matter in quebracho or as much as 16% in chestnut, and their use in traditional medicine is well recorded. Other usual sources of tannins are black wattle (Acacia mearnsii) for CT or valonea (Quercus macrolepis) and tara (Tara spinosa) for ET and GT, respectively [26]. Furthermore, as stated, brown algae (i.e., Arame, Eisenia bicyclis, Sargassum sp.) are also considered an adequate source of tannins, as well as other bioactive compounds, as they are easily harvested and currently underutilized while being the focus of research on bioactive compounds in recent years [27].

Taking into account the mentioned properties of tannins, it may be possible to explain the effectiveness of tannin-rich medicinal plants used in traditional medicine while these medicinal properties are also related to the synergy of tannins with other bioactive polyphenols present in these plants [28]. The recorded medicinal use of tannin extracts and tannin-rich plants will be addressed together with the study of the main chemical profile of the mentioned tannin-rich plants. Therefore, the main objective of this review is to relate the traditional knowledge gained after centuries of application of traditional medicine with scientific data that may point to the target molecules.

2. Traditional Applications of Rich-Tannins Plants

In the following sections and in Table 1, some examples of the traditional uses of plants and other sources of tannins will be explained. The selection of these species has been made according to their well-known content in tannins, their extensive recorded traditional applications (paying special attention to those orally administrated), their reported bioactivities and the availability of quantitative and qualitative studies that determined their chemical profile and their high levels of tannins.

### Table 1. Traditional applications of plants containing tannins. Selection of species and tissues rich in tannins traditionally applied under diverse administration ways (admin.) for treating different affections or diseases and the potential mechanism of action of their biomolecules.

| Plant | Admin. | Treatment, Remedy, Uses | Mechanism of Action | Ref. |
|-------|--------|-------------------------|---------------------|------|
| **PLANTS** |       |                          |                     |      |
| Acacia |        |                          |                     |      |
| *A. nilotica* | O, T | Gastrointestinal, respiratory, inflammatory, parasitic, neurological diseases, sexual disorders, skin issues, diabetes. Aphrodisiac, chemo-preventive, antimutagenic | Antioxidant, anti-inflammatory, anti-nociceptive, and antipyretic | [29–33] |
| *A. arabica* | O (G, S) | Used for sweetmeats (G) or roasted (S, India) |                     |      |
| *A. tortilis* | O, T | Gastrointestinal disorders in cameldias, skin issues (edema, allergic dermatitis, wound/burns healing) | Antiparasitic and anti-inflammatory | [34] |
| **Betula** |       |                          |                     |      |
| *B. pendula* | O (B in I/D) | Urinary, respiratory affections. Systematic diseases | Anti-viral | [35,36] |
| **Juglans** |       |                          |                     |      |
| *J. regia* | O (N), T | Hemorrhoids, rheumatism, varicose veins, skin wounds, fever, cough, toothache, infertility. Local analgesic. Hypercholesterolemic, antidiabetic, cardiotonic, vasodilator. Aromatizer. Antiparasitic | Anti-platelet, cardioprotective, antitherogenic and anti-inflammatory | [37–42] |
| Species            | Preparation modes | Food ingredients or supplements (Sp, L, F, R) | Breads-preparing flour or thicker in soups (B) | Antioxidant, antimicrobial, preservative | [43] |
|--------------------|-------------------|-----------------------------------------------|------------------------------------------------|------------------------------------------|------|
| **Picea**          |                   |                                               |                                                |                                          |      |
| *P. abies*         | O (Sp/L/F/R/B)    | Food ingredients or supplements (Sp, L, F, R) | Breads-preparing flour or thicker in soups (B) | Antioxidant, antimicrobial, preservative |      |
| **Pistacia**       |                   |                                               |                                                |                                          |      |
| *P. lentiscus*     | O, T (St, FR-oil) | Improvement of gastrointestinal function. Infected wounds, scabies, boil, constipation | Antiparasitic, anti-inflammatory |                   |      |
| **Phyllanthus**    |                   |                                               |                                                |                                          |      |
| *P. niruri*        | O (L and FR)      | Liver diseases (jaundice), urinary infections, inflammatory processes and malaria | Anti-inflammatory, antioxidant, hypoglycemic, hypolipidemic, hepatoprotective |                   |      |
| **Quercus**        |                   |                                               |                                                |                                          |      |
| *Quercus sp.*      | O, T (R/S in D/FR)| Skin injuries (burn, boil wound). Respiratory affections (cold and flu). Diabetes | Antioxidant, antidiabetic |                   | [37,42,50-52] |
| **Rhus**           |                   |                                               |                                                |                                          |      |
| *Rhus sp.*         | O                 | Gastrointestinal diseases (diarrhea, ulcers, hemorrhoids), dysentery, or stroke | Antimicrobial, anti-inflammatory, antiapoptotic, immunomodulatory, healing |                   |      |
| **Schinopsis**     |                   |                                               |                                                |                                          |      |
| *Schinopsis sp.*   | O, T (I/D of L/B/Rs/FR/Br/C/W/S) | Anti-inflammatory, antimicrobial, antipyretic, astringent and cicatrizing. Respiration affections (cold, cough, asthma), stomachache, headache, dysentery or fractures | Antioxidant, antimicrobial, antihelmintic |                   | [1,55-60] |
| **Smilax**         |                   |                                               |                                                |                                          |      |
| *S. aspera*        | O, T (D)          | Urinary retention, antiseptic in cows, enhancing health state of rabbits, treatment of purulent vesicles | Antioxidant, anti-inflammatory, diuretic |                   | [47,61] |
| **Umbilicus**      |                   |                                               |                                                |                                          |      |
| *U. rupestris*     | O, T (minced L)   | Infected wounds, diarrhea, fever, intoxications, antiparasitic in hens | Anti-inflammatory, antiparasitic |                   | [47,61,62] |
| **Urtica**         |                   |                                               |                                                |                                          |      |
| *U. dioica*        | O, T (L, direct application) | Arthritis, lumbago, rheumatism, muscular or limb paralysis. Rubefacient, blood circulation stimulant. Relief allergic rhinitis symptoms. Revitalizing. In animal promotes weight gain, growth and increases galactagogue production (ruminants) | Antioxidant, anti-inflammatory, antimicrobial, analgesic, anti-diabetic, antimutagenic. Emulsifier, gelling agent |                   | [63-68] |
| **Vitis**          |                   |                                               |                                                |                                          |      |
| *V. vinifera*      | O (raw sp, vinegar) | Gastrointestinal diseases, headaches, and colds. Thirst-quenching, revitalizing and anti-inflammatory | Antioxidant, anti-obesity, anti-inflammatory |                   | [42,69] |
| **Combination of plants** |               |                                               |                                                |                                          |      |
| “Triphala”         | Oral              | Restorative, revitalizing, boosting of the immune system, treatment for chronic gastrointestinal diseases | - |                   | [48,70] |
| **MACROALGAE**     |                   |                                               |                                                |                                          |      |
| **Sargassum**      |                   |                                               |                                                |                                          |      |
| *Sargassum sp.*    | O, T              | Nutritional value. Treatment for inflammations, goiter, dropsy, edema, dysuria, respiratory affections, angina pectoris, high blood pressure, skin diseases, neurosis, pregnancy-related depression and diabetes mellitus | Antioxidant, antibacterial, anti-proliferative, anti-inflammatory. Gelling hydrocolloid, emulsifier |                   | [71–74] |
| **Ecklonia**       |                   |                                               |                                                |                                          |      |
| *E. cava*          | Oral              | Common food ingredient, attenuation of goiter, treatment for mammary hyperplasia and diuretic | Antioxidant, anti-inflammatory |                   | [71,75,76] |

Definitions: preparation modes: D: decoction; I: infusion; Pp: plant parts: B: bark; Br: branches; Bu: buds; C: cortex; F: flowers; FR: fruits; G: gum; J: jam; L: leaves; N: nuts; Rs: resin; R: roots; S: sap; Sp: sprouts; St: stems; W: wood.

Among the species of the genus Acacia, A. nilotica is the most relevant from a medicinal point of view. Different parts of the plant have been used for very diverse affections. Even though all tissues have been described to possess activity, leaves, pods and bark present more healing properties. In general terms, this species has been described to treat...
gastrointestinal disorders or diseases (diarrhea, congestion, anthelmintic, diuretic, emetic, for burning sensation and it is also considered as nutritive), respiratory affections (pharyngitis, bronchitis, cough, cold, expectorant and for sore throat), skin issues (eczema, ulcers, leukoderma, wounds), variable inflammatory processes (toothache, conjunctivitis, menstrual pain, hemorrhoids, smallpox, biliousness) or diabetes. Its sedative and narcotic properties were applied for nervous system disorders, Alzheimer’s disease and its antimicrobial capacity was exploited as a remedy for dysentery, leprosy, tuberculosis or even malaria. It also possesses aphrodisiac properties, it can be used for treating spermatorrhoea and sexually transmitted diseases, but it was also claimed to possess chemo-preventive and antimutagenic activity [29,30]. The properties recognized for major tannins in A. nilotica include antioxidant, anti-inflammatory, anti-nociceptive, and antipyretic activities [31,32]. Another plant belonging to this genus with recognized properties is A. tortilis sap, whose seeds and bark recovered have been used for gastrointestinal ailments (stomachache, mild diarrhea or indigestion), eye conditions (treat white stains in the cornea or used in incipient cases of eye entropy), respiratory issues, as antipyretic, for jaundice, malaria, as wound healing and injuries disinfectant, as liver detoxifying and for bone strengthening. Roots soaked in water and crushed can be orally administrated to treat diphtheria [29,34]. A. tortilis also has been used for treating gastrointestinal disorders especially described for camelids. Their seeds, suckers, stipules and young spines have been found to be a remedy against sand colic that mostly to dromedaries. Moreover, its chewing gum has wound and burns healing properties, and when seeds or bark from A. tortilis are mixed with seeds from Vigna unguiculata, this mixture can be applied for treating skin issues (edema or allergic dermatitis) or as antiparasitic, respectively [34]. Pods from other species, like A. arabica or A. catechu, have also been reported for confectioning fodder for animals, particularly for sheep and goats [33,77]. In fact, A. arabica has been widely utilized in humans as a treatment for multiple affections and diseases, very similar to those already cited. The bark is considered a powerful astringent, and its extract has been used to allay irritation in acute gonorrhoea and leucorrhoea, cystitis, vaginitis and anal or uterus prolapsed. Decoctions or dry powder were used for treating hemorrhages, skin wounds, ulcers or leukoderma, diarrhea, dysentery, leprosy, diabetes, bronchitis, seminal weakness, as diuretic or anthelmintic agent. Noteworthy, its leaves have also been used for diarrheal disorders. Gargles were applied for cancerous and syphilitic affections, sore throat, cough or toothache since it has been described as tonic, demulcent, aphrodisiac and anti-viral. The ground bark of A. arabica mixed with seeds of Sesamum indicum have been used as food and the juice of their bark mixed with milk is dropped into the eye for treating conjunctivitis. Pods, fruits, flowers, roots, leaves and gum present very similar applications; additional ones include the treatment of eczema and abscess with leaves, the use of fried gum for preparing sweetmeats or flowers as antipyretic. Moreover, the gum obtained from this species can be fried using ghee, a kind of clarified butter traditionally confectioned in India, for preparing sweetmeats and roasted seeds which served as food during acute scarcity periods [33]. Bark decoctions of another species, Acacia catechu, also has been reported to cure cold and cough, severe diarrhea or piles (applied with lemon slice), as tonic for women after delivery (with cardamom) while heartwood can be used as antipyretic, for cold during the pregnancy and to cure ulcers both in skin and mouth/tongue [77].

Several plants have been used in labor and delivery, such as the fern Asplenium ceterach (accepted name of Ceterach officinarum), used in cows and ewes after delivery as depurative. This effect is attributed to the astringent tannins present in its composition [68]. Another example is the plant Capsella bursa-pastoris, known as shepherd’s purse, which presents anti-hemorrhaging properties associated with the presence of tannins [78]. In this case, a decoction of the plant was given to pregnant animals to avoid hemorrhage [68]. Different pharmacopeias worldwide, including Russia, India and some European countries (France and Deutschland), have described the healing properties of several tannin-based rich plants like Betula species. Most texts point to bark as the main plant target
to prepare decoction- or infusion-based extracts. Nevertheless, other parts like leaves, flowers, stems, roots or even sap or resin have also been exploited. *Betula pendula* is the species that has been further used and reported to have pharmacological properties. The principal applications of the extracts of *B. pendula* are aimed to treat or prevent urinary affections such as infections of the urinary tract or bladder, renal inflammation, renal stones or hindered diuresis. It also has been widely used for treating systematic diseases (rheumatism or arthritis), blood system disorders, respiratory tract ailments, or as wound healing, antipyretic or even anti-alopeciac agent. Other minor utilizations included it as a remedy for spleen affections, hypercholesterolemia, headache or even as anti-helminthic [35]. Betulinic acid, a triterpenoid acid extracted from *B. pendula*, is well-known for its antiviral, tested against HIV, and anti-inflammatory activity, which may act in synergy with the tannins present [36].

*Castanea sativa* has been referenced as alimentary or medicinal with applications as laxative or stomach regulator when chestnuts are consumed or even as hemoptysis agents. *C. sativa* episperma was, however, described as astringent. Nevertheless, its most relevant value has been underlined as a source of nutrients even though it also has been cited as a possible antidote to lip and esophagus lacerations caused by *Colchicum autumnale* poison [79].

Edible nuts from *Juglans regia* had been recognized since ancient times, but also other tissues were exploited with diverse purposes, such as its leaves, which have been used to wrap cheese in order to provide aroma, but also antiparasitic properties [38,42]. Moreover, it has been traditionally applied as an anti-inflammatory for rheumatism and hemorrhoids, antipyretic, antifungal, antitussive and for skin affections. Specific applications of each plant part include bark decoction to gargle it for toothache, direct application of fresh leaves to reduce varicose veins, mild skin inflammations and its use as a local analgesic, and immature fruits to color hair. Moreover, a dosage of one teacup of *J. regia* twice or three times a day during one month has been described to be able to provide antidiabetic, hypercholesterolemic (HDL cholesterol), cardiotonic and vasodilator properties and reduce infecundity [37,38]. In fact, scientific reports have described tannins from walnut to possess anti-platelet, cardioprotective, antiatherogenic and anti-inflammatory properties [39–41].

The genus *Lotus* has been traditionally utilized as forage for different ruminants [80,81]. *Lotus* species, rich in CT, have been demonstrated to provide different benefits, such as favoring the weight gain, the growth of wool, improvement of the production and composition of milk and reducing the number of anthelmintic products in farming animals [81]. In cattle, the production of methane was reduced and enhanced ruminal fermentation when the animals were fed with *Lotus corniculatus*, which was attributed to the CT [82]. The administration of *L. corniculatus* has shown positive effects on milk production and gastrointestinal function of sheep [80]. In addition, *L. cornicatus*, *Lespedeza cuneata* and *Hedysarum coronarium* have shown anti-helminthic effects on ewes, reducing the presence of fecal eggs and worms and inhibit the development of larvae [83,84].

