Continue



```
Tannins Tannins are a class of astringent, polyphenolic biomolecules that bind to and precipitate proteins and various other organic compounds including amino acids and alkaloids. The term tannin is widely applied to any large polyphenolic compounds including amino acids and alkaloids. The term tannin is widely applied to any large polyphenolic compounds including amino acids and alkaloids.
containing sufficient hydroxyls and other suitable groups to form strong complexes with various macromolecules. The tannin compounds are widely distributed in many species of plants, where they play a role in protection from predation (including as pesticides) and might help in regulating plant growth. The astringency from the tannins is what causes
the dry and puckery feeling in the mouth following the consumption of unripened fruit, red wine or tea. Likewise, the destruction or modification of tannins with time plays an important role when determining harvesting times. Tannins have molecular weights ranging from 500 to over 3,000 (gallic acid esters) and up to 20,000
(proanthocyanidins). Classification of tannins1. Hydrolysable tannins2. Condensed tannins3. Pseudotannins. Hydrolysable tannins are hydrolysable tannins are hydrolysable tannins are hydrolysable tannins are hydrolysable tannins.
 gallitannins and from that of ellagic acid are known as gallitannins. The gallic acid is found in rhubarb, clove and ellagic acid is found in eucalyptus leave and myrobalans and pomegranate bark. These tannins treated with ferric chloride to produced blue or black colour. 2. Condensed tannins: These tannins are resistant to hydrolysis and they derived from
the flavonols, catechins and flavan-3, 4-diols.On treatment with acids or enzymes they are decomposed into phlobaphenes. On dry distillation condensed tannins are found in cinchona bark, male fern, areca seeds, tea leaves and wild cherry bark, bahera fruits, Amla, etc. they
produce green colour with ferric chlorides. 3. Pseudotannins: They are phenolic compounds of lower molecular weight and do not show the goldbeater's test. They are found in catechu and nux-vomica properties of tannins: Tannins are
freely soluble in water, alcohol, glycerol, and acetone and dilute alkalies. They are precipitate with iron compounds. They are precipitate with iron compounds are precipitated by number of metallic salts are precipitated by number of me
sub acetate. They combine with skin and hide to form leather and with gelatin and isinglass to form an insoluble in water. Chemical tests of tannins: 1. Gelatin test: To a solution of gelatin and sodium chloride are added. A white buff coloured
precipitate is formed.2. Goldbeater's skin test: A small piece of goldbeater skin is soaked in 20% hydrochloric acid, ringed with distilled water and placed in a solution of ferrous sulphate. A brown or black colour is produced on the skin due presence of tannins. 3.
 Phenazone test: A mixture of aqueous extract of a drug and sodium acid phosphate is heated and cooled and filtered. A solution of phenazone is added to the filtrate. A bulky coloured precipitate is formed. 4. Match stick test (Catechin test): A match stick is dipped in aqueous plant extract, dried near burner and moistened with concentrated hydrochloric
acid. On warming near flame, the matchstick wood turns pink or red due to formation of phloroglucinol.5. Chlorogenic acid test:An extract of chlorogenic acid test:Sample solution and added vanillin- hydrochloric acid reagent
(Vanillin 1 gm, alcohol 10 ml, concentrated hydrochloric acid 10 ml). A pink or red colour is formed due to formation of phloroglucinol. Isolation of TanninsBoth hydrolysable and condensed tannins are highly soluble in water and alcohol but insoluble in organic solvents such as solvent ether, chloroform, and benzene. Tannin compounds can be easily
extracted by water or alcohol. The general method for the extraction of tannic acid from various galls is either with water-saturated ether, or with mixture of water, alcohol, and ether. In such cases, free acids such as Gallic and ellagic acid go along with ether while true tannin gets exracted in water. If the drug consists of chlorophyll or pigment, it may be
removed by ether. After extraction, the aqueous and ethereal layers are separately concentrated, dried, and subjected to further isolation and purification using various separation techniques of chromatographyMedicinal properties and usesTannins occur in crude drugs either as major active constituent as in oak bark, or as a subsidiary component as in
clove. In many cases, they synergistically increase the effectiveness of active principles. Tannins are medicinally significant due to their astringent properties. They promote rapid healing and the formation of new tissues on wounds as well as
inflammation of gums. Internally tannins are administered in cases of heavy metal poisoning as an antidote. Recently, these compounds have demonstrated their antiviral activities for treatment of viral diseases including AIDS. They are used as mordant in dyeing, manufacture of ink, sizing paper and silk, and for
printing fabrics. They are used along with gelatin and albumin for manufacture of imitation horn and tortoise shell. They are used for clarifying beer or wine, in photography or as a coagulant in rubber manufacture. They are used for the
manufacture of gallic acid and pyrogallol, and sometimes as a reagent in analytical chemistry. Award Abstract # 1120323 Hydrolyzable tannins are a group of plant polyphenolic compounds that act as chemical defenses against microbes, insects and vertebrate herbivores. Hydrolyzable tannins also
impact soil nutrient dynamics and affect the germination, growth and development of other plant species. Besides imparting astringent taste sensations, hydrolyzable tannins also enhance the nutritional quality of plant foods due to their antioxidant, anticancer and cardioprotective activities. Despite these important functions that hydrolyzable tannins play
in plants and humans, large and significant gaps remain in our understanding of the molecular and biochemical mechanisms underlying hydrolyzable tannin biosynthesis using strawberry and pomegranate as model systems. Cloning of hydrolyzable tannin biosynthesis using strawberry and pomegranate as model systems.