The genus *Phyllanthus* has a long clinical application in Asia. The fruit of *P. niruri*, *P. amarus*, *P. fraternus*, *P. debilis* and *P. maderaspatensis* and the leaves of *P. polyphyllus* has been applied for their tonic properties to liver diseases such as jaundice in India while for urinary affection were used *P. simplex*, *P. reticulatus*, and *P. acidis*. In India, these plants have also been utilized for wound healing, as antipyretic, anti-inflammatory or for treating diabetes. Similarly, this genus has been used as antipyretic and antitussive in China and for treating blood, bile disease, hypertension and anuria in Tibetan medicine. *P. urinaria* has been described to possess detoxifying properties and was also used for liver-based diseases (jaundice or hepatitis B), gastrointestinal (enteritis, diarrhea), or systematic affections (dropsy). As in India, other species like *P. reticulatus*, *P. niruri* and *P. simplex* were applied for treating urinary infection, among other inflammatory processes like rheumatism. In Thailand, *P. emblica* is used as the previously cited “Triphala” for chronic
gastrointestinal diseases. However, other species are utilized for treating the same affect-ions. *P. amarus*, *P. urinaria* and *P. virgatus* are aimed at treating liver diseases, diabetes or gonorrhea. *P. acidus* was the remedy for slightly different affections like hypertension, constipation, fever or skin issues, whereas urinary infections or malaria are treated with *P. taxodifolius*, *P. niruri*, and *P. reticulates*. However, in Africa, *P. muellerianus* is the most used species, and the one applied for malaria (and *P. reticulates*), tetanus, as antipyretic and wound healing. Instead, *P. polyanthus* is applied in Kenya for treating sexually transmitted diseases. Similar applications are found in South America, where leaves of *P. tenellus* have diuretic properties, *P. amarus* and *P. sellowianus* are used for treating diabetes, but also for jaundice and urinary infection, respectively [48]. For *P. niruri*, different bioactivities have been demonstrated, such as antioxidant, anti-inflammatory, anti-nociceptive, analgesic, hypoglycemic, lypolipidemic and hepatoprotective [49].

Different *P. abies* plant parts have been also applied in traditional culinary art. Young sprouts are used as food ingredients, while leaves (needles), flowers, pinecones and resin are utilized as food supplements. A Finnish novel food called “pettu” is prepared from the bark that is roasted and scratched of oozed substances or just boiled for 2 to 3 h. Then, the bark is dried, grounded and mixed with some cereals-based flour at equal parts since the consumption of pure bark can induce stomachache and constipation. This product can be used as bread-preparing flour; it can also be mixed with milk or animal fat, or blood or to prepare soup to where it provides a thickening effect [43]. This polyvalent flour was used in the 1860 s, during the famine, in Finland [85]. Other uses of different tissues of *P. abies* include animal treatments. Twigs serve for feeding calves, resin heals skin afflictions, and sores and ointments were used to treat or prevent respiratory affections like cough or pneumonia. This ointment of *P. abies*, when combined with other species like *Rumex obtusifolius* provides a remedy for mastitis [86]. Indeed, the veterinarian use of *P. abies* has been recognized by the European Medicines Agency through Veterinary Medicines and Inspections. The final preparation to administrate to animals is named *Piceae turiones recentes extractum* and can be obtained from boiling 10 to 15 cm long shoots, collected in spring, of fresh *P. abies*. This extract is then mixed with starch and an herbal powder. The final product that can be orally administrated (dosage: 0.6–6.4 mL solution, equivalent to 3.1 mg to 30. 6 mg spruce-tips extract, per kg body weight) is aimed to treat diarrhea in cattle, horses, pigs, sheep and poultry [87].

Plants such as *Parietaria officinalis*, *Pistacia lentiscus*, and *Prunus spinosa*, *rupestris*, also present tannins in their chemical composition, have been traditionally used to treat different disorders of domestic animals. The main use described for *Parietaria officinalis* is the treatment of diarrhea in domestic animals. *Pistacia lentiscus* and *Prunus spinosa* present a high content of tannins, and they have been reported to exert beneficial effects on the protein metabolism of ruminants, improving the absorption of amino acids in the small intestine [47]. *P. lentiscus*, known as lentisk, has also shown antiparasitic activity against intestinal helminths and coccidia on sheep and goats, which have been attributed to the presence of tannins and other compounds [44,45]. Additional traditional uses of this plant include the treatment of scabies, diarrhea, constipation, dermal affections and infected wounds [46,88]. In the case of *P. spinosa* or plum tree, this plant has also been applied externally to treat wounds infected by worms [46] and also to control diarrhea [89]. Similarly, *P. officinalis* was also effective in controlling diarrhea, which is attributed to the presence of astringent compounds such as tannins [68]. In addition, this plant was used to elaborate tisanes with anti-inflammatory and antiseptic properties in combination with other traditional plants, such as *Pisum sativum*, *Beta vulgaris*, *Lavandula latifolia* or *Malva sylvestris* [61].

*Punica granatum* has been used as itself or in combination with other plants to treat very variable affections. When used as a unique herb, mainly bark and roots were used to treat intestinal worms, decoctions of pomegranate hulls were described as strong astringents and a remedy for treating dysentery, diarrhea, and stomatitis. Pomegranate hulls and/or root extracts were also administrated orally and intravaginally to minimize fertility
and treat gynecological affections. Alternative uses include the application of pomegranate extracts for snakebite, diabetes, burns and leprosy, while the fresh fruit has been used as a refrigerant to ameliorate fever processes [90,91]. When used in combination, very assorted plants were used such as Achillea millefolium, Artemisia sp., Emblica officinalis, Nepeta sp., Tanacetum sp., Taraxacum officinale, Terminalia chebula, or Zingiber officinale, among many others. These mixtures of plants were mostly administrated to treat cold, cough and fever [92].

Among the genus Quercus, few examples of traditional medicinal or pharmacological uses can be found in the literature. A decoction of roots from Q. cerris and Q. cocifera can be applied as lotion twice a day for 2–3 weeks to treat skin burn, boil and wound. Fruits of Q. cocifera are edible and can represent a remedy for controlling diabetes. A teacup of a decoction of seeds from Q. ithaburensis administrated 2–3 times a day for one week can improve cold and flu processes [37]. A decoction of oak-apples from Q. pubescens together with other plants like mallow or chamomile was also used for healing wounds in newborn infants [42]. Tannins from Quercus had been described to have antioxidant and anti-diabetic activity [50–52].

Several species belonging to Rubus have been considered for their properties in different traditional medicines. Bud, fruits, leaves and roots of R. canescens can be eaten raw or drunk as an infusion (teacup twice a day for 2–3 weeks) or applied as a decoction for treating gastrointestinal issues (as carminative, dyspepsia and intestinal spasm) or diabetes. Similarly, fruits of R. idaeus can be eaten twice or three times a day for 2 to 5 days for mouth sores and as antiemetic. However, R. sanctus has wider applications, including treatment for atherosclerosis, stomachache, diabetes, eye diseases, nephralgia, kidney gravels, rheumatism, cold and flu, bronchitis, burn, boil and wound care, or as anti-hemorrhagic [37]. Leaves from R. ulmifolius can be topically administrated for hemostatic for cuts and for removing thorns; the extract of tender tips is useful for skin cuts and bruises, and jam obtained from fruits relief cough and sore throat. Moreover, R. ulmifolius sprouts can be mixed with walnut kernels, Verbena officinalis leaves, Sambucus nigra bark, cyclamen tubers and bramble buds to prepare a cream with beeswax and oil basis that can be administrated for inflammation processes [42].

Rhus genus has been traditionally applied and named as sumac. Its main uses included it as a food condiment, but also for the treatment of gastrointestinal diseases such as diarrhea, intestinal ulcers, rectal prolapse and hemorrhoids, oral diseases, dysentery, or stroke. Sumac has been described to possess anti-inflammatory, immunomodulatory, antimicrobial, antiviral, antioxidant, antifungal and antiapoptotic effects [53,54].

Several species from the genus Sapium have been described to be used as part of traditional medicine in different cultures. Most of the Sapium species were used to treat skin-related diseases such as eczema, dermatitis, wounds or snake bites. However, additional uses were pointed to this genus as a remedy for overstraining, hernia, constipation and hernia. For instance, Sapium baccatum has been used for treating eczema, roots bark and leaf from Sapium japonicum were applied for treating overstrain, lumbago and knee pain and similarly, the resin from Sapium glandulosum was used for hernias. Other uses included the treatment of digestive and urinary ailments (Sapium sebiferum root bark and seed), skin affections and antiparasitic (bark juice of Sapium insigne). Different plant tissues of Sapium ellipticum were applied with different purposes such as for respiratory complications (root decoction and dried stems), abdominal swelling, eye diseases and mumps (leaves), malaria (root decoction), anemia, fever, guinea worms, elephantiasis and rheumatic problems (stem bark decoction) [93].

Smilax aspera or sarsaparilla, another plant that has been reported to contain tannins in its chemical composition, has been administered orally as a diuretic and urinary anti-septic in cows and has been used in the alimentation of rabbits due to its beneficial effects on the health of the animals [61]. In addition, decoctions of this plant were applied to eliminate purulent vesicles [47].
To our knowledge, the traditional uses of the Schinopsis genus as medicinal and pharmacological remedies are few. Leaves, bark, resin and fruits from S. brasiliensis were used in the popular medicine as a general anti-inflammatory, for treating cold, cough, fever, diarrhea, dysentery, fractures and as antimicrobial [55]. S. lorentzii has been reported to be traditionally used for treating stomachache, headache or cough when prepared as infusion or decoction using leaves and tender branches. Nevertheless, leaves have been described to be useful as a cicatrizing agent and to relieve bruises while the bark may have anti-asthmatic properties [56,57]. The cortex of S. balansae also has cicatrizing properties accompanied by anti-inflammatory and antiseptic capacity. The wood of S. balansae has been referred to as astringent, and fresh sap may remove moles [57]. The main properties associated with Schinopsis are antioxidant, antimicrobial, anthelmintic [58–60].

Similarly, in the case of the genus Terminalia, many species had been contemplated as medicinal plants such as Terminalia bellirica, T. chebula, T. arjuna, T. catappa, etc. Among them, T. bellirica has been studied for being considered edible and for its multiple properties to treat edema, diarrhea, leprosy, bile congestion, indigestion, headache, fever, cough, dysentery or skin diseases [94]. Different plant structures have been suggested to have diverse applications. For instance, fruits can be utilized for respiratory tract affections like cough (decoction), hoarseness, asthma or bronchitis; for digestive issues (indigestion, diarrhea, edema or hemorrhoids that can be treated with pulp fruit), menstrual disorders, hepatitis, as purgative or even as a hair tonic. Fruit kernel has been described as narcotic, and its oil was purgative like bark gum. Seed oil has anti-rheumatic activity while leaves improve health status by improving immunity, acting as anti-aging, enhance appetite, relieve hemorrhoids and can reduce cholesterol and blood pressure [70]. Extracts obtained from the bark of T. arjuna are aimed as cardioprotective and antihyperlipidemic, but also as a remedy for muscle sores, contusions, fractures, ulcers, treatment of bile infection, dysentery or as poison antidote [94,95]. For T. chebulla, the fruit has also been widely used for digestive alterations to improve appetite, as an astringent, antiemetic, stomach tonic, mild laxative, for hemorrhoids or as antispasmodic [96]. T. chebulla can also be applied for infertility, asthma, sore throat, dental caries, urticaria, dysentery, bleeding, ulcers, gout and bladder disease [94]. A paste obtained by mixing grounded T. chebulla with water has anti-inflammatory, analgesic and wound healing capacities while its decoction helps to treat oral ulcers or sore throat [96]. A combination of dried fruits obtained from these two species, T. chebula and T. bellirica, and Phyllanthus emblica, is known as “Triphala,” being long-used as a restorative and revitalizing natural formulation that boosts the immune system against infectious diseases [70].

The nutritional value of Urtica dioica has been recognized from ancient times for both humans and animals. It was administrated as a revitalizing agent for humans [63]. In animals, it is also restorative and promotes weight gain and growth of chicks, Turkey cocks and pigs, and it was also described to increase the production of galactagogue (a substance that promotes lactation) in ruminants [63,66,68]. Currently, U. dioica is consumed as part of curry, soup, vegetable complement or as the main ingredient of an omelet. Within its chemical composition, tannins have been quantified in 0.93 mg/100 g, 38% of proteins, 9% of crude fiber and 0.2% for both calcium and iron. The fresh plant has been applied both directly and as an infusion for treating arthritis, lumbago, rheumatism, muscular or limb paralysis. The direct use of U. dioica has been described as a rubefacient; thus, it was utilized for the stimulation of blood circulation, which helped the warmth of joints and extremities. This plant was also stated to relieve symptoms of allergic rhinitis and to provide vitality to people [63]. Indeed, scientific works have described antioxidant, anti-inflammatory, antimicrobial, analgesic, antidiabetic, and antimutagenic activities for U. dioica extracts [64,65]. Another plant used in animal feeding is U. dioica (traditionally named nettle), which has been given to chicks, Turkey cocks and pigs as restorative to promote weight gain and the growth of the animals [66,68]. It has also been described to increase the production of galactagogue (a substance that promotes lactation) in ruminants [67]. Different compounds have been identified in U. dioica, including tannins [46].
The traditional veterinarian applications of the species *Umbilicus rupestris*, also known for its common name navelwort, are well documented. This plant, which has been described to possess tannins, has been used externally to treat wounds of animals [61,62] and orally to control diarrhea, fever, intoxications [47] and has been used as an antiparasitic in hens [61]. *Vitis vinifera* has been widely and repeatedly used as food and beverage ingredients, and its consumption has been associated with different beneficial health effects. It has been used for gastrointestinal diseases; sprouts can be eaten as thirst-quenching, but also for treating headaches (as vinegar), colds (mixed with honey, cinnamon and cloves), and wine baths were used for children to strengthen them or to treat inflammations [42]. Most of their traditionally and currently exploited bioactivities are directly related to their high content in molecules with antioxidant properties such as proanthocyanidins and anthocyanins [97]. Among their recognized benefits, extracts obtained from seed grapes have been described to possess anti-obesity and antidiabetic capacity by downregulating the lipid metabolism. The administration of grape seed extracts rich in proanthocyanidins revealed a high increase in the expression of several genes involved in β-oxidation, involved in lipid catabolism, and which ultimately suggests their potential to prevent fat accumulation [98]. These extracts demonstrated to increase energy expenditure, and thermogenesis was also found to diminish the expression of TNF-α, a proinflammatory factor augmented in chronic diseases, such as obesity [99]. Proanthocyanidins present in *V. vinifera*, besides inhibiting fat gain, have shown the potential to alter the small intestinal gut microbiota. This has been suggested to be related to their capability to improve glucose tolerance and insulin sensitivity, and hence described as antidiabetic [100]. Other tannin classes present in several species that possess antidiabetic or hypoglycemic properties are valonie acid di-lactone, TGG and PGG from *C. sativa*, both HTs (TGG, PGG) and CTs (catechin derivatives) from *S. lorentzii* or chebulanic, chebulagic acid and chebulinic acid from *T. chebula* [59,101,102].

Another source of tannins recently demonstrated is brown macroalgae with a high content in phlorotannins. Macroalgae have been used for nutritional purposes since ancient times, especially in the Far East Asiatic cultures, such as *Sargassum* and *Ecklonia*. *Sargassum*, among other algae species, has been historically used as edibles and folk medicine. Seaweed consumption was supported for its nutritional value but also because its regular ingestion was related to an effective reduction of depressive symptoms during pregnancy and with a diminution of suicide rate in Japan, while in Korea was associated with minor diabetes mellitus incidence. Additionally, these algae have been used as hydrocolloids, emulsifiers and gelling agents in various food product preparations [71,74]. Different species belonging to the genus *Sargassum* have been used in traditional Chinese medicine. *S. pallidum*, *S. confusum*, *S. fusiforme*, *S. fulvellum*, *S. siliquastrum*, *S. thunbergii*, *S. muticum* or *S. hornerii* have served as a treatment for goiter, inflammation-based diseases like scrofula, arteriosclerosis, hepatosplenomegaly or testes swelling, dropsy, edema due to retention of phlegm and morbid fluids, dysuria, respiratory affections like sore throat, cough, acute esophagitis or chronic bronchitis, angina pectoris and high blood pressure, skin diseases like furuncle, and even neurosis [71]. The potential mechanism through which *Sargassum* may exert its activity includes its capacity as antioxidant, antibacterial, antiproliferative, and anti-inflammatory [72,73]. *Ecklonia cava* is a highly valued edible brown seaweed in Japan, China and South Korea, where it is consumed daily. It is foremost intake as part of salads, miso soup, or powdered as a condiment in rice cakes, candies or kimchi [103]. It is recorded in Chinese Pharmacopoeia as part of preparations with other seaweeds like *Sargassum* sp. as “Laminaria Thallus”, and it is attributed to attenuate goiter, diuretic and treatment for mammary hyperplasia [71]. Additionally, it is allegedly held as “health-promoting” in Korea [104]. *E. cava* ethanolic extract, highly rich in PT (> 90%), has been approved for use as a food ingredient by both Food & Drug Administration (FDA) and European Food Safety Authority (EFSA) [75,76]. This approval is justified...
on the evidence regarding its antioxidant, antiviral or anti-inflammatory, as well as anti-diabetic and anti-obesity properties [105,106]. In fact, an in vivo experiment determined significantly lower carbohydrate absorbance and metabolization in rats when administered said E. cava extract [107].

As a final mention to this section, in Figure 2, an illustrative description of the traditional uses of tannins with pharmacological, medicinal, nutritional, veterinarian and botanical applications is briefly depicted.

**3. Chemical and Quantitative Composition of Rich Tannins Plants Traditionally Used**

In traditional medicine, it is of great pharmacological interest to study the composition of plant extracts due to the direct relationship among chemical structures of compounds and their beneficial effect [108]. Plant polyphenols are suggested to exert their bioactivities in synergy and to be present in tannin extracts; therefore, some of these relevant compounds are also reported to offer a complete view of the beneficial potential of plant extracts [109]. Furthermore, some non-tannin molecules like several flavonoids, phenolic acids or phenolic glucosides have also been suggested or evidenced to contribute to polymerization or conformation of several tannins.

Therefore, in the present section, we describe the chemical composition of plant species used in traditional applications (Table 2), the molecular structures of representative tannins of each structural group (Figure 3) and their quantitative presence in different species (Table 3).
**Table 2.** Rich-tannins species of plant and macroalgae with the main tannin and tannin-based compounds.

| Genera          | Species       | Representative Tannins and Relevant Related Molecules                                                                 | Ref.     |
|-----------------|---------------|------------------------------------------------------------------------------------------------------------------------|----------|
| **A. catechu**  | CT monomers, dimers and trimers: trihydroxyflavan, profisetidin, gallo-catechin, prorobinetidin, 3,5,7,4′-tetrahydroxyflavan | [110]    |
|                 | **A. mearnsii** | Relevant dimers:                                                                                                       | [111,112]|
| **Acacia sp.**  |               | robinetinidol-(4α-8)-gallocatechin                                                                                      |          |
|                 |               | fisetinidol-(4α-8)-catechin and robinetinidol-(4α-8)-catechin                                                          |          |
|                 |               | robinetinidol-(4α-8″)-robinetinidol (4′α-6″)-catechin                                                                     |          |
| **Betula sp.**  | B. pendula    | **Phenolic acids**: glycosylated flavonoids and salicylates                                                            | [114,115]|
| **Castanea sp.** | C. sativa     | **Phenolic acids**: EA                                                                                                  |          |
|                 |               | **GT and ET**: chesantin, chesatin, isocbesatin, chebulagic acid, pedunculagin, tellimagrandin I, castalagin/vescalagin, stachyurin or casuarinin, deoxyhexoside | [101,116–118]|
|                 |               | **Other molecules**: cocciferin d2, castacrenin A-C isomers, trimethyl-ellagic acid hexoside, cretanin, methylvescalagin, vescavaloninic acid |          |
| **Ecklonia sp.** | E. cava       | **Phenolic acids**: EA                                                                                                  |          |
|                 |               | **PT**: phloroglucinol, eckol, dieckol, 7-phloroeckol, 2,7-phloroglucinol-6,6-bieckol, phlorofucofuroeckol-A, pyrogallol-phloroglucinol-6,6-bieckol | [104,119]|
| **Juglans sp.** | J. regia      | **Phenolic acids**: EA                                                                                                  |          |
|                 |               | **Tannin heteropolymers**: units of catechin/epicatechin and gallocatechin/epigallocatechin                            | [120]    |
| **Lotus sp.**   | L. corniculatus| **Phenolic acids**: GA and EA                                                                                        |          |
| **Picea sp.**   | P. abies      | **Ellagitannins**: castalagin, grandinin, castalina, vescalinagin, vescalin                                              | [50]     |
|                 |               | **Triterpenoid glycosides**: polygalloylquinic acid derivatives                                                        |          |
| **Quercus sp.** | Q. robur      | **Phenolic acids**: GA                                                                                                  |          |
|                 |               | **QUERING**                                                                                                           |          |
|                 |               | **CYANG derivatives**:                                                                                                  |          |
|                 |               | cyanidin-3-(2′′-galloyl)-galactoside and methyl delphinidin aglycone                                                     | [54,123]|
|                 |               | 7-methyl-delphinidin-3-(2′′-galloyl)-galactoside                                                                      |          |
|                 |               | 7-methyl-cyanidin-3-(2′′-galloyl)-galactoside                                                                         |          |
| **Rhus sp.**    | R. coriaria   | **Other bioactive compounds**:                                                                                          |          |
|                 |               | galloylhexose, benzoic acid, galloylquinic acid and quinic acid                                                        |          |
|                 |               | 3,4, 5-trihydroxy-2-oxo-1,3-propanediyl ester                                                                       |          |
|                 |               | myricetin galloylhexoside, triGA                                                                                        |          |
| **Rubus sp.**   | R. fruticosus | **Phenolic acids**: GA                                                                                                  | [124]    |
|                 |               | **CYANG and vanillic acid**                                                                                            |          |
|                 |               | **Flavonoids**: flavanone naringenin                                                                                  |          |
Anthocyanins and anthocyanidins: malvidin-3-galactoside, cyanidin-3-galactoside and delphinidin-3-galactoside

**Foods Terminalia**

| Foods | Flavonoid quercetin 3-α-L-arabinopyranoside tannins: |
|-------|----------------------------------------------------|
| Sapium sp. | S. baccatum, methyl gallate, corilagin and tercatain chebulagic acid and chebulinic acid |
| Sargassum sp. | S. fusiforme, GT: fufalols, fucols, ethols, caramalol derivatives |
| Schinopsis sp. | S. muticum, PT: fufalols (hydroxytrifufalol B, hydroxypentafufalol A, hydroxyheptafufalol B and hydroxynonafufalol A) |
| Schinopsis sp. | S. lorentzii, GT: TGG, PGG, FIS catechin polymers and quinic acid-GA esters. |
| Schinopsis sp. | S. balansae, CT: fisetinidol and robinetinidol polymers |
| Terminalia sp. | T. chebula, Phenolic acids: EA, GA, chebulinic acid, chebulic acid. |
| Vitis sp. | V. vinifera, Epicatechins: epigallocatechin, epicatechin-3-gallate and procyanidins B, catechin-gallocatechin dimers and fisetinidin dimers |

Definitions: CAST: castalagin, CYANG: cyanidin-3-glucoside, EA: ellagic acid, ET: elagtatin, FIS: fisetinidin, GA: gallic acid, GT: gallotannin, PC: procyanidin, PD: prodelphinidin, PG: phloroglucinol; PGG: pentagalloylglucone, PoGG: polygalloylglucone PT: phlorotannins, QUERG: quercetin-3-glucoside TGG: trigalloylglucone, VES: vescalagin.

There are hundreds of species of the genus *Acacia* globally distributed. Among them, *A. nilotica* has been widely documented for its traditional uses. The highest tannins levels are located in their fruits (22%), while leaves and bark account for half of this quantity [113]. Among the tannins identified in *A. nilotica* some of the most representatives are methyl gallate and polygalloyl units like ethyl gallate-1-galloyl-β-D-glucose, 1,6-di-galloyl-β-D-glucose, galloctein-5-gallate, epigallocatechin-7-gallate and -5,7-digallate, diGA, dicatechin, and the phenolic acids GA and EA [30]. The tannin fraction of *A. mearnsii* is also of interest for pharmacists, and in fact, it is commercially available as a food supplement after hot water extraction. The composition is based on flavan-3-ols units, mainly the monomers fisetinidol, robinetinidol, quercetin, myricetin, catechin and galloctein, among others. They are linked by C-C bonds, so that the resulting polymeric flavonoids are bioflavonoids like fisetinidol-(4α-8)-catechin and robinetinidol-(4α-8)-catechin androbinetinidol-(4α-8)-gallocatechin and triflavanoids such as robinetinidol-(4α-8′)-robinetinidol-(4′α-6′)-gallocatechin and rospinetinidol-(4α-8′)-robinetinidol (4′α-6′)-catechin [111]. Similarly, *A. arabica* has been described to possess a 12–20% of tannins in the bark, accounting for these some tannin units like GA, (+)-catechin, (+)-catechin-5-gallate, (-)-epicatechin, (-)-epigallocatechin-7-gallate and -5,7-digallate, (+)-dicatechin or pyrocatechol. Fruit also contains 32% of tannins identified as oligomers or as structural units (digallic and GA with its methyl and ethyl esters, protocatechuic and EA, leucocyanidin, 3,4,5,7-tetrahydroxy flavan-3-ol, 3,4,5,7-tetrahydroxy flavan 3,4-diol and 3,4,5,7-tetrahydroxy flavan-3-ol and (-)-epicatechol) [33]. *A. catechu* leaves possess high amounts of esterified monomers, such as epicatechin- and epigallocatechin-3-gallate, and some flavonoids like quercetin and kaempferol. Aqueous extracts were characterized for containing rhamnetin, 4-hydroxyphenylethanol or profisetidin [110].

The genus *Betula* also contains a hundred species worldwide distributed; however, pharmacologists mainly focus on *B. pendula*. In general terms, *B. pendula* possess a wide
range of phenolics, mainly glycosylated flavonoids and salicylates and high concentrations of CT (oligomeric and polymeric flavan-3-ols) [114]. In particular, B. pendula from southeastern Finland possess tannins and flavonoid-aglycones (apigenin, luteolin and chrysoeriol derivatives) [115]. Other work focused on B. pubescens collected from the same country revealed the content of CT and quercetin, apigenin, naringenin derivatives, kaempferol and myricetin derivatives [131].

Bark, resin, fruits and/or leaves of two common trees have been widely applied as traditional remedies and are well known to contain tannins. This is the case of the genus Castanea, being the most common representative C. sativa. Organic and aqueous extracts obtained from burs of C. sativa were evaluated with HPLC-UV-HRMS (high-performance liquid chromatography coupled to ultraviolet high-resolution mass spectrometry). Chromatograms from chestnut revealed that the most relevant tannins present in C. sativa are EA (5–79 mg/g) and chestanin (1–13 mg/g). However, the presence of many other several HT has been repeatedly demonstrated, such as trimethyl-ellagic acid hexoside or deoxyhexoside, chesnin, chesnatin, isochesnatin, crenatin, castalagin/vescalagin, methylvescalagin, pedunculagin, stachyurin or casuarinin, tellimagrandin I, chebulagic acid, castavalonic acid, cociferin d2 and castacrenin A-C isomers [101,116–118]. Other molecules described in chestnuts include ETs such as castalin, acutissimin A and B, grandinin or to its isomer roburin E, valoneic acid dilactone, tannin T1 and T2, MGG, TGG, TeGG, PGG, and HHDP-glucose derivatives (pedunculagin, casuarinin or tellimagrandin I) as well as the phenolic acid and GA [101,116,118]. Other minor compounds, present at trace levels, are 5-galloylhamamelose, (3,5-dimethoxy-4-hydroxyphe- nol)-1-β-D-(6′-o-galloyl)-glucoside isomer, m-digallic acid and kurigalin isomer [117].

Walnuts obtained from J. regia were analyzed in terms of polyphenol content. The main phenolic compounds were ET, even though they are more abundant in seeds, together with GT. Many of these HT found in J. regia were identified through the presence of the HHDP group. HT present in J. regia were tentatively identified using an LTQ-Orbitrap based on MS/MS results. The major ones semiquantitatively determined were EA and HHDP-glucose. Many derivatives of the latter one were suggested to be present such as pedunculagin or casuarinin (bis-HHDP-glucose), valoneoyl, sanguisorbyl, tergalloyl or macaranoyl (HHDP-glucose+trigalloyl group), tellimagrandin I (digalloyl-HHDP-glucose), precocin A and its isomers such as flosin A, platycarin or platycaryanin B (trigalloyl-HHDP-glucose), glansrin C, alnusnin B, asuarinin/casuaricin isomers (galloyl-bis-HHDP-glucose), strictitin/isostictitin isomers (galloyl-HHDP-glucose), stenophyllains A-C, malabathrin A, eucalbanin A or its isomer cornusan B, heterophylliin E, pterocarinin, breginin A (dimer of casuarinin and pendunculagin) and alienanin B (dimer of casuarinin and stachyurin), and flavogallionic acid dilactone [39].

More than 500 compounds have been isolated from Phyllanthus, although tannins together with lignins are considered the main bioactive compounds of this genus [48]. The species P. niruri contains ETs (HT) and flavonoids (CT). It is worth mentioning that the final hydrolysis of ETs gives the phenolic acids EA and GA, and many of them display activity against some viruses [132].
Figure 3. Chemical structure of main tannins present in the selected species.

The characterization of the chemical profile of aqueous extracts of four Phyllanthus species (P. amarus, P. stipulatus, P. niruri and P. tenellus) have revealed C-glycosylated flavones, O-glycosylated flavonols and the ETs geraniin A and B, phyllanthussin C, pelargoniin A, chebulagic acid A and geraniinic acid A. Moreover, the flavonol quercetin-3-O-β-D-glucuronopyranoside was purified from the aqueous extract of P. stipulates [133]. It was also reported the isolation of corilagiri, a tannin with antihyperalgesic activity, from the species P. niruri [134]. The HT have been shown as the main therapeutically active molecules of P. amarus [132], including different kinds of ETs: geraniin, amaritin, furosin, geraniinic acid B, amarinic acid, amarulone, repandusinic acid A, corilagin, isocorilagin, elaeocarpusin, phyllanthussin A, B, C, D and melatonin [135]. Phyllanthus phillyreifolius var. commersonii from Mauritius has also been documented as a potent source of bioactive phytochemicals. Its aqueous and methanolic extracts are abundant in ETs (including phyllanthusin B and granatin B), while phenolic acids, GA and flavonoids, quercetin and derivatives, were also present [136].