tannin biosynthetic genes will facilitate modification of plant composition for improved protein utilization in forage crops. Underpinning hydrolyzable tannin biogenesis will also broaden our understanding of plant defense mechanisms, as well as plant-soil and plant-plant (allelopathic) interactions. Broader Impacts In addition to the scientific impacts,
various aspects of the research will be used to provide multidisciplinary training opportunities, encompassing molecular biology, biochemistry, and cell biology, to high school, undergraduate encompassing molecular biology, biochemistry, and cell biology
opportunities to new UC Davis transfer students, promoting career access among women and underrepresented minority students from low-income families. Another major focus of the educational activities is to prepare graduate students and postdoctoral scholars for their future independent careers in science. An outreach
program is currently being developed to expose high school students to research activities and biotechnological applications through internships in the PI's laboratory. PUBLICATIONS PRODUCED AS A RESULT OF THIS RESEARCH Note: When clicking on a Digital Object Identifier (DOI) number, you will be taken to an external site maintained by the
 publisher. Some full text articles may not yet be available without a charge during the embargo (administrative interval). Some links on this page may take you to non-federal websites. Their policies may differ from this site. Ono, N.N., Britton, M.T., Fass, J.N., Nicolet, C.M., Lin, D.W. and Tian, L. "Exploring the transcriptome landscape of pomegranate
(Punica granatum) fruit peel for natural product biosynthetic gene and SSR marker discovery." Journal of Integrative Plant Science, v.180, 2011, p.800 Ono, N.N., Bandaranayake, P.G. and Tian, L. "Establishment of pomegranate (Punica granatum) fruit peel for natural product biosynthetic gene and SSR marker discovery." Journal of Integrative Plant Science, v.180, 2011, p.800 Ono, N.N., Bandaranayake, P.G. and Tian, L. "Establishment of pomegranate (Punica granatum) fruit peel for natural product biosynthetic gene and SSR marker discovery." Journal of Integrative Plant Science, v.180, v
granatum) hairy root cultures for genetic interrogation of the hydrolyzable tannin biosynthetic pathway." Planta, v.236, 2012, p.931-941 PROJECT OUTCOMES REPORT Disclaimer This Project Outcomes Report for the General Public is displayed verbatim as submitted by the Principal Investigator (PI) for this award. Any opinions, findings, and
conclusions or recommendations expressed in this Report are those of the PI and do not necessarily reflect the views of the National Science Foundation; NSF has not approved or endorsed its content. Plants synthesize specialized chemicals that play important roles in ensuring optimal plant growth and effective defense against pathogens and predators
healthy plants can provide abundant food and medicine for human nutrition and health, as well as biomass for biofuel production. Our investigations centered on understanding how a group of specialized chemicals named hydrolyzable tannins in
 animals and humans, there is a gap in our understanding of their production in plants, knowledge that is necessary for dissecting the mechanistic basis of their biological activities in mammals. Through our current research, we obtained genes involved in hydrolyzable tannin biosynthesis and demonstrated for the first time their functions in plants.
Isolation of hydrolyzable tannin biosynthetic genes provides critical molecular tools for modification of hydrolyzable tannin composition and content in plants with the goal of delineating cancer suppression mechanisms of these specialized chemicals in humans or improving protein utilization in forage crops for animal consumption. Elucidation of
hydrolyzable tannin biosynthesis will also broaden our understanding of general plant defense mechanisms, as well as plant-soil and plant-plant interactions. Various aspects of this research were used to provide multidisciplinary training opportunities, encompassing molecular biology, biochemistry and cell biology, to high school, undergraduate and
graduate students and postdoctoral researchers. In addition, we focused our educational activities on promoting graduate students and preparing graduate students and postdoctoral researchers for their future independent careers in science. The PI has also
 incorporated topics on phytonutrients and human health into her classroom curriculum and developed an outreach program that exposed high school students to research activities and biotechnological applications through internships in the PI's laboratory. Last Modified: 07/17/2015 Modified by: Li Tian Please report errors in award information by
 writing to: awardsearch@nsf.gov. The hydrolysable tannin family perhaps is the most fascinating group of tannins, since they show both structural simplicity and complexity within both monomeric and oligomeric forms Fig. 1. Examples of the structural simplicity and complexity within both monomeric and oligomeric forms Fig. 1. Examples of the structural simplicity and complexity within both monomeric and oligomeric forms Fig. 1.
of tannins are the hydrolysable tannins (HTs). HTs are first divided into three subclasses such as simple gallic acid derivatives contain five or less galloyl groups (Fig. 1) that are most commonly esterified to either glucose (monogalloyl and pentagalloyl glucoses in Fig. 1b, d) or quinic
acid (monogalloyl quinic acid in Fig. 1c). Gallic acid derivatives that contain six or more galloyl groups are defined as GTs and are further characterized by having one or more digalloyl groups (heptagalloyl groups are defined as GTs and are further characterized by having one or more digalloyl groups are defined as GTs and are further characterized by having one or more digalloyl groups (heptagalloyl groups are defined as GTs and are further characterized by having one or more digalloyl groups (heptagalloyl groups are defined as GTs and are further characterized by having one or more digalloyl groups (heptagalloyl groups are defined as GTs and are further characterized by having one or more digalloyl groups (heptagalloyl groups are defined as GTs and are further characterized by having one or more digalloyl groups (heptagalloyl groups are defined as GTs and are further characterized by having one or more digalloyl groups (heptagalloyl groups are defined as GTs and are further characterized by having one or more digalloyl groups (heptagalloyl groups are defined as GTs and are further characterized by having one or more digalloyl groups (heptagalloyl groups are defined as GTs and are further characterized by having one or more digalloyl groups (heptagalloyl groups are defined as GTs are much representation of the further characterized by having one or more digalloyl groups (heptagalloyl groups are defined as GTs are much representation of the further characterized by having one or more digalloyl groups (heptagalloyl groups are defined as GTs are much representation of the further characterized by having one or more digalloyl groups (heptagalloyl groups are defined as GTs are much representation of the further characterized by having one or more digalloyl groups (heptagalloyl groups are defined as GTs are much representation of the further characterized by having one or more digalloyl groups (heptagalloyl groups are defined as GTs are much representation of the further characterized by having one or more digallo
divided into six subgroups: hexahydroxydiphenoyl (HHDP) esters (Fig. 2b), dehydro-HHDP esters (Fig. 2c), and their modifications (Fig. 2d), nonahydroxytriphenoyl (NHTP) esters (Fig. 2e), flavonoellagitannins (Fig. 2d), nonahydroxytriphenoyl (NHTP) esters (Fig.
structures of the ellagitannin subgroups. Condensed tannins and hydrolysable tannins are two types of tannins are known as proanthocyanidins, are polymers of flavan-3-ols that are linked together. They are commonly found in fruits, such as grapes and berries, as well as in tea and cocoa. Condensed tannins are known
for their astringent taste and are responsible for the bitterness in some foods. On the other hand, hydrolysable tannins are esters of gallic acid and glucose. They are found in various plant parts, including bark, leaves, and fruits. Hydrolysable tannins are known for their antioxidant properties and are often used in traditional medicine. Unlike condensed
tannins, hydrolysable tannins can be easily hydrolyzed by acids or enzymes, releasing gallic acid and glucose. Overall, both types of tannins have distinct chemical structures and properties, contributing to their different roles in plants and potential applications in various industries. Tannins are a diverse group of plant secondary metabolites that play
important roles in various biological processes. They are widely distributed in nature and can be found in different parts of plants, such as leaves, bark, fruits, and seeds. Tannins are known for their ability to bind and precipitate proteins, which gives them astringent properties. They have been used for centuries in various industries, including leather
tanning, wine production, and traditional medicine. Condensed tannins are a type of tannin that are formed by the polymerization of flavan-3-ol monomers. They are commonly found in fruits, such as grapes, apples, and berries, as well as in the bark and wood of trees. Condensed tannins are
characterized by their ability to form insoluble complexes with proteins, which makes them effective in preventing protein degradation and inhibiting microbial growth. One of the key attributes of condensed tannins is their antioxidant activity. They have been shown to scavenge free radicals and protect cells from oxidative damage. This property is
believed to contribute to their health benefits, including their potential role in reducing the risk of cardiovascular diseases and certain types of cancer. Condensed tannins also have antimicrobial properties. They can inhibit the growth of various bacteria and fungi, making them useful in food preservation and as natural alternatives to synthetic
antimicrobial agents. Additionally, condensed tannins have been found to have anti-inflammatory effects, which may be beneficial in the treatment of inflammatory diseases. Furthermore, condensed tannins have been shown to have positive effects on animal nutrition. They can improve the digestibility of proteins and carbohydrates, enhance the absorption
of minerals, and reduce the risk of gastrointestinal disorders in livestock. These properties make condensed tannins valuable in animal feed formulations. However, condensed tannins can also have negative effects. In some cases, they can bind to dietary proteins and reduce their bioavailability, leading to potential nutrient deficiencies. Additionally, high
 levels of condensed tannins in certain plants can impart a bitter taste, which may limit their use in food and beverage applications. Hydrolysable Tannins and gallotannins, are another type of tannin that are formed by the esterification of gallic acid or ellagic acid with a sugar molecule. They are commonly
 implicated in various diseases, including cancer, cardiovascular diseases, and neurodegenerative disorders. Hydrolysable tannins have been extensively studied for their potential anticancer properties, which may contribute to their health benefits. Hydrolysable tannins have been extensively studied for their potential anticancer properties. They have been shown to inhibit the growth of
cancer cells, induce apoptosis (programmed cell death), and inhibit angiogenesis (the formation of new blood vessels). These effects are believed to be mediated by their antioxidant and anti-inflammatory activities, as well as their ability to modulate signaling pathways involved in cell proliferation and survival. Furthermore, hydrolysable tannins have been
found to have antimicrobial properties. They can inhibit the growth of various bacteria and fungi, making them useful in the treatment of infections. Hydrolysable tannins can also have negative effects. In some cases, they can form
complexes with dietary proteins and reduce their digestibility, leading to potential nutrient deficiencies. Additionally, high levels of hydrolysable tannins and hydrolysable tannins are two distinct types of tannins with
different chemical structures and properties. While both types of tannins exhibit antioxidant, antimicrobial, and anti-inflammatory activities, they also have some unique attributes. Condensed tannins are known for their ability to form insoluble complexes with proteins, which makes them effective in preventing protein degradation and inhibiting microbial
 have negative effects, such as reducing the bioavailability of dietary proteins and imparting a bitter taste. Further research is needed to fully understand the mechanisms of action and potential applications of these tannins in various fields, including medicine, food science, and agriculture. Comparisons may contain inaccurate information about people
 places, or facts. Please report any issues. Tannins are non-nitrogenous organic compounds with astringent properties. They are a large group of compounds with free phenolic groups in multiple units. They form a colloidal solution in water. They are soluble in water
 alkali, alcohol, and glycerin. Tannins are partially soluble in ethyl acetate. They are soluble in acetate but insoluble in other organic solvents Tannins can bind to protein to heartwood and bark. They are classified into two groups, based on the
 tanning test or Goldbeater's test. Tannins can combine with animal hides and are detected by their ability to absorb standard hide powder. This process is called true tanning and those who fail the test are called pseudotannins. High molecular
 weight compounds such as polyphenols are true tannins. These true tannins are classified based on its hydrolysable tannins are classified based on its hydrolysable tannins are hydrolysable tannins are classified based on its hydrolysable tannins are classified by the classified based on its hydrolysable tannins are classified by the classified based on its hydrolysable tannins.
known as pyrogallol tannins, as the phenolic acids are converted into pyrogallol derivatives on dry distillation. They are water-soluble, and the solution turns blue with ferric chloride. Hydrolysable tannins mainly contain polyphenolic acids like gallic acid, etc., which bond through ester linkages to a glucose molecule. They can be further
classified based on the phenolic acids formed after hydrolysis. Gallotannins that are non-hydrolysable by mineral acids or enzymes. They are also called proanthocyanidins. Compounds with condensed tannins containing cont
 phenolic nuclei are related to flavonoids. They can form more complex tannins with proteins and carbohydrates. On treatment with enzymes or mineral acids, these non-hydrolysable tannins produce insoluble red-colored phlobaphenes due to the polymerization reaction. These are characteristics of drugs like cinchona, cherry bark, etc. Condensed tannins
are soluble in water and the solution turns green colored with ferric chloride. Catechin is flavan-3, 4-diol. Non-hydrolysable tannins are commonly seen in plants of families Rosaceae, Leguminosae, Rubiaeae, Geraniaceae, Combretaceae, etc. Pseudo tannins are simple, phenolic tannins having low
molecular weight. They do not respond to Goldbeater's skin test. They are found in dead tissues and dying cells. Eg. Chlorogenic acid, gallic acids, catechin, etc. Tannins are extracted using water or alcohol since they are soluble in these solvents. They are insoluble in all other organic solvents such as benzene, ether, or chloroform. Water-saturated
ether is used to extract tannic acid from all galls. A mixture of water, ether, and alcohol may also be used. When the mixture of all three solvents is used, free acids like ellagic and gallic acids go along with ether while the true tannins go with water. Ether removes chlorophyll content as well. After extraction, the ethereal and aqueous layers are
separated, concentrated, dried, and subjected to filtration to purify tannins. Isolation of tannins from plants can be done using different methods. Solvent extraction uses an appropriate solvent and the dried plant powder is mixed in. The solution is allowed to sit for a while and the tannins are extracted through osmosis. Decoction method uses a heat