Bark, resin, fruits and/or leaves of two common threes that have been widely applied as traditional remedies and are well known to contain tannins are the genus Picea. One of the most utilized species for treating human and animal affections is P. abies. Leaves of P. abies have been analyzed and have shown to contain mono-terpenes (bornyl acetate, α-pinene, camphene, and limonene), di-terpenes (manool and dehydroabietate), sesqui- and triterpenes; phenolic compounds (CT; flavonoids like kaempferol, quercetin, myricetin; stilbenes and lignans) and alkaloids. The group of phenolic compounds represents 23%
without counting the 25% the group of the CT, triterpene saponins/glycosides are a 3%, essential oils account for 2% and flavone glycosides [87]. The resin of P. abies is a very useful product that may account for up to 19 g dry plant equivalent/100 g finished product [86].

The traditional medicinal plant P. lentiscus, typically found in the Mediterranean countries, has revealed at least 46 compounds, including flavonoids, hydroxycinnamic acid derivatives, phenolic acid derivatives and other polar compounds. Among them, the most prevalent flavonoids are catechin, myricetin galactoside, myricetin galloy, rhamno-pyranoside, myricetin-xiloside, myricetin-rhamnoside isomers and quercetin glycoside and the phenolic acid derivatives comprised galloyl quinic acid, digalloyl quinic acid, digalloyl quinic acid, dallic acid methyl ester and pistafolin A [137]. In addition, active components like polyphenols, flavonoids, A-type proanthocyanidins, anthocyanins, coumariins and phenolic acids were identified in P. spinosa [138].

An ethanolic extract obtained from the wood of Q. robur was analyzed and observed to possess HHDP-glucose, castalin, vescalin, vescalagin, castalagin, grandinin or to its isomer roburin E, polygalloylglucose isomers (TGG, TeGG, PGG isomers), and triterpenoid glycosides, among others like triterpenoid or polygalloylquinic acid (tri-, tetra-, penta-, esa-galloylquinic acid) derivatives, as well as the phenolic acids, EA and GA [50]. Bark from Q. petraea has been characterized to contain ETs such as 2,3-(S)-hexahydroxydiphenoyl-glucose, pedunculagin, vescalagin, and castalagin, the flavanoellagitannins acutissimin A, acutissimin B, eugenigrandin A, guajavin B, and stenophyllan C; and the procyandin ET [139].

Rhus coriaria mainly contains HT that, in general terms, have a common chemical base, the GA unit. Some works described its content as GA, quercetin-glucoside or cyanidin-3-glucoside equivalents and described its cyanidin-derivatives content as follows: cyanidin-3-(2"galloyl)-galactoside, 7-methyl-delpininidin-3-(2"galloyl)-galactoside, methyl delphinidin aglycone, 7-methyl-cyanidin-3-(2"galloyl)-galactoside [54]. Among the HT present in R. coriaria, it is worth mentioning galloylhexose, benzoic acid, 3,4,5-trihydroxy-, 2-oxo-1,3-propanediyl ester, galloylnorbergenin isomers, digalloylhexose, galloylshikimic acid, methyl digallate isomers, galloylquinic acid, quinic acid, isomers of tri-galloylllevoglucosan, myricetin galloylhexose, trGA, galloyl arbutin, arbutin, digalloylhexoyl-EA, pentagalloylhexose, hexagalloyl-hexose and dihydroxybenzoic acetate-digallate and galloyl-valoneic acid bilactone [123].

Extracts obtained from the seeds of Rubus occidentalis were demonstrated to contain EA derivatives and ETs such as sanguin H-10 isomer, lambertianin C without ellagic moiety, sanguin H-10 isomer, lambertianin C and sanguin H-6, proanthocyanidin trimers, galloyl-HHDP glucose or galloyl-bis-HHDP glucose isomer [140]. The number of anthocyanins quantified in fruit extracts obtained from R. idaeus accounted for 5.7 mg/g (73% of total polyphenols), being the major ones cyanidin-3-sophoroside cyanidin-3-glucoside, cyanidin-3-glucosyl-rutinoside and cyanidin-3-rutinoside [141]. Similarly, the most abundant anthocyanin identified in the juice of R. fruticosus was cyanidin-3-glucoside, and as minor ones malvidin-3-galactoside, cyanidin-3-galactoside and delphinidin-3-galactoside. Other compounds present in the juice were the phenolic acids GA and vanillic acid or flavanones such as naringenin, but in much lesser amounts [124].

From Sapium baccatum, apart from the phenolic acid, GA, and the flavonoid, quercetin 3-α-L-arabinopyranoside, the following tannins have been identified: methyl gallate, corilagin, tercatain, chebulagic acid and chebulinic acid [125].

Among other relevant bioactive compounds such as fucoxanthin, sulfated polysaccharides (i.e., fucoidan), tocopherols or vitamins, the main PT described in Sargassum fusiforme or S. horneri are fuhalols, fucols, fucols, ethols, fucophloroetols and several carmalol derivaties [73]. Many studies have attempted to elucidate the specific structure of some of these phlorotannins by, i.e., HPLC/MS methods, but only main groups of PT are reported. However, research on other Sargassum species such as S. muticum or S. spinuligerum show colliding results regarding the main PT, which are fuhalols such as hydroxytrufuhalol B,
hydroxypentafulanol A, hydroxyheptafuhalol B and hydroxynonafulanol A [126]. Conversely, structurally different PT like eckol derivatives have only been reported in algae from _Ecklonia_ sp. and _Eisenia bicyclis_ such as dieckol, 2,7-phloroglucinol-6,6-bieckol, phlorofucofuroeckol-A, pyrogallol-phloroglucinol-6,6-bieckol have been recently described in _Ecklonia cava_ by HPLC [119].

Red quebracho species ( _S. lorentzii_ and _S. balansae_) are, as mentioned, one of the most common and abundant sources of CT (14–26% of heartwood), and commercial extracts are even employed as quantification standards (about 300 mg/g) [1,6]. Extracts are usually obtained from bark or heartwood and have been used since the 19th-Century for leather tanning, but also exhibit other industrial and bioactive properties. Quebracho extracts are generally composed of 95% CT and 5% polysaccharides. Of these CT, some authors have determined that they are almost entirely profisenitidin polymers, formed by fisetinidol extenders bonded through a catechin subunit by C4-C8 linkage [58]. In fact, recent work has described the presence of the following CT: dimer constituted by catechin-fisetinidol isomer, dimers of catechin-3-gallate and fisetinidol, trimers of catechin-3-gallate and two fisetinidol, trimers of one catechin and two fisetinidol units, tetramers of one catechin and three fisetinidol units, a tetramer of one catechin-3-gallate and three fisetinidol. Moreover, it also revealed some of the HT present in _S. lorentzii_: TGG and PGG isomer, as well as esters of quinic acid with different units of GA [59].

The genus _Smilax_, typically found in tropical areas of Asia and the United States, possesses more than 350 species. Moreover, finally, the NMR characterization of root extracts from _Smilax aspera_ with antifungal activity have shown steroid saponins, resveratrol (phenolic compound), curillin G, asparagoside E, asparoside A and asparoside B [142].

Other plants used in traditional medicine are those from the genus _Terminalia_, which comprises 200 species. These plants have been revealed the occurrence of several classes of tannins and pseudotannins. For instance, the species _T. chebula_, _T. bellerica_ and _T. horrida_ are rich sources of GA and other simple gallate esters like methyl gallate, 1,6-di-galloyl-β-D-glucose, 3,4,6-tri-galloyl-β-D-glucose, 1,3,4,6-tetra-galloyl-β-D-glucose and 1,2,3,4,6-penta-galloyl-β-D-glucose [95,128]. It was also reported the identification of chebulic acid and ET (chebulic and non-chebulic) in fruit and leaves from several _Terminalia_ spp., being chebulanic, methyl neo-chebulanic, corilagin, punicalagin and terflavin the most frequent molecules. In addition, it is widely reported the isolation of EA and their derivatives flavogallonic acid, gallagic acid and methyl flavogallonate and the identification of several molecules from the EA glycosides group [95].

In the same way, antioxidants omega-3 polyunsaturated fatty acids, tocopherols, polyphenols, flavonoids, phenolic acids and a phenylpropanoid glucoside were characterized from hydroethanolic extracts of _U. rupestris_, which also showed antibacterial activities [143]. _U. dioica_ is the unique species of the _Urtica_ genus provided by the pharmaceutical industry. The powder from medicinal herbs includes phenolic acids, flavonoids, tannins, curcuminoinds, coumarins and lignans, among others [63].

Mainly seeds and skin of _V. vinifera_ have been analyzed to test the presence of tannins since they are the tissues with major abundances. While tannins from grape seeds are smaller in size due to a low polymerization degree, skin tannins are conversely heavier because of the higher polymerization degree. Seed tannins are mainly procyandins polymers. Grape skin mostly contains epicatechins, which can be present as epigallocatechin, catechin dimers (procyandins B) or catechin-gallocatechin dimers, but it also possesses fisetinidin dimers [129,130].
Table 3. Important species as sources of tannins. Quantitative data of hydrolyzable and condensed tannins (expressed in mg/g of dry weight (dw), except when other units were indicated) determined using different detection methods in specific tissues of the indicated species.

| Species          | Tissue                             | Type | Method               | Concentration (mg/g dw) | Ref.     |
|------------------|------------------------------------|------|----------------------|-------------------------|----------|
| *Acacia* sp.     | Leaves, bark                        | HT, CT | Folin–Ciocâlcateu   | 84–256                  | [144]    |
|                  |                                     | CT    | HPLC-UV-MS           | 108                     | [145]    |
| *Betula* sp.     | Leaves                             | CT    | Abs. 550 nm          | 73–81                   | [115]    |
| *Castanea* sativa| Bark, heartwood, peel              | HT    | HPLC-DAD-MS          | 47.5–167.3 (bark), 62.8 (heartwood), 4.9 (peel) | [22,146,147] |
| *Ecklonia* cava  | Whole alga                         | PT    | HPLC                 | 6.07                    | [148]    |
| *Hedysarum* sp.  | Whole plant                        | CT    | -                    | 68                      | [149]    |
| *Juglans* regia  | Seeds                              | CT, ET| -                    | 35–87 (CT), 36–59 (ET)  | [5]      |
| *Lespedeza* procumbens | Leaves                      | CT    | Abs. 550 nm          | 60–130                  | [150]    |
| *Lotus* sp.      | Flowers, leaves, stems and roots   | CT    | Abs. 550 nm          | 25–54                   | [151]    |
| *Parietaria* sp. | Whole plant                        | CT    | Abs. 550 nm          | 10 mg DE/g dw           | [47]     |
| *Pistacia* sp.   | Leaves                             | CT    | Folin–Ciocâlcateu   | 21.7–25.1               | [152]    |
|                  | Hulls                              | HT    | HPLC-DAD-MS          | 20.4–33.1               | [153]    |
| *Prunus* sp.     | Fruits and leaves                  | CT    | Abs. 550 nm          | 2.2–37.6 (fruit), 74 (leaves) | [154,155] |
| *Punica* granatum| Whole fruit                         | HT    | Abs. 550 nm          | 62.71–139.63 mg TAE/g dw| [156]    |
| *Quercus* sp.    | Whole fruit                         | HT    | Abs. 270–325 nm      | 8.18–47.26              | [157,158]|
| *Rhus* sp.       | Leaves                             | GT    | Folin–Ciocâlcateu   | 13–550 mg GAE/g dw      | [159]    |
|                  | Plant                              | HT    | LC–MS/MS             | 230.7 mg/kg             | [160]    |
| *Schinopsis* sp. | Barks                              | CT    | Folin–Ciocâlcateu   | 453 mg TAE/g dw         | [161]    |
|                  | Heartwood                          | CT    | HPLC                 | 164                     | [145]    |
| *Smilax* sp.     | Leaves                             | CT    | Abs. 550 nm          | 11.36 mg DE/g dw        | [47]     |
| *Umbilicus* sp.  | Whole plant                        | CT    | Abs. 550 nm          | 5.45 mg DE/g dw         | [47]     |
| *Urtica* sp.     | Whole plant                        | CT    | Abs. 550 nm          | 8 mg DE/g dw            | [47]     |
| *Vitis* sp.      | Skins and seeds                    | CT    | Abs. 500 nm          | 6–165 mg CE/g dw (skins), 3–241 mg CE/g dw (seed) | [162]   |

*TAE:* tannic acid equivalents, *GAE:* gallic acid equivalents, *DE:* delphinidin equivalents, *CE:* catechin equivalents. *HPLC:* high-performance liquid chromatography, *DAD:* diode array detector, *LC–MS/MS:* liquid chromatography–tandem mass-spectrometry, *UV:* ultraviolet.

Finally, few different legume species, including *L. corniculatus*, *L. pedunculatus*, *Lespedeza* sp., *Leucaena* sp., *D. ovalifolium*, *Gliricidia* sepium, *Manihot* esculenta, *Arachis* pintoi or *Medicago* sativa L., have been repeatedly described to possess high amounts of CT. However, the relative information of the chemical profile of these molecules is not easily accessible [7,163–166]. Nevertheless, we have compiled the chemical profile data relative to the genus *Lotus* to provide an example of this family of legumes with traditional applications for veterinarian aims mainly. Two *L. corniculatus* varieties (Fergus and Viking) were deeply analyzed by MALDI-TOF MS. The MS spectra revealed the presence of tetramers to hexamers (consisting of procyanidin or catechin/epicatechin units) but also included oligomers up to the decamer range. The most abundant tannins in *L. corniculatus* are heteropolymers, containing both catechin/epicatechin (procyanidin, PC) and galloatechin/epigallocatechin units (prodelphinidin, PD) or homopolymers (PDs were not detected as homopolymer). Even though most of the heteropolymers were constituted by one or two PD units, few molecules displayed a maximum substitution degree of three or four units [120]. Another work used HPLC-ESI-MS for examining the CT content in *L. corniculatus* and compared it against *L. pedunculatus*. The analysis was performed after a strong acid-catalyzed cleavage in the presence of PG or benzyl mercaptan. The average
In concordance with the previous work, a transport of 23, 13 and 16% was determined for transportation of procyanidins A2 and B2, \((\text{methylation})\), besides slight metabolization into monomeric epicatechin was observed. Presence of tetramers improved the absorption of B2 dimers. The monomeric epicatechin among the dimers A1 and A2, they showed better absorption than B2, even though the monomeric epicatechin mostly possesses PD subunits (ratio PC:PD of 2:8), which are mainly located in extender units. Terminal units differ from extender ones since they have a lower content of epigallocatechin and epicatechin \([81]\).

Therefore, plants and extracts reported to be used as remedies for human and animal ailments or affections have been found to possess high concentrations in tannins, which given their reported bioactivities, can be suggested to be responsible for the alleged benefits of these species.

4. Bioavailability and Bioaccessibility of Tannins

Traditionally, the most common application of rich-tannins plants has been through oral and topical administration, while as mentioned, several tannin-rich sources are commonly used as a foodstuff (i.e., \(\text{Sargassum sp.}, \ E. \text{cava}, \ C. \text{sativa}, \ P. \text{granatum}, \ V. \text{vinifera}\)) \((\text{Table 1})\). The oral intake of tannins has two potential mechanisms of action; they may exert their biological effects as non-absorbable complexes or as absorbable simpler units. Non-absorbable complexes are created due to their binding properties that prompt their union with other present molecules in the organism, like proteins. These resultant complexes may produce local effects in the gastrointestinal tract (antioxidant, radical scavenging, antimicrobial, antiviral, antimitogenic and antinutrient). Absorbable tannins are simpler metabolites, characterized to have low-molecular-weight; thus, they are mostly dimers and trimers. These absorbable tannins can be present in the preparation administrated or can be the metabolic product of more complex structures that get fermented along the digestive tract. Either the origin of these absorbable tannins they are capable of reaching blood circulation and get transported into other organs, being then able to induce systemic effects \([5,20]\). Yet, despite evidence regarding tannin bioaccessibility on humans is scarce, some experiments have tested their absorbability in vitro and animal models. The bioaccessibility and bioavailability of tannins are both directly related to their chemical structure, the matrix into which they are embedded, but also with the digestibility capacity of the organism that intakes them. In general terms, highly polymerized tannins, with high molecular weight, are more poorly absorbed in the small intestine and rely on fragmentation and gut microbiota \([167]\). The conjugation of tannins with other molecules present in the matrix can enhance their transport as biotransformed polyphenols. For example, anthocyanins have been demonstrated to possess higher bioaccessibility when embedded into lipidic matrixes while protein ones prevent their degradation by small intestine conditions, which prompt their further metabolism at the colon, after which they can reach blood circulation \([168]\) \((\text{Figure 4})\). This could be explained by the preferential absorption of lipophilic molecules by the gut, a feature that has able to enhance the bioaccessibility of many modern manufactured drugs \([169]\). Different research works have addressed the absorption and metabolism of tannins or their purified units. In accordance with their chemical nature, HT are more easily absorbed once they reach the small intestine since they are subjected to partial hydrolyzation by digestive acids. An experiment performed on rats analyzed the absorption of procyanidin dimers A1 \([\text{epicatechin}(2\text{-O}-7, 4\text{-8})\text{-catechin}]\), A2 \([\text{epicatechin}(2\text{-O}-7, 4\text{-8})\text{-epicatechin}]\), B2 \([\text{epicatechin}(4\text{-8})\text{-epicatechin}]\), and other types and mixtures of procyanidins. All the three dimers were absorbed at the small intestine level and showed no conjugation or further chemical modifications (methylation), besides slight metabolization into monomeric epicatechin was observed. Among the dimers A1 and A2, they showed better absorption than B2, even though the presence of tetramers improved the absorption of B2 dimers. The monomeric epicatechin got partially methylated and totally conjugated. A-type trimers were not absorbed \([170]\).

In another study developed with human adenocarcinoma stomach cell line \((\text{MKN-28})\), the transportation of procyanidins A2 and B2, \((-\text{epicatechin and +catechin})\) was analyzed. In concordance with the previous work, a transport of 23, 13 and 16% was determined for
A2, (−)-epicatechin and (+)-catechin, respectively, showing a pH- and time-dependent transport pattern [171].

A review paper has evaluated the absorption, metabolism, distribution and excretion of (−)-epicatechin. As the previous study has pointed (−)-epicatechin is absorbed in the small intestine and can be detected in plasma at amounts under the μmol/L level one hour after its ingestion. Up to twelve structural-related (−)-epicatechin metabolites (SREMs) can be detected; however, the chemical profile is different between species. Indeed, in humans, the main SREMs are (−)-epicatechin-3′-sulfate and -glucuronide, while in rats are 3′-methyl(−)-epicatechin and the -5-glucuronide form as well as the (−)-epicatechin-5-glucuronide. Later, flavan-3-ol units that reach the colon are transformed by microbiota gut into 5C-ring fission metabolites (5C-RFMs) 5-(hydroxyphenyl)-γ-valerolactones and 5-(hydroxyphenyl)-γ-hydroxyvaleric. These metabolites were quantified as 42% of the ingested (−)-epicatechin after nearly 6 h after its ingestion. The total (−)-epicatechin in urine and plasma can be quantified in terms of 5C-RFMs equivalents. Its presence in urine was determined at 95%, suggesting its high bioavailability. Similarly, a porcine model showed that acorns (Quercus sp.) ET were gradually fragmented to ellagic acid glucuronides and several urolithins. Subsequent decarboxylation, and dehydroxylation reactions loss of hydroxyl groups from ellagic acid to urolithins D, C, A and finally B decreased its antioxidant capacity by the lower hydroxyl groups but raised its lipophilicity. These urolithins were detected in bile and plasma, which indicates active circulation [172]. Urolithin A is also considered a biomarker of ET intake, as it is also detected in human plasma and urine. Administration of R. idaeus in healthy, and ileostomy patients showed the presence of urolithin A and B glucuronides in the urine of healthy subjects, while these were significantly lower in those with ileostomy [173]. This preeminent role of gut microbiota in improving the bioaccessibility of tannins in humans and animals has been addressed in other studies. One tested fermenting walnuts and punicalagin with human fecal bacteria, determining the production of urolithin A from ellagic acid. Results showed great variations
among the subjects, with some bacterial samples displaying no detectable production, which supports the hypothesis that individual gut differences have a considerable effect on the bioaccessibility of molecules [174].

Thus, differences in the chemical profile of metabolites obtained from (−)-epicatechin depending on the studied species must be considered for extrapolating results between species. Moreover, it is necessary to establish appropriate concentrations, determine the adequate metabolites to experiment with, as well as the biomarkers that are going to be used for quantification purposes [175].

5. Traditional and Scientific Knowledge: Building Bridges

Considering records on the traditional use of selected plants and knowledge on their high levels of tannins, known to exert various bioactivities, a correlation could be suggested.

Some of the traditional uses with pharmacological applications of the genus *Acacia* indicated it as useful plants for treating gastrointestinal, respiratory or skin mild inflammatory processes, as well as having a narcotic effect useful to treat nervous system disorders [29,30]. Currently, it has been demonstrated that tannins present in *A. mearnsii* like robinetinidol-(4-β-8)-epigallocatechin 3-gallate was capable of restoring the oxidative damage induced in neuroblastoma cells [176]. Fisetinidol-derivatives from *A. mearnsii* also reduced the oxidative stress but also minimized the presence of inflammatory markers in macrophages, concordant effects of those from *A. nilotica* (provided anti-nociceptive, anti-inflammatory and antipyretic) tested in vivo [30–32].

Another plant with an important presence of tannins, *J. regia*, has also been applied as an anti-inflammatory (for rheumatism, hemorrhoids, mild skin inflammations) to reduce varicose veins or toothache [37,38]. These traditional uses can be related to the demonstrated capacity of EA as antioxidant, anti-inflammatory and antiatherogenic. EA, present in *J. regia* both free or as part of ETs, possesses the capacity of reducing the activity of lactate dehydrogenase, superoxide dismutase, catalase, and levels of hydroperoxides and oxidized glutathione (antioxidant capacity directly related with the anti-inflammatory) and avoids the cellular activity of serum creatine kinase-MB, VCAM-1 and ICAM-1 (antiatherogenic) [39–41].

Traditional uses of *Quercus* sp. with pharmacological aims have also been supported by scientific evidence. *Quercus* sp. was traditionally reported to be utilized for controlling diabetes, and, in fact, extracts obtained from *Quercus* sp. were demonstrated to inhibit α-glucosidase, a molecule used to evaluate antidiabetic properties in vitro [37,50]. Other traditional uses such as the treatment of mild inflammations may be connected with its demonstrated antioxidant properties that may reduce oxidative stress triggered by inflammatory cascades and reduce their impact [51].

The *Rubus* genus has a wide variety of traditional applications that cover the treatment of gastrointestinal, urinary, respiratory, eye and skin affections coursing inflammation, diabetes or atherosclerosis (was also used as anti-hemorrhagic [37,42]. Among them, *R. idaeus* was specifically evaluated as an inhibitor of platelet aggregation showing its capacity to modulate gene expression of proteins involved in the activation of platelets accompanied by a reduction in the oxidative status of the cell model [177]. These capacities are consistent with the reduction of the oxidative stress of hypertrophied adipocytes, where *R. idaeus* was also claimed to mobilize lipids [141]. These combined properties point to its potential use as a cardioprotective and key ingredient in the prevention of obesity. Antioxidant and anti-inflammatory general properties of *Rubus* are summed to the anti-diabetic and gastroprotective ability demonstrated in vivo assays for *R. fruticosus* [124,178] or the healing capacity of *R. imperialis* [179]. These functions may be further supported by the potential antifungal and antibacterial capacities of plants belonging to this genus. *R. ulmifolius* was demonstrated to inhibit bacteria present in gastrointestinal, urinary or genital microbiota such as *Helicobacter pylori* [180], *Escherichia coli* or *Staphylococcus agalactiae* [181]. *R. ulmifolius* has been proven to possess antifungal activity against *C. albicans*, a
common genital yeast [181]. It also has an antifungal effect against Beauveria sp. or F. solani involved in mycotic keratitis or endophthalmitis (eye care suggested by traditional uses), M. canis, P. verrucosa and S. brevicaulis, reported to cause skin and nail infections and lesions (treatment of mild skin affections was also traditionally reported) [182].

Rhus is a genus widely explored through scientific methods that concord with some of its traditional uses (gastrointestinal diseases such as dysentery, intestinal ulcers, rectal prolapse, or hemorrhoids, among others) [53]. The most studied species R. coriaria was demonstrated in vitro as capable of inhibiting TNF-α-induced inflammatory cascades [54] whereas, in vivo, it prevented necrotizing enterocolitis by reversing mild and focalized injuries [53], which can support its traditional use for gastrointestinal affections, including the treatment of intestinal ulcers, rectal prolapse or hemorrhoids. For these last properties, it is critical to know the accelerating healing capacity (prompted by both anti-inflammatory and antibacterial activity against Staphylococcus aureus or Pseudomonas aeruginosa) of this plant [183], while for its application against dysentery its role as anti-helminthic may provide some scientific basis [184].

Among the variability of the traditional uses of Terminalia, those related to gastrointestinal issues can be associated with the scientific finding. T. chebula was demonstrated to inhibit maltase, an enzyme present in the small intestine that catalyzes the maltose hydrolysis [102]. Moreover, T. chebula and T. bellerica also modulate genes involved in the storage and mobilization of lipids, glucose metabolism, morphogenesis and inflammatory response [185]. The capacity of improving the appetite of T. chebula may be indirectly related to its potential ability to ameliorate the expression of GABA receptors implied in relaxing mechanisms [186].

6. Discussion and Conclusions

Tannin-rich plants have been traditionally used in very different geographical areas, with autochthon species being used to treat a huge variety of affections. Some species showed several applications and are still used nowadays, which shows the great acceptance of bioactive molecules from these plants over the years. Moreover, it is estimated that 70% of the global population from underdeveloped countries do not have access to novel commercial drugs, being medicinal plants the only therapeutic solution.

This review offers an overview of the traditional uses of more than twenty-one genera of plants and the macroalgae Sargassum sp., all known to possess considerable amounts of tannins as a part of their tissues. Many species reported like V. vinifera, J. regia, C. sativa or Sargassum sp. are part of the diet of many countries without medicinal purposes, and its bioavailable low-polymerized tannins may be readily absorbed. Most typical applications in human bodies include the treatment of mild skin inflammations and gastrointestinal and respiratory affections. Therefore, this paper constitutes a useful tool to satisfy the global market, which demands natural phytomedicinal for diseases with difficult treatment like obesity, insomnia, anxiety, stress, constipation, etc. Plant applications in animals are mainly attributed to the anti-helminthic or antidiarrheal properties.

The chemical analysis of phytochemicals in traditionally used plants has been performed to figure out the composition of tannins and tannin-related molecules. Plants pose some common molecules like phenolic acids, GT, ET and polymeric flavonoids, and macroalgae contain PT, mainly fuhalols, fucols, ethols and carmalol derivatives. However, the variability in the chemical profile is high and mostly depended on the analyzed tissue, extraction procedure, selected solvent, geographical area and moment of collection, etc.

In summary, this review aimed to interconnect the knowledge collected along centuries in the traditional application of rich-tannins plants with scientific results to establish bridges between ethnology and science. We understand that ethnology compiles useful information achieved by trial and error of many generations, and now, based on works developed under the scientific methodology, this knowledge can be accepted or refuted. As previously exposed, some traditional uses have already been demonstrated by scientific data. Thus, those still not scientifically confirmed may represent an important source
of information to develop innovative applications using tannins, natural ingredients with huge potential.

Author Contributions: Conceptualization, M.F.-C., M.A.P. and J.S.-G.; methodology, C.L.-L., J.E., M.C., M.F.-C., P.G.-O., P.O. and F.C.; formal analysis, C.L.-L., J.E., L.C., M.C., M.F.-C., P.G.-O., P.O. and F.C.; investigation, C.L.-L., J.E., M.C., M.F.-C., P.G.-O., P.O. and F.C.; writing—original draft preparation, C.L.-L., J.E., M.C., M.F.-C., P.G.-O., L.C., P.O. and F.C.; writing—review and editing, M.F.-C., M.A.P. and J.S.-G.; supervision, M.F.-C., M.A.P. and J.S.-G.; project administration, M.F.-C., M.A.P. and J.S.-G. All authors have read and agreed to the published version of the manuscript.

Funding: The research leading to these results was funded by FEDER under the program Interreg V-A Spain-Portugal (POPTEC) 2014–2020 ref. 0377_IBERPHENOL_6_E and ref. 0181_NANOEATERS_01_E; to Xunta de Galicia supporting with the Axudas Conecta Peme the IN852A 2018/58 NeuroFood Project and the program EXCELENCIA-ED431F 2020/12; to Ibero-American Program on Science and Technology (CYTED—AQUA-CIBUS, P317RT0003) and by the Bio-Based Industries Joint Undertaking (JU) under grant agreement No 888003 UP4HEALTH Project (H2020-BBI-JTI-2019), the JU receives support from the European Union’s Horizon 2020 research and innovation program and the Bio-Based Industries Consortium. The project SYSTEMIC Knowledge hub on Nutrition and Food Security has received funding from national research funding parties in Belgium (FWO), France (INRA), Germany (BLE), Italy (MIPAAF), Latvia (IZM), Norway (RCN), Portugal (FCT), and Spain (AEI) in a joint action of JPI HDHL, JPI-OCEANS and FACCE-JPI launched in 2019 under the ERA-NET ERA-HDHL (n° 696295).

Institutional Review Board Statement: Not applicable.

Informed Consent Statement: Not applicable.

Data Availability Statement: Not applicable.

Acknowledgments: The research leading to these results was supported by MICINN supporting the Ramón&Cajal grant for M.A. Prieto (RYC-2017-22891) and the Juan de la Cierva_ incorporación grant for P. Otero (IJCI-2016-27774); by Xunta de Galicia and the University of Vigo supporting the post-doctoral grant of M. Fraga-Corral (ED481B-2019/096), the pre-doctoral grant for P. García-Oliveira (ED481A-2019/295); to EcoChestnut Project (Erasmus+ KA202) that supports the work of M. Carpena.