source to extract tannins from the solvent. The heat is usually 100°C and then it is allowed to cool down before filtering it. Pressurized water extraction uses static or dynamic water pressure to extract tannins from the solvent. Ultrasound method uses sound waves to destroy plant structures and yield tannins. Microwave-assisted extraction as the name
suggests uses a microwave as the heat source. Infrared-assisted extraction uses ionic solution to soak the material and is heated in a microwave. Infrared-assisted extraction subjects the solvent-dissolved
 tannins to Co-60 gamma radiation Enzyme-assisted extraction uses cellulase enzymes in sea plants that have higher cost. Shah, Biren N,
Avinash Seth. (2010). Textbook of Pharmacognosy and Phytochemistry. Elsevier. Tannins: Extraction from Plants. DOI: 10.5772/intechopen.86040 As a library, NLM provides access to scientific literature. Inclusion in an NLM database does not imply endorsement of, or agreement with, the contents by NLM or the National Institutes of Health. Learn
more: PMC Disclaimer | PMC Copyright Notice . 2016 Oct 21;174(11):1244-1262. doi: 10.1111/bph.13630 Tannins are a heterogeneous group of high MW, water-soluble, polyphenolic compounds, naturally present in cereals, leguminous seeds and, predominantly, in many fruits and vegetables, where they provide protection against a wide range of biotic
and abiotic stressors. Tannins exert several pharmacological effects, including antioxidant and free radical scavenging activity as well as antimicrobial, anti-cancer, anti-nutritional and cardio-protective properties. They also seem to exert beneficial effects on metabolic disorders and prevent the onset of several oxidative stress-related diseases. Although
the bioavailability and pharmacokinetic data for these phytochemicals are still sparse, gut absorption of these compounds seems to be inversely correlated with the degree of polymerization. Further studies are mandatory to better clarify how these molecules and their metabolites are able to cross the intestinal barrier in order to exert their biological
properties. This review summarizes the current literature on tannins, focusing on the main, recently proposed mechanisms of action that underlie their pharmacological and disease-prevention properties, as well as their bioavailability, safety and toxicology. This article is part of a themed section on Principles of Pharmacological Research of
 Nutraceuticals. To view the other articles in this section visit GSE grape seed extract HTs hydrolyzable tannins NOAEL no-observed-adverse effect level OPCs oligomeric proanthocyanidins Tannins are a heterogeneous group of water-soluble polyphenolic compounds of high molecular weight (500-3000 Daltons) - with as many as 20 hydroxyl groups - and
are present in plants, foods and beverages (de Jesus et al., 2012). Being phenolic compounds, tannins are chemically reactive and form inter- and intra-molecular hydrogen bonds that are able to interact with, and precipitate macromolecules, such as proteins and carbohydrates. They are also responsible for the astringent taste of many fruits and
 vegetables (de Jesus et al., 2012; Lamy et al., 2016). With one to five hydroxyl groups, astringency is increased, while from seven groups upwards, it decreases, given that steric hindrance starts to counterbalance the strength of the hydrogen bonds (Zou et al., 2015). Tannins can be classified into two groups: hydrolysable tannins and condensed tannins
(also named catechin tannins or proanthocyanidins). Hydrolysis do not yield just sugar and gallic acid but also ellagic acid (see Lamy et al., 2016). These compounds, as the name suggests, are hydrolyzed by weak
 acids and decomposed by high temperatures to yield pyrogallol, a hepatotoxic and highly irritant compound (Jiménez et al., 2014). The second class, condensed tannins, also referred to as proanthocyanidins, is the most abundant plant-derived polyphenols. They are oligomers of flavan-3-ol (catechin monomers) and/or flavan-3,4-diol, usually linked by C-C
(4-8 or 6-8) and occasionally by C-O-C bonds with a wide structural diversity (de Jesus et al., 2012; Lamy et al., 2016) and are also called oligomeric proanthocyanidins (OPCs). These compounds are not readily hydrolyzed; they decompose in acidic alcoholic conditions giving red pigments called phlobaphenes. To date, though, the chemistry of
proanthocyanidins is only partly known. Despite their abundance in our diet (estimated daily intake 0.1-0.5 g), tannins have received little attention, probably due to their polymeric nature and high structural complexity (Serrano et al., 2009). In recent years, considerable attention has been paid to proanthocyanidins and their monomers due to the
potential beneficial effects on human health, including immunomodulatory, anti-inflammatory, anti-inflammato
and toxicological behaviour. In fact, although many plant-derived proanthocyanidins are widely used now as nutritional supplements, evidence of their safety and potential for long-term toxicity is still lacking (Berry et al., 2016). Here we have reviewed the latest developments and knowledge on the occurrence, dietary intake and biological effects of their safety and potential for long-term toxicity is still lacking (Berry et al., 2016).
tannins, with particular attention on the pharmacological and toxicological aspects. Tannins (proanthocyanidins and hydrolysable tannins) are one of the main secondary metabolites found in cacao beans, tea, wines (mainly red), fruits, juices, nuts, chocolate, legumes and cereal grains (Table 1). There are many ways to define tannins based on their
properties, solubility and presence of substituents (Okuda and Ito, 2011). Taking into account, for instance, the structural features of hydrolysable tannins, they can be identified as follows: gallotannins, they can be identified as
 Ellagitannins Gallotannins Fruits Cranberries Vaccinium oxycoccus L. 194-496 — Chokeberries Aronia melanocarpa (Michx.) Elliott 553-2106 — Plums Prunus domestica L. 32-334 — Black diamond Prunus spp 210-267 — Blueberries Vaccinium myrtillus L. 87-274 — - Vaccinium corymbosum L. 311-335 — Black currants Riges nigrum L.
105-255\ 3-6 — Red currants Ribes rubrum L. 30-61 — Blackberries Rubus fructicosus L. 5-46\ 150-270 — Crowberries Empetrum nigrum L. 153-173 — Red Grapes Vitis Vinifera L. 2180-6050 — Strawberries Fragaria × ananassa Duchesne 15-183\ 71-83
— Peaches Prunus persica L. 29-110 — Apricot Prunus armeniaca L. 8-73 — Raspberries Rubus occidentalis L. 3-74 160-326 — Pears Pyrus communis L. 5-81 — Apple Malus domestica Borkh. 46-278 — Pomegranate Punica granatum L. -58-177 — Guava Pisidium spp. — 20-25 — Mango Mangifera indica L. -30-160 Juices Cranberry -20-20 — Pomegranate Punica granatum L. -58-177 — Guava Pisidium spp. — 20-25 — Mango Mangifera indica L. -30-160 Juices Cranberry -20-200 — Pomegranate Punica granatum L. -58-177 — Guava Pisidium spp. — 20-25 — Mango Mangifera indica L. -30-160 Juices Cranberry -20-200 — Pomegranate Punica granatum L. -58-177 — Guava Pisidium spp. — 20-25 — Mango Mangifera indica L. -30-160 Juices Cranberry -20-200 — Pomegranate Punica granatum L. -58-177 — Guava Pisidium spp. — 20-25 — Mango Mangifera indica L. -30-160 Juices Cranberry -20-200 — Pomegranate Punica granatum L. -58-177 — Guava Pisidium spp. — 20-25 — Mango Mangifera indica L. -30-160 Juices Cranberry -30-1000 — -30-1000 — -30-1000 — -30-1000 — -30-1000 — -30-1000 — -30-1000 — -30-1000 — -30-1000 — -30-1000 — -30-1000 — -30-1000 — -30-1000 — -30-1000 — -30-1000 — -30-1000 — -30-1000 — -30-1000 — -30-1000 — -30-1000 — -30-1000 — -30-1000 — -30-1000 — -30-1000 — -30-1000 — -30-1000 — -30-1000 — -30-1000 — -30-1000 — -30-1000 — -30-1000 — -30-1000 — -30-1000 — -30-1000 — -30-1000 — -30-1000 — -30-1000 — -30-1000 — -30-1000 — -30-1000 — -30-1000 — -30-1000 — -30-1000 — -30-1000 — -30-1000 — -30-1000 — -30-1000 — -30-1000 — -30-1000 — -30-1000 — -30-1000 — -30-1000 — -30-1000 — -30-1000 — -30-1000 — -30-1000 — -30-1000 — -30-1000 — -30-1000 — -30-1000 — -30-1000 — -30-1000 — -30-1000 — -30-1000 — -30-1000 — -30-1000 — -30-1000 — -30-1000 — -30-1000 — -30-1000 — -30-1000 — -30-1000 — -30-1000 — -30-1000 — -30-1000 — -30-1000 — -30-1000 — -30-1000 — -
fibre Ceratonia siliqua L. 1-19 — Cowpeas Vigna unguiculata (L.) Walp. 17-319 — Lentils Lens culinaris Medik. 1-2 — Peanuts Arachis hypogaea L. 121-141 — Cereal grains Barley Hordeum vulgare L. 59-153 — Rice Oryza sativa L.
9-91 — Beverages Wine - 1-53 2-5 — Tea - 1-5 — Cacao beans Theobroma cacao L. 6100-8100 — Chocolate - 828-1332 — Proanthocyanidins are oligomers or polymers of flavan-3-ols, where the monomeric units are linked mainly by C-4 \rightarrow C-8 bonds, although less frequently also C-4 \rightarrow C-6 linkages can be found. These types of linkages lead to
the formation of the so-called B-type proanthocyanidins. A-type proanthocyanidins, on the other hand, are characterized by an additional bond between C-2 	o C-7 of the basic flavan-3-ol units (Figure 1). Proanthocyanidins are composed of different flavan-3-ol units (Figure 1).
are the diastereomers of (epi)catechin, (epi)afzelechin and (epi)afzelechin and (epi)afzelechin and they are joined by a three-atom carbon bridge. Their C ring features a hydroxyl group at the C-3 position, and it lacks a double bond between C-2 and C-3. The most
abundant proanthocyanidins in vegetables are those composed of catechin and epicatechin or (epi)gallocatechin basic units (Figure 1), present in foods such as barley, broad beans, red kidney beans, redcurrants, pinto beans, black tea and
 cinnamon (Landete, 2011; de Jesus et al., 2012; Mateos-Martín et al., 2012; Mateos-Martín et al., 2016). Procyanidin B1-B8, procyanidin C1 and C2, selligueain A and B), tetramers and oligomeric structures with a degree of polymerization ranging from 5 to 11
The most common acyl substituent (as in the case of tea- or wine-derived species) is a galloyl group bound to the hydroxyl group in the C-3 position. The carbohydrate moieties are usually linked to the C-5 position in glycosylated proanthocyanidin oligomers. Basic chemical features of B- and A-type proanthocyanidins and their monomeric units
Gallotannins represent the simplest class of hydrolyzable tannins (HTs), containing gallic acid substituents esterified with a polyol residue (mainly D-glucose). The β anomer of glucose hydroxyl groups can be partly or totally
substituted by phenol units to produce initially β-glucogylin (1-O-galloyl-β-D-glucopyranose). The biosynthetic pathway, starting from this molecule and after the galloylglucoses. Of these, 1,2,3,4,6-penta-O-galloyl-β-D-glucopyranose is usually employed as the prototypical molecule of these, 1,2,3,4,6-penta-O-galloyl-β-D-glucopyranose is usually employed as the prototypical molecule of these, 1,2,3,4,6-penta-O-galloyl-β-D-glucopyranose is usually employed as the prototypical molecule of these, 1,2,3,4,6-penta-O-galloyl-β-D-glucopyranose is usually employed as the prototypical molecule of these, 1,2,3,4,6-penta-O-galloyl-β-D-glucopyranose is usually employed as the prototypical molecule of these, 1,2,3,4,6-penta-O-galloyl-β-D-glucopyranose is usually employed as the prototypical molecule of these and after the galloyl-β-D-glucopyranose is usually employed as the prototypical molecule of the prototypica
gallotannins (Figure 2). The formation of meta- or para-depside bonds is characteristic of these molecules and involves esterification of the aromatic hydroxyl group rather than those present in aliphatic structures. However, many other derivatives can be found, for example gallotannins with 10 or more (up to 12) units of gallic acid esterified to a single gallotannins with 10 or more (up to 12) units of gallic acid esterified to a single gallotannins with 10 or more (up to 12) units of gallic acid esterified to a single gallotannins with 10 or more (up to 12) units of gallic acid esterified to a single gallotannins with 10 or more (up to 12) units of gallic acid esterified to a single gallotannins with 10 or more (up to 12) units of gallic acid esterified to a single gallotannins with 10 or more (up to 12) units of gallic acid esterified to a single gallotannins with 10 or more (up to 12) units of gallic acid esterified to a single gallotannins with 10 or more (up to 12) units of gallic acid esterified to a single gallotannins with 10 or more (up to 12) units of gallic acid esterified to a single gallotannins with 10 or more (up to 12) units of gallotannins with 10 or more (up to 12) units of gallotannins with 10 or more (up to 12) units of gallotannins with 10 or more (up to 13) units of gallotannins with 10 or more (up to 13) units of gallotannins with 10 or more (up to 13) units of gallotannins with 10 or more (up to 13) units of gallotannins with 10 or more (up to 13) units of gallotannins with 10 or more (up to 13) units of gallotannins with 10 or more (up to 13) units of gallotannins with 10 or more (up to 13) units of gallotannins with 10 or more (up to 13) units of gallotannins with 10 or more (up to 13) units of gallotannins with 10 or more (up to 13) units of gallotannins with 10 or more (up to 13) units of gallotannins with 10 or more (up to 13) units of gallotannins with 10 or more (up to 13) units of gallotannins with 10 or more (up to 13) units of gallotannins with 10 or more (up to 13) units of 
 glucose moiety, as in the case of tannins obtained from sumac (Rhus semialata) or oak galls (Quercus infectoria), utilized since ancient times to tan animal hides to produce leather. Although glucose is by far the most abundant polyol identified in tannins, glucitol, fructose, shikimic acid, xylose, hamamelose, saccharose, quercitol and quinic acid may
constitute the core molecules for the subsequent galloylation processes. However, these derivatives are not very common and have only been isolated in maple, chestnut and witch hazel. Chemical structure of pentagalloyl-glucose. Different from gallotannins (rarely found in nature), ellagitannins are present in many plant families, and almost 500
molecules have been isolated and identified to date (Okuda and Ito, 2011; Lamy et al., 2016). Although not all ellagitannins are hydrolyzable, they continue to be classified as hydrolyzable tannins for historical reasons. They can be found in numerous forms: monomeric (e.g. nupharin A, punicalagin, geraniin, eugeniin, davidiin, casuarictin and corilagin)
dimeric (e.g. sanguiin), oligomeric (e.g. agrimoniin, nupharin E, 
 solution spontaneously lactonizes into ellagic acid (Figure 3). Ellagitannins and ellagic acid have been identified in both fruits as well as in nuts and seeds (Landete, 2011), see Table 1. The oxidative coupling commonly involves C-4 and C-3, leading to the formation of casuarictin (Figure 4). Other
carbon atoms involved in this reaction are the C-3/C-6, C-2/C-4 or C-1/C-6 pairs. Hexahydroxydiphenoyl acid can undergo esterification not only with plucose but also with hamamelose and terpenoids. Ellagitannins can yield dimers following intermolecular oxidative coupling with other hydrolyzable tannins (as in the case of euphorbins) or high MW
 oligomers. Formation of ellagic acid in aqueous solution. Chemical structure of eugeniin and casuarictin. The reaction of gallotannins or ellagitannins with catechin units yields complex tannins are camelliatannins A and B, malabatrin A and acutissimin A
(Okuda and Ito, 2011). Tannins, in particular proanthocyanidins, are one of the most widespread compounds present in food ingested daily. They are commonly found in plants and have been identified to date, and these compounds
continue to be of interest to researchers due to the wide range of applications and the numerous biological processes influenced by their presence. These compounds are found in tea, wine, cereals, cacao and fruits in amounts of up to 184 mg·100 g-1, with epicatechin being the most abundant component, followed by catechin and type B-procyanidin (deep to 184 mg·100 g-1, with epicatechin being the most abundant component, followed by catechin and type B-procyanidin (deep to 184 mg·100 g-1).