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

Abbreviations

CoT Complex tannin
CT Condensed tannins
EA Ellagic acid
ET Ellagitannin
GA Gallic acid
GT Gallotannin
HHDP Hexahydroxydiphenol
HT Hydrolyzable tannins
NHTP Nonahydroxytriphenoyl
PC Procyanidin
PD Prodelphinidin
PG Phloroglucinol
TGG Trigalloylglucose
PT Phlorotannins
GABA Gamma-Aminobutyric acid
ICAM Intercellular adhesion molecule
TNF-α Tumor necrosis factor-α
VCAM Vascular cell adhesion protein
53. Isik, S.; Tayman, C.; Cakir, U.; Koyuncu, I.; Taskin Turkmenoglu, T.; Cakir, E. Sumac (Rhus coriaria) for the prevention and treatment of necrotizing enterocolitis. *J. Food Biochem.* 2019, 43, e13068, doi:10.1111/jfbi.13068.

54. Khalilpour, S.; Sangiovanni, E.; Piazza, S.; Fumagalli, M.; Beretta, G.; Dell’Agli, M. In vitro evidences of the traditional use of *Rhus coriaria* L. fruits against skin inflammatory conditions. *J. Ethnopharmacol.* 2019, 238, 111829, doi:10.1016/j.jep.2019.111829.

55. Saraiva, A.M.; Saraiva, C.L.; Cordeiro, R.P.; Soares, R.R.; Xavier, H.S.; Caetano, N. Atividade antimicrobiana e sinérgica das frações das folhas de Schinopsis brasiliensis Engl. frente a clones multirresistentes de Staphylococcus aureus. *Rev. Bras. Plantas Med.* 2013, 15, 199–207, doi:10.1590/S15572021000200006.

56. Del Carrizo, E.V.; Palacio, M.O.; Roic, L.D. Uso medicinal de algunas especies nativas en Santiago del Estero (República Argentina). *Dominica* 2005, 21, 25–32.

57. Barboza, G.E.; Cantero, J.I.; Núñez, C.; Ariza Espinar, L.; del Pacciaroni, A.V. Medicinal plants: A general review and a phytochemical and ethnopharmacological screening of the native Argentine Flora. *Kurztania* 2009, 34, 7–365.

58. Venter, P.B.; Van Der Merwe, M.J.; Bonnet, S.L.; Van Der Westhuizen, J.H. Analysis of commercial proanthocyanidins. Part 1: The chemical composition of quebracho (*Schinopsis lorentzii* and *Schinopsis balansa*) heartwood extract. *Phytochemistry* 2012, 73, 95–105, doi:10.1016/j.phytochem.2011.10.006.

59. Cardullo, N.; Muccilli, V.; Cunsolo, V.; Tringali, C. Mass Spectrometry and 1H-NMR Study of *Schinopsis lorentzii* (Quebracho) Tannins as a Source of Hypoglycemic and Antioxidant Principles. *Molecules* 2020, 25, 3257, doi:10.3390/molecules25143257.

60. Fruet, A.P.B.; Giotto, F.M.; Fonseca, M.A.; Nörnborg, J.L.; De Mello, A.S. Effects of the Incorporation of Tannin Extract from Quebracho Colorado Wood on Color Parameters, Lipid Oxidation, and Sensory Attributes of Beef Patties. *Foods* 2020, 9, 667, doi:10.3390/foods9050667.

61. Bonet, M.A.; Valles, J. Ethnobotany of Montseny biosphere reserve (Catalonia, Iberian Peninsula): Plants used in veterinary medicine. *J. Ethnopharmacol.* 2007, 110, 130–147, doi:10.1016/j.jep.2006.09.016.

62. Bullitta, S.; Re, G.A.; Manunta, M.D.I.; Piluzza, G. Traditional knowledge about plant, animal, and mineral-based remedies to treat cattle, pigs, horses, and other domestic animals in the Mediterranean island of Sardinia. *J. Ethnobiol. Ethnomed.* 2018, 14, 1–26, doi:10.1186/s13002-018-0250-7.

63. Adhikari, B.M.; Bajracharya, A.; Shrestha, A.K. Comparison of nutritional properties of Stinging nettle (*Urtica dioica*) flour with wheat and barley flours. *Food Sci. Nutr.* 2015, 119–124, doi:10.1002/fsn3.259.

64. Dar, S.A.; Ganai, F.A.; Yousuf, A.R.; Balkhi, M.-H.; Bhat, T.M.; Sharma, P. Pharmacological and toxicological evaluation of *Urtica dioica*. *Pharm. Biol.* 2013, 51, 170–180, doi:10.3109/13880209.2012.715172.

65. Jan, K.N.; Zarafshan, K.; Singh, S. Stinging nettle (*Urtica dioica* L.): A reservoir of nutrition and bioactive components with great functional potential. *J. Food. Med. Charact.* 2017, 11, 423–433, doi:10.1007/s11694-016-9410-4.

66. Guerrera, P.M. Traditional phytotherapy in Central Italy (Marche, Abruzzo, and Latium). *Fitoterapia* 2005, 76, 1–25, doi:10.1016/j.fitote.2004.09.006.

67. Uncini Manganelli, R.E.; Camangi, F.; Tomei, P.E. Curing animals with plants: Traditional usage in Tuscany (Italy). *J. Ethnopharmacol.* 2001, 78, 171–191, doi:10.1016/S0378-8741(01)00341-5.

68. Viegi, L.; Pieron, A.; Guerrera, P.M.; Vangelisti, R. A review of plants used in folk veterinary medicine in Italy as basis for a databank. *J. Ethnopharmacol.* 2003, 89, 221–244, doi:10.1016/j.jep.2003.08.003.

69. Rodríguez-Pérez, C.; García-Villanova, B.; Guerra-Hernández, E.; Verardo, V. Grape seeds proanthocyanidins: An overview of in vivo bioactivity in animal models. *Nutrients* 2019, 11, 2435, doi:10.3390/nu1102435.

70. Gupta, A.; Kumar, R.; Bhattacharyya, P.; Bishaya, A.; Pandey, A.K. *Terminalia bellirica* (Gaertn.) roxb. (Bahera) in health and disease: A systematic and comprehensive review. *Phytomedicine* 2020, 77, 153278, doi:10.1016/j.phymed.2020.153278.

71. Liu, L.; Heinrich, M.; Myers, S.; Dworjany, S.A. Towards a better understanding of medicinal uses of the brown seaweed *Sargassum* in Traditional Chinese Medicine: A phytochemical and pharmacological review. *J. Ethnopharmacol.* 2012, 142, 591–619, doi:10.1016/j.jep.2012.05.046.

72. Casas, M.P.; Rodríguez-Hermida, V.; Pérez-Larrán, P.; Conde, E.; Liveri, M.T.; Ribeiro, D.; Fernandes, E.; Domínguez, H. In vitro bioactive properties of phlorotannins recovered from hydrothermal treatment of Sargassum muticum. *Sep. Purif. Technol.* 2016, 167, 117–126, doi:10.1016/j.seppur.2016.05.003.

73. Li, Y.; Fu, X.; Duan, D.; Liu, X.; Xu, J.; Gao, X. Extraction and Identification of Phlorotannins from the Brown Alga, Sargassum fusiforme (Harvey) Satchell. *Mar. Drugs* 2017, 15, 49, doi:10.3390/md15020049.

74. Ganesan, A.R.; Tiwari, U.; Rajauria, G. Seaweed nutraceuticals and their therapeutic role in disease prevention. *Food Sci. Hum. Wellness* 2019, 8, 252–263.

75. European Commission. Commission Implementing Regulation (EU) 2018/460 of 20 March 2018 authorising the placing on the market of Ecklonia cava phlorotannins as a novel food under Regulation (EU) 2015/2283 of the European Parliament and of the Council and amending Commiss. Off. J. Eur. Union 2018, 46–119.

76. Park, J.; Kim, J.H.; Kwon, J.M.; Kwon, H.; Jeong, H.J.; Kim, Y.M.; Kim, D.; Lee, W.S.; Ryu, Y.B. Dieckol, a SARS-CoV 3CLpro inhibitor, isolated from the edible brown algae Ecklonia cava. *Bioorg. Med. Chem.* 2013, 21, 3730–3737, doi:10.1016/j.bmc.2013.04.026.

77. Singh, K.N.; Lal, B. Notes on traditional uses of khair (*Acacia catechu* Willd.) by inhabitants of shivalik range in Western Himalaya. *Ethnobot. Leafl.* 2006, 2006, 12.
78. Ghalandari, S.; Kariman, N.; Sheikhan, Z.; Mojafi, F.; Mirzaei, M.; Shahrahmani, H. Effect of Hydroalcoholic Extract of Capsella bursa pastoris on Early Postpartum Hemorrhage: A Clinical Trial Study. *J. Altern. Complement. Med.* 2017, 23, 794–799, doi:10.1089/acm.2017.0095.

79. Conedera, M.; Krebs, P.; Tinner, W.; Pradella, M.; Torriani, D. The cultivation of *Castanea sativa* (Mill.) in Europe, from its origin to its diffusion on a continental scale. *Veg. Hist. Archaeobot.* 2004, 13, 161–179.

80. Aguere, M.J.; Duval, B.; Powell, J.M.; Vadas, P.A.; Wattiaux, M.A. Effects of feeding a quebracho–chestnut tannin extract on lactating cow performance and nitrogen utilization efficiency. *J. Dairy Sci.* 2010, 103, 2264–2271, doi:10.3168/jds.2019-17442.

81. Meagher, L.P.; Lane, G.; Sivakumaran, S.; Tavernade, M.H.; Fraser, K. Characterization of condensed tannins from Lotus species by thiolic degradation and electrospray mass spectrometry. *Anim. Feed Sci. Technol.* 2004, 117, 151–163, doi:10.1016/j.anifeedsc.2004.08.007.

82. Christensen, R.G.; Eun, J.S.; Yang, S.Y.; Min, B.R.; MacAdam, J.W. In vitro effects of birdsfoot trefoil (*Lotus corniculatus*L.) pasture on ruminal fermentation, microbial population, and methane production. *Prof. Anim. Sci.* 2017, 33, 451–460, doi:10.15322/pas.2016-01558.

83. Lange, K.C.; Olcott, D.D.; Miller, J.E.; Mosjidis, J.A.; Terrill, T.H.; Burke, J.M.; Kearney, M.T. Effect of sericea lespedeza (*Lespedeza cuneata*) fed as hay, on natural and experimental *Haemonchus contortus* infections in lambs. *Vet. Parasitol.* 2006, 141, 273–278, doi:10.1016/j.vetpar.2006.06.001.

84. Katiki, L.M.; Ferreira, J.F.S.; Gonzalez, J.M.; Zajac, A.M.; Lindsay, D.S.; Chagas, A.C.S.; Amarante, A.F.T. Anthelmintic effect of plant extracts containing condensed and hydrozable tannins on Caenorhabditis elegans, and their antioxidant capacity. *Vet. Parasitol.* 2013, 192, 218–227, doi:10.1016/j.vetpar.2012.09.030.

85. Jyske, T.; Kuroda, K.; Keriö, S.; Pranovich, A.; Linnakoski, R.; Hayashi, N.; Aoki, D.; Fukushima, K. Localization of (+)-Catechin in Picea abies Phloem: Responses to Wounding and Fungal Inoculation. *Molecules* 2020, 25, 2952, doi:10.3390/molecules25122952.

86. Disler, M.; Ivenmeyer, S.; Hamburger, M.; Vogl, C.R.; Tesic, A.; Klarer, F.; Meier, B.; Walkenhorst, M. Ethnoveterinary herbal remedies used by farmers in four north-eastern Swiss cantons (St. Gallen, Thurgau, Appenzell Innerrhoden and Appenzell Ausserrhoden). *J. Ethnobiol. Ethnomed.* 2014, 10, 32, doi:10.1186/1746-4269-10-32.

87. Agency, E.M.; Medicines, V. EMA 2004 Committee for Medicinal Products for Veterinary Use; EMA: Amsterdam, The Netherlands, 2005; pp. 1–3.

88. Landau, S.Y.; Muklada, H.; Abu-Rabia, A.; Kaadan, S.; Azaiez, H. Traditional Arab ethno-veterinary practices in small ruminant breeding in Israel. *Small Rumin. Res.* 2014, 119, 161–171, doi:10.1016/j.smallrumres.2014.01.004.

89. Piluzza, G.; Virdis, S.; Serralutzu, F.; Bullitta, S. Uses of plants, animal and mineral substances in Mediterranean ethno-veterinary practices for the care of small ruminants. *J. Ethnopharmacol.* 2015, 168, 87–99, doi:10.1016/j.jep.2015.03.056.

90. Lanský, E.P.; Newman, R.A. Punica granatum (pomegranate) and its potential for prevention and treatment of inflammation and cancer. *J. Ethnopharmacol.* 2007, 109, 177–206, doi:10.1016/j.jep.2006.09.006.

91. Lanský, E.; Shubert, S.; Neeman, I. Pharmacological and therapeutic properties of pomegranate. In *Production, Processing and Marketing of Pomegranate in the Mediterranean Region: Advances in Research and Technology*; Options Méditerranéennes: Série A. Séminaires Méditerranéens; CIHEAM: Zaragoza, Spain, 2000; pp. 231–235.

92. Ballabh, B.; Chaurasia, O.P. Traditional medicinal plants of cold desert Ladakh—Used in treatment of cold, cough and fever. *J. Ethnopharmacol.* 2007, 112, 341–349, doi:10.1016/j.jep.2007.03.020.

93. Al Muqarrabun, L.M.R.; Ahmat, N.; Aris, S.R.S. A review of the medicinal uses, phytochemistry and pharmacology of the genus Sapium. *J. Ethnopharmacol.* 2014, 155, 9–20, doi:10.1016/j.jep.2014.05.028.

94. Zhang, X.-R.; Kaunda, J.S.; Zhu, H.-T.; Wang, D.; Yang, C.-R.; Zhang, Y.-J. The Genus *Terminalia* (Combretaceae): An Ethnopharmacological, Phytochemical and Pharmacological Review. *Nat. Prod. Bioprospect.* 2019, 9, 357–392, doi:10.1007/s13659-019-00222-3.

95. Fahmy, N.M.; Al-Sayed, E.; Singab, A.N. Genus *Terminalia*: A phytochemical and biological review. *Med. Aromat Plants* 2015, 4, 1–22.

96. Bag, A.; Bhattacharyya, S.K.; Chattopadhyay, R.R. The development of *Terminalia chebula* Retz. (Combretaceae) in clinical research. *Asian Pac. J. Trop. Biomed.* 2013, 3, 244–252, doi:10.1016/S2221-1691(13)60059-3.

97. Ćurko, N.; Tomašević, M.; Bubalo, M.C.; Gracin, L.; Redovniković, I.R.; Ganić, K.K. Extraction of proanthocyanidins and anthocyanins from grape skin by using ionic liquids. *Food Technol. Biotechnol.* 2017, 55, 429–437, doi:10.17113/ftb.55.03.17.5200.

98. Caimari, A.; del Bas, J.M.; Crescenti, A.; Arola, L. Low doses of grape seed procyanidins reduce adiposity and improve the plasma lipid profile in hamsters. *Int. J. Obes.* 2013, 37, 576–583, doi:10.1038/ijo.2012.75.