 Jesus et al., 2012; Lamy et al., 2016). They are also the principal components found in ripe fresh nectarines, peaches and plums (Table 1). Recently, the presence of epicatechin and B-type dimers and trimers of proanthocyanidins has been detected in the pulp of Annona cherimola Mill (Barreca et al., 2011). In red wine, the content of catechin, epicatechin
 procyanidin B1, B2, B3 and B4 amounts to ~18 mg·100 g-1, more than double that found in white wine (Sanchez-Moreno et al., 2003). Catechin and procyanidin B2 were the two principal components found in white wine (Sanchez-Moreno et al., 2003).
database of Proanthocyanidin Content of Selected Foods (http://www.nal.usda.gov/fnic/foodcomp/Data/PA/PA.html). Gallotannins are present only in selected woody and herbaceous dicotyledons. Cereals are sources of hydrolyzable phenols due to phenolic compounds being linked to cell wall components. β-Glucogallin has been reported to be one of the
components of mango fruit pulp (Oliveira et al., 2016). Sumac and Chinese gallnuts (or nutgalls) are particularly rich in gallotannins. Sumac (Rhus coriaria L.) is a shrub grown in Spain, Italy, Turkey and some Mediterranean Arab countries from which a powder is obtained that has long been used as a tanning agent. The main compounds are D-glucose
derivatives esterified with gallic acid, such as penta-, hexa-, hepta-, octa-, nona-, deca-, undeca- and dodeca-galloyl-D-glucose (Lu et al., 2013). Ellagitannins are present in only a few fruits and nuts (especially pecans and walnuts) consumed in the Western diet, and dietary intake (most probably far below 5 mg·day-1) is mainly resulting from the
consumption of red fruits (strawberries, raspberries and blackberries or beverages and jams made from these) (Okuda and Ito, 2011), see Table 1. The principal derivatives identified in foods so far are as follows: sanguiin H-6, punicalagin, roburin E, casuarictin, pedunculagin, potentillin and lambertianin C. Estimates
of the amount of ellagitannins present in food are based on detection of ellagic acid (after hydrolysis of these compounds) followed by HPLC detection, although care is needed during quantification to avoid underestimation deriving from solubility issues. Sanguiin H-6, casuarictin, potentillin and pedunculagin are the predominantly ellagitannins identified
in strawberries, raspberries and blackberries (Zorenc et al., 2016). These compounds are mainly contained in the peel and seed, while very low quantities or traces have been detected in the pulp. Pomegranates (fruits, juices and jams) are also a rich source of ellagitannins, mainly punicalagin and ellagic acid (Masci et al., 2016). Ellagitannins have been
 found in significant amount (Table 1) also in walnuts and pecan nuts (Landete, 2011), with pedunculagin being the main derivative present in walnuts. Aside from the pharmacological effects exerted locally in the gut, tannins have to be bioavailable in order to exert their health effects, and therefore, absorption, bioavailability and metabolism of these
compounds must be carefully evaluated. Although the pharmacokinetics of simple phenols have been extensively investigated in animal and human studies (Velderrain-Rodríguez et al., 2014), the same cannot be said for tannins, where results are still scarce and controversial. High MW tannins apparently are not absorbed intact, as demonstrated by Wiese
et al. (2015), who reported that almost 90% of apple juice-derived procyanidins consumed were retrieved in ileostomy effluent and were able to enter the colon (Wiese et al., 2015). The polymerization rate appears to play a major role in the fate of these compounds and seems to be indirectly related to the absorption of these molecules through the gut
barrier and to their metabolism by gut microbiota to the monomers (i.e. catechin and epicathechin) (Zhang et al., 2016). Some in vivo and in vitro studies have investigated the hydrolysis mechanism of polymeric proanthocyanidins and whether it is possible for the derived oligomeric molecules to be absorbed by the small intestine; often the molecules that
appear in biological fluids can be very different from those ingested (Zhang et al., 2016). Even though small quantities of proanthocyanidins monomers and dimers were found in the plasma compartment, methylated and glucuronidated derivatives seem to be the main metabolites. Furthermore, in the colon, the proanthocyanidins are catabolized by the gut
microflora into a series of simpler metabolites such as phenyl valerolactone, phenylacetic and phenylpropionic acids (Zhang et al., 2016). However, these results are still controversial. Some in vitro experiments have suggested, for example that cocoa procyanidins are hydrolyzed into a mixture of epicatechin monomers and dimers under conditions similared.