99. Zhou, F.; Yin, M.; Liu, Y.; Han, X.; Guo, J.; Ren, C.; Wang, W.; Huang, W.; Zhan, J.; You, Y. Grape seed flour intake decreases adiposity gain in high-fat-diet induced obese mice by activating thermogenesis. *J. Funct. Foods* 2019, 62, 103509, doi:10.1016/j.jff.2019.103509.

100. Griffin, L.E.; Witrick, K.A.; Klotz, C.; Dorenkott, M.R.; Goodrich, K.M.; Fundaro, G.; McMillan, R.P.; Hulver, M.W.; Ponder, M.A.; Neilson, A.P. Alterations to metabolically active bacteria in the mucosa of the small intestine predict anti-obesity and anti-diabetic activities of grape seed extract in mice. *Food Funct.* 2017, 8, 3510–3522, doi:10.1039/C7FO01236E.

101. Cardullo, N.; Muccilli, V.; Saletti, R.; Giovanio, S.; Tringali, C. A mass spectrometry and 1H NMR study of hypoglycemic and antioxidant principles from a *Castanea sativa* tannin employed in oenology. *Food Chem.* 2018, 268, 585–593, doi:10.1016/j.foodchem.2018.06.117.
Foods 2021, 10, 251

Senthilkumar, G.P.; Subramanian, S.P. Biochemical studies on the effect of Terminalia chebula on the levels of glycoproteins in streptozotocin-induced experimental diabetes in rats. J. Appl. Biomed. 2008, 6, 105–115, doi:10.3272/jab.2008.01.04.

Turck, D.; Bresson, J.; Burlingame, B.; Dean, T.; Fairweather-Tait, S.; Heinonen, M.; Hirsch-Ernst, K.J.; Mangelsdorf, I.; Mc Ardle, H.J.; Naska, A.; et al. Safety of Ecklonia cava phlorotannins as a novel food pursuant to Regulation (EC) No 258/97. EFSA J. 2017, 15, doi:10.2903/j.efsa.2017.5003.

Li, Y.; Qian, Z.J.; Ryu, B.M.; Lee, S.H.; Kim, M.M.; Kim, S.K. Chemical components and its antioxidant properties in vitro: An edible marine brown alga, Ecklonia cava. Bioorg. Med. Chem. 2009, 17, 1963–1973, doi:10.1016/j.bmc.2009.01.031.

Kim, S.K.; Lee, D.Y.; Jung, W.K.; Kim, J.H.; Choi, I.; Park, S.G.; Seo, S.K.; Lee, S.W.; Lee, C.M.; Yea, S.S.; et al. Effects of Ecklonia cava ethanol extract on airway hyperresponsiveness and inflammation in a murine asthma model: Role of suppressor of cytokine signaling. Biomed. Pharmacother. 2008, 62, 289–296, doi:10.1016/j.biopha.2007.07.009.

Kang, M.C.; Ahn, G.; Yang, X.; Kim, K.N.; Kang, S.M.; Lee, S.H.; Ko, S.C.; Ko, J.Y.; Kim, D.; Kim, Y.T.; et al. Hepatoprotective effects of dieckol-rich phlorotannins from Ecklonia cava, a brown seaweed, against ethanol induced liver damage in BALB/c mice. Food Chem. Toxicol. 2012, 50, 1986–1991, doi:10.1016/j.fct.2012.03.078.

Roy, M.C.; Anguenot, R.; Fillion, C.; Beaulieu, M.; Bérubé, J.; Richard, D. Effect of a commercially-available algal phlorotannins extract on digestive enzymes and carbohydrate absorption in vivo. Food Res. Int. 2011, 44, 3026–3029, doi:10.1016/j.foodres.2011.07.023.

Wang, T.; Li, Q.; Bi, K. Bioactive flavonoids in medicinal plants: Structure, activity and biological fate. Asian J. Pharm. Sci. 2018, 13, 12–23, doi:10.1016/j.ajps.2017.08.004.

Hooper, B.; Frazier, R. Polyphenols in the diet: Friend or foe? Nutr. Bull. 2012, 37, 297–308, doi:10.1111/j.1467-3010.2012.02001.x.

Duval, A.; Avérous, L. Characterization and Physicochemical Properties of Condensed Tannins from Acacia catechu. J. Agric. Food Chem. 2016, 64, 1751–1760, doi:10.1021/acs.jafc.5b05671.

Ogawa, S.; Yazaki, Y. Tannins from Acacia mearnsii De Wild. Bark: Tannin determination and biological activities. Molecules 2018, 23, 837.

Crestini, C.; Lange, H.; Bianchetti, G. Detailed Chemical Composition of Condensed Tannins via Quantitative 31P NMR and HSQC Analyses: Acacia catechu, Schinopsis balansae, and Acacia mearnsii. J. Nat. Prod. 2016, 79, 2287–2295, doi:10.1021/acs.jnatprod.6b00380.

Elgailani, I.E.H.; Ishak, C.Y. Determination of Tannins of Three Common Acacia Species of Sudan. Adv. Chem. 2014, 2014, 192708, doi:10.1155/2014/192708.

Julkunen-Tiitto, R.; Sorsa, S. Testing the effects of drying methods on willow flavonoids, tannins, and salicylates. J. Chem. Ecol. 2001, 27, 779–789, doi:10.1023/A:1010358120482.

Yamaji, K.; Julkunen-Tiitto, R.; Rousi, M.; Freiwald, V.; Oksanen, E. Ozone exposure over two growing seasons alters root-to-shoot ratio and chemical composition of birch (Betula pendula Roth). Glob. Chang. Biol. 2003, 9, 1363–1377, doi:10.1046/j.1365-2486.2003.00669.x.

Barretra, J.C.M.; Ferreira, I.C.F.R.; Oliveira, M.B.P.P. Bioactive Compounds of Chestnut (Castanea sativa Mill.) BT; In Bioactive Compounds in Underutilized Fruits and Nuts; Murthy, H.N., Bapat, V.A., Eds.; Springer International Publishing: Cham, Switzerland, 2020; pp. 303–315. ISBN 978-3-030-31082-8.

Chiariini, A.; Micucci, M.; Malaguti, M.; Budriesi, R.; Ioan, P.; Lenzi, M.; Fimognari, C.; Gallina Toschi, T.; Comandini, P.; Hrelia, S. Sweet Chestnut (Castanea sativa Mill.) Bark Extract: Cardiovascular Activity and Myocyte Protection against Oxidative Damage. Oxidative Med. Cell. Longev. 2013, 47190, doi:10.1155/2013/47190.

Esposito, T.; Celano, R.; Pane, C.; Piccinelli, A.L.; Sansone, F.; Picerno, P.; Zaccardelli, M.; Aquino, R.P.; Mencherini, T. Chestnut (Castanea sativa Miller.) Burs Extracts and Functional Compounds: UHPLC-UV-HRMS Profiling, Antioxidant Activity, and Inhibitory Effects on Phytopathogenic Fungi. Molecules 2019, 24, 3020, doi:10.3390/molecules24202032.

Lee, J.H.; Ko, J.Y.; Oh, J.Y.; Kim, C.Y.; Lee, H.J.; Kim, J.; Jeon, Y.J. Preparative isolation and purification of phlorotannins from Ecklonia cava using centrifugal partition chromatography by one-step. Food Chem. 2014, 158, 433–437, doi:10.1016/j.foodchem.2014.02.112.

Hedqvist, H.; Mueller-Harvey, I.; Reed, J.D.; Krueger, C.G.; Murphy, M. Characterisation of tannins and in vitro protein digestibility of several Lotus corniculatus varieties. Anim. Feed Sci. Technol. 2000, 87, 41–56, doi:10.1016/S0377-8401(00)00178-4.

Behrens, A.; Maie, N.; Knicker, H.; Kögel-Knabner, I. MALDI-TOF mass spectrometry and PSD fragmentation as means for the analysis of condensed tannins in plant leaves and needles. Phytochemistry 2003, 62, 1159–1170, doi:10.1016/S0031-9422(02)00660-X.

Bianchi, S.; Gloess, A.N.; Kroslakova, I.; Mayer, I.; Pichelin, F. Analysis of the structure of condensed tannins in water extracts from bark tissues of Norway spruce (Picea abies [Karst.] and Silver fir (Abies alba [Mill.]) using MALDI-TOF mass spectrometry. Ind. Crops Prod. 2014, 61, 430–437, doi:10.1016/j.indcrop.2014.07.038.

Sulaiman, T.; Kakakhan, H.; Sijam, K. Antifungal effects of Rhus coriaria L. fruit extracts against tomato anthracnose caused by Colletotrichum acutatum. Ind. Crops Prod. 2013, 113, 391–397, doi:10.1016/j.indcrop.2018.01.066.

Monforte, M.T.; Smeriglio, A.; Germano, M.P.; Pergolizzi, S.; Circosta, C.; Galati, E.M. Evaluation of antioxidant, antiinflammatory, and gastroprotective properties of Rubus fruticosus L. fruit juice. Phyther. Res. 2018, 32, 1404–1414, doi:10.1002/ptr.6078.

Vu, T.T.; Kim, H.; Tran, V.K.; Vu, H.D.; Hoang, T.X.; Han, J.W.; Choi, Y.H.; Jang, K.S.; Choi, G.J.; Kim, J. Antibacterial activity of tannins isolated from Sapium baccatum extract and use for control of tomato bacterial wilt. PLoS ONE 2017, 12, e0181499, doi:10.1371/journal.pone.0181499.
126. Isaza Martínez, J.H.; Torres Castañeda, H.G. Preparation and chromatographic analysis of phlorotannins. *J. Chromatogr. Sci.* 2013, 51, 825–838, doi:10.1093/chromsci/bmt045.

127. Vivas, N.; Nonier, M.F.; De Gaulejac, N.V.; Absalon, C.; Bertrand, A.; Mirabel, M. Differentiation of proanthocyanidin tannins from seeds, skins and stems of grapes (*Vitis vinifera*) and heartwood of Quebracho (*Schinopsis balansae*) by matrix-assisted laser desorption/ionization time-of-flight mass spectrometry and thiacoaldehyde/liquid c. *Anal. Chim. Acta* 2004, 513, 247–256, doi:10.1016/j.aca.2003.11.085.

128. Pfundstein, B.; El Desouky, S.K.; Hull, W.E.; Haubner, R.; Erben, G.; Owen, R.W. Polyphenolic compounds in the fruits of Egyptian medicinal plants (*Terminalia bellerica, Terminalia chebula* and *Terminalia horsid*): Characterization, quantitation and determination of antioxidant capacities. *Phytochemistry* 2010, 71, 1132–1148, doi:10.1016/j.phytochem.2010.03.018.

129. Kyraeleou, M.; Kallithraka, S.; Theodorou, N.; Teisseder, P.-L.; Kotseridis, Y.; Koundouras, S. Changes in Tannin Composition of Syrah Grape Skins and Seeds during Fruit Ripening under Contrasting Water Conditions. *Molecules* 2017, 22, 1453, doi:10.3390/molecules22091453.

130. Ricci, A.; Parpinello, G.P.; Palma, A.S.; Teslić, N.; Brilli, C.; Pizzi, A.; Versari, A. Analytical profiling of food-grade extracts from grape (*Vitis vinifera* sp.) seeds and skins, green tea (*Camellia sinensis*) leaves and Limousin oak (*Quercus robur*) heartwood using MALDI-TOF-MS, ICP-MS and spectrophotometric methods. *J. Food Compos. Anal.* 2017, 59, 95–104, doi:10.1016/j.jfca.2017.01.014.

131. Stark, S.; Julkunen-Tiitto, R.; Holappa, E.; Mikkola, K.; Nikula, A. Concentrations of foliar quercetin in natural populations of white birch (*Betula pubescens*) increase with latitude. *J. Chem. Ecol.* 2008, 34, 1382–1391, doi:10.1007/s10886-008-9554-8.

132. Malayaman, V.; Sisubalan, N.; Senthilkumar, R.P.; Sheikh Mohamed, S.; Ranjithkumar, R.; Ghous Basha, M. Chitosan mediated enhancement of hydrolysable tannin in *Phyllanthus debilis* Klein ex Willd via plant cell suspension culture. *Int. J. Biol. Macromol.* 2017, 104, 1656–1663, doi:10.1016/j.ijbiomac.2017.03.138.

133. Sprenger, F.; Cass, Q.B. Characterization of four *Phyllanthus* species using liquid chromatography coupled to tandem mass spectrometry. *J. Chromatogr. A* 2013, 1291, 97–103, doi:10.1016/j.chroma.2013.03.030.

134. Cechinel, V.; Moreira, J.; Klein-ju, L.C. Anti-hyperalgesic activity of corilagin, a tannin isolated from *Phyllanthus niruri* L. (*Eu- phorbiaceae*). 2013, 146, 318–323, doi:10.1016/j.jep.2012.02.052.

135. Ram, J.; Tripathi, P.; Sharma, V.; Singh, N.; Kumar, V. *Phyllanthus amarus*: Ethnomedicinal uses, phytochemistry and pharmacology. A review. *J. Ethnopharmacol.* 2011, 138, 286–313, doi:10.1016/j.jep.2011.09.040.

136. Fawzi, M.; Yerlikaya, S.; Llorent-prat, E.J.; Uğurlu, A. Pharmacological and polyphenolic profiles of *Phyllanthus phillyreifolius* var. commersonii Müll. Arg: An unexplored endemic species from Mauritius. *Food Res. Int.* 2019, 115, 425–438, doi:10.1016/j.foodres.2018.10.075.

137. Rodríguez-pérez, C.; Quirantes-piné, R.; Amessis-ouchemoukh, N.; Madani, K. Journal of Pharmaceutical and Biomedical Analysis A metabolite-profiling approach allows the identification of new compounds from *Pistacia lentiscus* leaves. *J. Pharm. Biomed. Anal.* 2013, 77, 167–174, doi:10.1016/j.jpba.2013.01.026.

138. Marchelak, A.; Owczarek, A.; Matczak, M.; Pawłak, A.; Kolodziejczyk-Czepas, J.; Nowak, P.; Olszewska, M.A. Bioactivity Potential of *Prunus spinosa* L. Flower Extracts: Phytochemical Profiling, Cellular Safety, Pro-inflammatory Enzymes Inhibition and Protective Effects Against Oxidative Stress In Vitro. *Front. Pharmacol.* 2017, 8, 680.

139. König, M.; Scholz, E.; Hartmann, R.; Lehmann, W.; Rimpler, H. Ellagitannins and complex tannins from *Quercus petraea* bark. *J. Nat. Prod.* 1994, 57, 1411–1415, doi:10.1021/np00112a010.

140. Park, M.; Cho, H.; Jung, H.; Lee, H.; Hwang, K.T. Antioxidant and anti-inflammatory activities of tannin fraction of the extract from black raspberry seeds compared to grape seeds. *J. Food Biochem.* 2014, 38, 259–270, doi:10.1111/jfbc.12044.

141. Kowalska, K.; Olejnik, A.; Zielinska-Wasielica, J.; Olkowicz, M. Raspberry (*Rubus idaeus* L.) fruit extract decreases oxidation markers, improves lipid metabolism and reduces adipose tissue inflammation in hypertrophied 3T3-L1 adipocytes. *J. Funct. Foods* 2019, 62, 103568, doi:10.1016/j.jff.2019.103568.