to those present in the human stomach. Nevertheless, other studies have demonstrated that no significant depolymerization of cocoa procyanidins occurs in the stomach environment (Ellam and Williamson, 2013; Kim et al., 2014). However, despite these
conflicting observations, what is certain is that during digestion, high MW proanthocyanidins can form complexes and this property is indirectly related to the degree of polymerization. Indeed, small molecules such as dimeric and trimeric
proanthocyanidins can be more readily absorbed (Zhang et al., 2016). Absorption of OPCs has been reviewed recently by Ou and Gu, 2014. They reported that procyanidin A-type dimers, trimers and tetramers were slowly transported across Caco-2 cells monolayers (transport ratio of 0.6%, 0.4% and 0.2% respectively), suggesting their possible absorption
after dietary intake. Furthermore, they reported similar permeability coefficients for (+)-catechin and a proanthocyanidin dimer and trimer, while the permeability of proanthocyanidins with high polymerization was found to be approximately 10 times lower. As described above, most ingested tannins reach the colon. At this level, the gut microbiota play a
 phenylbutyric acids (Marín et al., 2015). The low concentration of 14C-labelled metabolites detected indicates controversial results (Depréz et al., 2000). However, these underestimates may be due to the ability of some polyphenols to bind strongly to various molecules in gut cells and dietary fibres in the colonic lumen. There is currently no data available
 regarding the intestinal bacteria responsible for the degradation of proanthocyanidins and their metabolites. Hydrolysable tannins are metabolized to gallic acid, pyrogallol, phloroglucinol and finally to acetate and butyrate via several bacterial enzymes (Marín et al., 2015). Despite some evidence to the contrary, the OPCs appear to be hydrolyzed into
epicatechin in rat isolated small intestine (Zhang et al., 2016). Nevertheless, orally administered procyanidins in rat plasma and trace amounts of procyanidin trimers and dimers can be absorbed in vivo, also due to the similarity of the permeability
coefficient to that of mannitol, and limited polymer bioavailability in the gut lumen (Ou and Gu, 2014). Moreover, 16 metabolites, including phenylacetic, phenylpropionic and phenylbutyric acids, have been detected in rat urine after administration of proanthocyanidin isolated from willow tree catechins. The total yields significantly decreased in relation to
 the polymerization degree of the precursors: catechin monomer > dimer > trimer > polymer (Brenes et al., 2016). Analysis of luminal content, after administration of grape seed extract (GSE) to Sprague-Dawley rats, showed distinct native and metabolite profiles for each region (caecum and proximal, mid and distal colon) allowing insight to be gained
into the distribution and delivery of procyanidins and their microbial metabolites throughout the colon. In particular, procyanidins reached maximum concentrations from 3 to 18 h post-gavage appearing later in more distall
 regions (Goodrich et al., 2015). Recently, the systemic absorption and metabolism of dietary procyanidin B4, after oral administration, were evaluated in urine. In addition, it was degraded to the monomeric subunits cathechin and epicathechin that were then
further metabolized to methylated and glucuronidated conjugates (Bittner et al., 2014). Unlike condensed tannins, few studies on the bioavailability of hydrolysable tannins are currently available. However, the absorption of main compounds
after oral administration of pomegranate juice detected low concentrations of ellagic acid in plasma after 0.5-3 h, while no intact forms of ellagic acid is probably due to its low water solubility and to its ability to complex calcium and magnesium ions in the
  intestine and thus compromise gut absorption (Serrano et al., 2009). The main ellagic acid derivatives have been found in humans is relatively slow (tmax, 87 min), as also found in rats (tmax, 60 min) (Serrano et al., 2009). Two different speeds of gastric
 absorption have been suggested for this simple phenol: rapid permeation for the unchanged molecule and slow permeation for the metabolite of gallic acid (Serrano et al., 2009). A plausible mechanism for ellagitannin degradation by human microbiota, via hydrolysis into ellagic acid and
its microbial transformation into urolithin B, has been proposed. A study performed on human volunteers fed with a single dose of ellagitannin-rich dietary sources demonstrated a large inter-individual variation in the metabolite profiles among subjects within each group, suggesting the involvement of variable colonic microbiota (Espín et al., 2013). It is
known that tannins are partially bioavailable for absorption in the gastrointestinal tract, small intestine for hydrolyzable tannins (Kamiloglu et al., 2016). It may be concluded that absorption through the
gut barrier is probably limited to the absorption of tannins with a low degree of polymerization and of their metabolites formed in the colon. In view of this, it is critical to evaluate bioavailability studies in order to gain a better understanding of the effects of these phytochemicals on human health. In addition, the above findings highlight the necessity to
choose appropriate biomarkers for the in depth study of the pharmacokinetics of these molecules. For some polyphenols, this has already been achieved (Espín et al., 2013; Stalmach et al., 2014). However, there is a great deal still to be done in this area.
Marchese, 2014; Katiyar, 2015; Salvadó et al., 2015; Verstraeten et al., 2015). Many of the in vitro and in vivo (human and animal) studies performed suggest that tannin intake may prevent the onset of several chronic diseases, as reported by recent reviews, systematic reviews and meta-analysis (Holt et al., 2012; Blumberg et al., 2013; Wang et al., 2014;
Salvadó et al., 2015; Turati et al., 2015). The recognized pharmacological activities have been ascribed to dietary monomeric flavan-3-ol derivatives and to various medicinal plants (Table 2). Tannins exert their biological effects not
only as an un-absorbable (high MW) complex structure with binding properties that may produce local effects in the gastrointestinal tract but also as absorbable tannins (dimers and trimers) with their metabolites producing systemic effects (Jiménez et al., 2014; Nuñez-Sánchez et al., 2014; Velderrain-Rodríguez et al., 2014; Sieniawska,
2015). In addition to their well-documented free radical scavenging and antioxidant activity, tannins seem able to exert antibacterial, antiviral, anticarcinogenic, anti-inflammatory, 
pharmacological activities ascribed to these compounds is provided in Table 3 and described in detail below. Main herbal medicines containing tannins and their therapeutic indications. Source: www.ema.europa.eu Herbal drugs Active constituents Herbal drugs Active constituents Herbal drugs Active constituents.