142. Elhouchet, Z.B.; Autour, M.S.; Iyamoto, T.M.; Ubois, M.L.A. Steroidal Saponins from the Roots of *Smilax aspera* subsp. *mauritanica*. *Chem. Pharm. Bull.* 2008, 56, 1324–1327.

143. Harumi, J.; Fernandes, A.; Calhelha, R.C.; José, M.; Dias, F.; Barros, L.; Amaral, J.S.; Ferreira, I.C.F.R. Nutritional composition and bioactivity of Umbilicus rupes-tris (Salisb.) Dandy: An underexploited edible wild plant. *Food Chem.* 2019, 295, 341–349, doi:10.1016/j.foodchem.2019.05.139.

144. Rubanza, C.D.K.; Shem, M.N.; Otisyna, R.; Bakengesa, S.S.; Ichinohe, T.; Fujihara, T. Polyphenolics and tannins effect on in vitro digestibility of selected Acacia species leaves. *Anim. Feed. Sci. Technol.* 2005, 119, 129–142, doi:10.1016/j.anifeedsci.2004.12.004.

145. Kardel, M.; Taube, F.; Schulz, H.; Schütze, W.; Giers, M. Different approaches to evaluate tannin content and structure of selected plant extracts—Review and new aspects. *Appl. Bot. Food Qual.* 2013, 86, 154–166.

146. Comandini, P.; Lerma-García, M.J.; Simó-Alfonso, E.F.; Toschi, T.G. Tannin analysis of chestnut bark samples (*Castanea sativa* Mill.) by HPLC-DAD–MS, *J. Food Chem.* 2014, 570, 295–297, doi:10.1016/j.foodchem.2014.02.003.

147. Sanz, M.; Cadahia, E.; Estebuelas, E.; Muñoz, A.M.; De Simón, B.F.; Hernández, T.; Estrella, I. Phenolic compounds in chestnut (*Castanea sativa* Mill.) heartwood. Effect of toasting at cooperage. *J. Agric. Food Chem.* 2010, 58, 9631–9640, doi:10.1021/jf102718t.

148. Chowdhury, M.T.H.; Bangoura, I.; Kang, J.Y.; Park, N.G.; Ahn, D.H.; Hong, Y.K. Distribution of phlorotannins in the brown alga Ecklonia cava and comparison of pretreatments for extraction. *Fish. Aquat. Sci.* 2011, 14, 198–204, doi:10.5657/FAS.2011.0198.

149. Waghorn, G.C.; Tavernale, M.H.; Woodfield, D.R. Methanogenesis from forages fed to sheep. *Proc. N. Z. Grassl. Assoc.* 2002, 167–171, doi:10.3384/jnzg.2002.64.2462.
150. Pawelek, D.L.; Muir, J.P.; Lambert, B.D.; Wittie, R.D. In sacco rumen disappearance of condensed tannins, fiber, and nitrogen from herbaceous native Texas legumes in goats. *Anim. Feed Sci. Technol.* 2008, 142, 1–16.

151. Häring, D.A.; Suter, D.; Amrhein, N.; Lüscher, A. Biomass allocation is an important determinant of the tannin concentration in growing plants. *Ann. Bot.* 2007, 99, 111–120, doi:10.1093/aob/mcl227.

152. Decandia, M.; Sitzia, M.; Cabiddu, A.; Kababja, D.; Molle, G. The use of polyethylene glycol to reduce the anti-nutritional effects of tannins in goats fed woody species. *Small Rumin. Res.* 2000, 38, 157–164, doi:10.1016/S0921-4488(00)00145-0.

153. Ersan, S.; Güçlü Üstündag, Ö.; Carle, R.; Schweiggert, R.M. Subcritical water extraction of phenolic and antioxidant constituents from pistachio (*Pistacia vera L.*) hulls. *Food Chem. 2013*, 253, 46–54, doi:10.1016/j.foodchem.2018.01.116.

154. Song, W.; Qin, S.-T.; Fang, F.-X.; Gao, Z.-J.; Liang, D.-D.; Liu, L.-L.; Tian, H.-T.; Yang, H.-B. Isolation and purification of condensed tannin from the leaves and branches of Prunus cerasifera and its structure and bioactivities. *Appl. Biochem. Biotechnol.* 2018, 185, 464–475.

155. Cao, J.; Jiang, Q.; Lin, J.; Li, X.; Sun, C.; Chen, K. Physicochemical characterisation of four cherry species (*Prunus spp.*) grown in China. *Food Chem.* 2015, 173, 855–863.

156. Elfalleh, W. Total phenolic contents and antioxidant activities of pomegranate peel, seed, leaf and flower. *J. Med. Plants Res.* 2012, 6, 4724–4730, doi:10.5897/JMPR11.995.

157. Cadahia, E.; Varea, S.; Muñoz, L.; de Simón, B.F.; García-Vallejo, M.C. Evolution of Ellagitannins in Spanish, French, and American Oak Woods during Natural Seasoning and Toasting. *J. Agric. Food Chem.* 2001, 49, 3677–3684, doi:10.1021/jf010288r.

158. De Simón, B.F.; Cadahía, E.; del Alamo, M.; Nevaro, I. Effect of size, seasoning and toasting in the volatile compounds in toasted oak wood and in a red wine treated with them. *Anal. Chim. Acta* 2010, 660, 211–220, doi:10.1016/j.aca.2009.09.031.

159. Tian, F.; Li, B.; Ji, B.; Yang, J.; Zhang, G.; Chen, Y.; Luo, Y. Antioxidant and antimicrobial activities of consecutive extracts from Galla chinensis. The polarity affects the bioactivities. *Food Chem.* 2009, 113, 173–179, doi:10.1016/j.foodchem.2008.07.062.

160. Tohma, H.; Altay, A.; Köksal, E.; Gören, A.C.; Gülcin, I. Measurement of anticancer, anti-diabetic and anti-cholinergic properties of sumac (*Rhus coriaria*): Analysis of its phenolic compounds by LC–MS/MS. *J. Food Meas. Charact.* 2019, 13, 1607–1619, doi:10.1007/s11694-019-00779-9.

161. Saraiva, A.M.; Castro, R.H.A.; Cordeiro, R.P.; Peixoto Sobrinho, T.J.S.; Castro, V.T.N.A.; Xavier, H.S.; Pisciotano, M.N.C. In vitro evaluation of antioxidant, antimicrobial and toxicity properties of extracts of Schinus brasiliensis engl. (*Anacardiaceae*). *Afri. J. Pharm. Pharmacol.* 2011, 5, 1724–1731, doi:10.5897/AJPP11.428.

162. Travaglia, F.; Bordiga, M.; Locatelli, M.; Coisson, J.D.; Arlorio, M. Polymeric Proanthocyanidins in Skins and Seeds of 37 Vitis vinifera L. Cultivars: A Methodological Comparative Study. *J. Food Sci.* 2011, 76, 742–749, doi:10.1111/j.1750-3841.2011.02194.x.

163. Schofield, P.; Mbugua, D.; Pell, A. Analysis of condensed tannins: A review. *Anim. Feed Sci. Technol.* 2001, 91, 21–40, doi:10.1016/S0377-8401(01)00228-0.

164. Giner-Chavez, B.I.; Van Soest, P.J.; Robertson, J.B.; Lascano, C.; Pell, A.N. Comparison of the Precipitation of Alfalfa Leaf Protein and Bovine Serum Albumin by Tannins in the Radial Diffusion Method. *J. Sci. Food Agric.* 1997, 74, 513–523, doi:10.1002/(SICI)1097-0010(199705)74:4<513::AID-JSFA825>3.0.CO;2-B.

165. Fagundes, G.M.; Benetel, G.; Santos, K.C.; Welter, K.C.; Melo, F.A.; Muir, J.P.; Bueno, I.C.S. Tannin-rich plants as natural manipulators of rumen fermentation in the livestock industry. *Molecules* 2020, 25, 2943, doi:10.3390/molecules25122943.

166. McAllister, T.A.; Martínez, T.; Bae, H.D.; Muir, A.D.; Yanke, L.J.; Jones, G.A. Characterization of Condensed Tannins Purified From Legume Forages: Chromophore Production, Protein Precipitation, and Inhibitory Effects on Cellulose Digestion. *J. Chem. Ecol.* 2005, 31, 2049–2068, doi:10.1007/s10886-005-6077-4.

167. Landete, J.M. Ellagitannins, ellagic acid and their derived metabolites: A review about source, metabolism, functions and health. *Food Res. Int.* 2011, 44, 1150–1160, doi:10.1016/j.foodres.2011.04.027.

168. Martínez, K.B.; Mackert, J.D.; McIntosh, M.K. Chapter 18—Polyphenols and Intestinal Health. In *Nutrition and Functional Foods for Healthy Aging*; Watson, R.R., Ed.; Academic Press: Cambridge, MA, USA, 2017, pp. 191–210, ISBN 978-0-12-805376-8.

169. Arnott, J.A.; Planey, S.L. The influence of lipophilicity in drug discovery and design. *Expert Opin. Drug Discov.* 2012, 7, 863–875, doi:10.1517/17464412.2011.714363.

170. Appeldoorn, M.M.; Vincken, J.-P.; Gruppen, H.; Hollman, P.C.H. Procyanidin dimers A1, A2, and B2 are absorbed without conjugation or methylation from the small intestine of rats. *J. Nutr.* 2009, 139, 1469–1473, doi:10.3945/jn.109.106756.

171. Li, S.; Li, J.; Sun, Y.; Huang, Y.; He, J.; Zhu, Z. Transport of Flavanolic Monomers and Procyanidin Dimer A2 across Human Adenocarcinoma Stomach Cells (MKN-28). *J. Agric. Food Chem.* 2019, 67, 3354–3362, doi:10.1021/acs.jafc.9b00378.

172. Espín, J.C.; González-Barrio, R.; Cerdá, B.; López-Bote, C.; Rey, A.I.; Tomás-Barberán, F.A. Iberian pig as a model to clarify obscure points in the bioavailability and metabolism of ellagitannins in humans. *J. Agric. Food Chem.* 2007, 55, 10476–10485, doi:10.1021/jf0723864.

173. González-Barrio, R.; Borges, G.; Mullen, W.; Crozier, A. Bioavailability of anthocyanins and ellagitannins following consumption of raspberries by healthy humans and subjects with an ileostomy. *J. Agric. Food Chem.* 2010, 58, 3933–3939, doi:10.1021/jf100315d.

174. Cerdá, B.; Periago, P.; Espín, J.C.; Tomás-Barberán, F.A. Identification of urolithin A as a metabolite produced by human colon microflora from ellagic acid and related compounds. *J. Agric. Food Chem.* 2005, 53, 5571–5576, doi:10.1021/jf050384i.

175. Borges, G.; Ottaviani, I.L.; van der Hoolt, J.J.; Schroeter, H.; Crozier, A. Absorption, metabolism, distribution and excretion of (−)-epicatechin: A review of recent findings. *Mol. Asp. Med.* 2018, 61, 18–30, doi:10.1016/j.mam.2017.11.002.
176. Huang, W.; Niu, H.; Xue, X.; Li, J.; Li, C. Robinetinidol-(4β→8)-epigallocatechin 3-O-gallate, A Galloyl Dimer Prorobinetinidin From Acacia Mearnsii De Wild, Effectively Protects Human Neuroblastoma SH-SY5Y Cells Against Acrolein-Induced Oxidative Damage. J. Alzheimer’s Dis. 2010, 21, 493–506, doi:10.3233/JAD-2010-090886.

177. Dudzinska, D.; Bednarska, K.; Bonczer, M.; Luzak, B.; Watala, C. The influence of Rubus idaeus and Rubus caesius leaf extracts on platelet aggregation in whole blood. Cross-talk of platelets and neutrophils. Platelets 2016, 27, 433–439, doi:10.3109/09537104.2015.1131254.

178. Mirazi, N.; Hosseini, A. Attenuating properties of Rubus fruticosus L. on oxidative damage and inflammatory response following streptozotocin-induced diabetes in the male Wistar rats. J. Diabetes Metab. Disord. 2020, doi:10.1007/s40200-020-00649-3.

179. Tonin, T.D.; Thiesen, L.C.; de Oliveira Nunes, M.L.; Broering, M.F.; Donato, M.P.; Goss, M.J.; Petreanu, M.; Niero, R.; Machado, I.D.; Santin, J.R. Rubus imperialis (Rosaceae) extract and pure compound nigamigchoside F1: Wound healing and anti-inflammatory effects. Naunyn. Schmiedebergs. Arch. Pharmacol. 2016, 389, 1235–1244, doi:10.1007/s00210-016-1285-8.

180. Martini, S.; D’Addario, C.; Colacevich, A.; Focardi, S.; Borghini, F.; Santucci, A.; Figura, N.; Rossi, C. Antimicrobial activity against Helicobacter pylori strains and antioxidant properties of blackberry leaves (Rubus ulmifolius) and isolated compounds. Int. J. Antimicrob. Agents 2009, 34, 50–59, doi:10.1016/j.ijantimicag.2009.01.010.

181. Hajaji, S.; Jabri, M.A.; Sifaoui, I.; López-Arencibia, A.; Reyes-Battle, M.; B’chir, F.; Valladares, B.; Pinero, J.E.; Lorenzo-Morales, J.; Akkari, H. Amoebicidal, antimicrobial and in vitro ROS scavenging activities of Tunisian Rubus ulmifolius Schott, methanolic extract. Exp. Parasitol. 2017, 183, 224–230, doi:10.1016/j.exppara.2017.09.013.

182. Sisti, M.; De Santi, M.; Fraternale, D.; Ninfali, P.; Scoccianti, V.; Brandi, G. Antifungal activity of Rubus ulmifolius Schott standardized in vitro culture. LWT Food Sci. Technol. 2008, 41, 946–950, doi:10.1016/j.lwt.2007.05.012.

183. Gabr, S.A.; Alghadir, A.H. Evaluation of the Biological Effects of Lyophilized Hydrophilic Extract of Rhus coriaria on Myeloperoxidase (MPO) Activity, Wound Healing, and Microbial Infections of Skin Wound Tissues. Evid.-Based Complement. Altern. Med. 2019, 2019, 5861537, doi:10.1155/2019/5861537.

184. El-Saber Batiha, G.; Magdy Beshbishy, A.; Stephen Adeyemi, O.; Hassan Nadwa, E.; kadry Mohamed Rashwan, E.; Alkazmi, L.M.; Elkelish, A.A.; Igarashi, I. Phytochemical Screening and Antiprotozoal Effects of the Methanolic Berberis vulgaris and Acetonic Rhus Coriaria Extracts. Molecules 2020, 25, 550, doi:10.3390/molecules25030550.

185. Matsumoto, K.; Yokoyama, S.I. Induction of uncoupling protein-1 and -3 in brown adipose tissue by kaki-tannin in type 2 diabetic NSY/Hos mice. Food Chem. Toxicol. 2012, 50, 184–190, doi:10.1016/j.fct.2011.10.067.

186. Chandrasekhar, Y.; Phani Kumar, G.; Navya, K.; Ramya, E.M.; Anilakumar, K.R. Tannins from Terminalia chebula fruits attenuates GABA antagonist-induced anxiety-like behaviour via modulation of neurotransmitters. J. Pharm. Pharmacol. 2018, 70, 1662–1674, doi:10.1111/jphp.13007.