proanthocvanidins and small amount of ellagitannins) Comminuted herbal substance; Tincture (1:5), extraction solvent ethanol 25% (V/V). Mild diarrhoea; Minor inflammation of the skin and small superficial wounds. Hamamelis virginiana L. (dried
or fresh leaves) 3-10% tannins (gallotannins and proanthocyanidins) Tincture prepared from fresh leaves (1:1) extraction solvent ethanol 45% V/V; Liquid extract from dried leaves (1:1) extraction solvent ethanol 45% V/V; Liquid extract from dried leaves (1:1) extraction solvent ethanol 45% V/V; Liquid extract from dried leaves (1:1) extraction solvent ethanol 45% V/V; Liquid extract from dried leaves (1:1) extraction solvent ethanol 45% V/V; Liquid extract from dried leaves (1:1) extraction solvent ethanol 45% V/V; Liquid extract from dried leaves (1:1) extraction solvent ethanol 45% V/V; Liquid extract from dried leaves (1:1) extraction solvent ethanol 45% V/V; Liquid extract from dried leaves (1:1) extraction solvent ethanol 45% V/V; Liquid extract from dried leaves (1:1) extraction solvent ethanol 45% V/V; Liquid extract from dried leaves (1:1) extraction solvent ethanol 45% V/V; Liquid extract from dried leaves (1:1) extraction solvent ethanol 45% V/V; Liquid extract from dried leaves (1:1) extraction solvent ethanol 45% V/V; Liquid extract from dried leaves (1:1) extraction solvent ethanol 45% V/V; Liquid extract from dried leaves (1:1) extraction solvent ethanol 45% V/V; Liquid extract from dried leaves (1:1) extraction solvent ethanol 45% V/V; Liquid extract from dried leaves (1:1) extraction solvent ethanol 45% V/V; Liquid extract from dried leaves (1:1) extraction solvent ethanol 45% V/V; Liquid extract from dried leaves (1:1) extraction solvent ethanol 45% V/V; Liquid extract from dried leaves (1:1) extraction ethanol 45% V/V; Liquid extract from dried leaves (1:1) extraction ethanol 45% V/V; Liquid extract from dried leaves (1:1) extraction ethanol 45% V/V; Liquid extract from dried leaves (1:1) extraction ethanol 45% V/V; Liquid extract from dried leaves (1:1) extraction ethanol 45% V/V; Liquid extract from dried leaves (1:1) extraction ethanol 45% V/V; Liquid extract from dried leaves (1:1) extraction ethanol 45% V/V; Liquid extract from dried leaves (1:1) extraction ethanol 45% V/V; Liquid extract
solvent ethanol 60% V/V. Minor skin inflammation and dryness; Temporary relief of the symptoms associated with haemorrhoids, such as itching, burning sensation or pain; Minor inflammatory conditions of the oral mucosa. Vaccinium myrtillus L. (ripe, dry fruits) Proanthocyanidins Comminuted herbal substance Mild diarrhoea; Minor inflammations of the
oral mucosa. Quercus robur L. (cortex) Hydrolyzable tannins (predominant) and proanthocyanidins Comminuted herbal substance; Powdered herbal substance; Powd
haemorrhoids; Potentilla erecta (L.) Raeusch. (rhizoma) 5-22% total tannins (15-20% condensed tannins, about 3.5% hydrolyzable tannins) Comminuted herbal substance; Tincture (1:5), extraction solvent ethanol 45% (V/V); Liquid extract (DER 1:1), extraction solvent ethanol 25% (V/V); Dry extraction solvent ethanol 45% (V/V); Liquid extract (DER 1:1), extraction solvent ethanol 45% (V/V); Dry extraction solvent ethanol 45% (V/V); Liquid extract (DER 1:1), extraction solvent ethanol 45% (V/V); Dry extraction solvent ethanol 45% (V/V); Liquid extract (DER 1:1), extraction solvent ethanol 45% (V/V); Dry extraction solvent ethanol 45% (V/V); Liquid extract (DER 1:1), extraction solvent ethanol 45% (V/V); Dry extraction solvent ethanol 45% (V/V); Liquid extract (DER 1:1), extraction solvent ethanol 45% (V/V); Dry extraction solvent ethanol 45% (V/V); Liquid extract (DER 1:1), extraction solvent ethanol 45% (V/V); Dry extraction solvent ethanol 45% (V/V); Liquid extract (DER 1:1), extraction solvent ethanol 45% (V/V); Dry extraction ethanol 45% (V/V); Dry extract
(DER 3.5-4.5:1), extraction solvent ethanol 60% (V/V) Mild diarrhoea; Minor inflammations of the oral mucosa; Rosa centifoglia L. (dried petals) Proanthocyanidins Comminuted herbal substance Mild inflammations of the oral and pharyngeal mucosa; Minor skin inflammation. Main pharmacological activities ascribed to tannins Properties Effects
References Antioxidant and radical scavenging Scavengers of hydroxyl, superoxide, and peroxyl radicals (Proanthocyanidins); Inhibition of lipid peroxidation and lipoxygenases (Ellagitannins); Stronger antioxidant activity than ascorbic acid or α-tocopherol (Procyanidins B1 and B3); Dose-dependent radical scavenging action of galloylated condensed
tannins. Nile and Park, 2014 Skrovankova et al., 2015 Kancheva and Kasaikina, 2013 Sieniawska, 2015 Anti-cancer Apoptosis p53-dependent and Bax/Bcl-2 proteins and caspase-3 activation mediated in JB6 C141 cells (Grape seed proanthocyanidins); Reduction of UV-induced oxidative stress-mediated phosphorylation and activation of NF-kB in NHEK
cells (Grape seed proanthocyanidins); Inhibition of cell viability, proliferation and expression of MMP-2 and -9 in DU145 and LNCaP cells (Grape seed proanthocyanidins); Dose-dependent inhibition of cell viability, proliferation and apoptosis in 4 T1, HT29 and LoVo cells (Grape seed proanthocyanidins); Dose-dependent inhibition of cell viability, proliferation and apoptosis in 4 T1, HT29 and LoVo cells (Grape seed proanthocyanidins); Dose-dependent inhibition of cell viability, proliferation and apoptosis in 4 T1, HT29 and LoVo cells (Grape seed proanthocyanidins); Dose-dependent inhibition of cell viability, proliferation and apoptosis in 4 T1, HT29 and LoVo cells (Grape seed proanthocyanidins); Dose-dependent inhibition of cell viability, proliferation and apoptosis in 4 T1, HT29 and LoVo cells (Grape seed proanthocyanidins); Dose-dependent inhibition of cell viability, proliferation and apoptosis in 4 T1, HT29 and LoVo cells (Grape seed proanthocyanidins); Dose-dependent inhibition of cell viability, proliferation and apoptosis in 4 T1, HT29 and LoVo cells (Grape seed proanthocyanidins); Dose-dependent inhibition of cell viability, proliferation and apoptosis in 4 T1, HT29 and LoVo cells (Grape seed proanthocyanidins); Dose-dependent inhibition of cell viability, proliferation and apoptosis in 4 T1, HT29 and LoVo cells (Grape seed proanthocyanidins); Dose-dependent inhibition of cell viability and the cell viability and t
protein levels and decrease of cyclins and cyclin-dependent kinases in MCF-7, and A-427 cells (Grape seed proanthocyanidins); Inhibition of KB, CAL-27, MCF-7, HT-29, HCT116, DU145 and LNCaP cells growth and apoptosis induction (blackberry, black raspberry, blac
UVB-induced immune suppression in mice with induction of IL-12 (Grape seed proanthocyanidins); Inhibition of a T1 murine mammary tumours in Sprague-Dawley rats (Grape seed proanthocyanidins); In vitro and in vivo inhibition of HT29 cell
growth (Grape seed proanthocyanidins); Inhibition of prostate tumour growth and progression in TRAMP mice (Grape seed proanthocyanidins); Inhibition of E. coli adherence to uroepithelium (Cranberry
proanthocyanidins); Activity against Staphylococcus aureus, Candida albicans and Campylobacter jejuni (Ellagitannins); Inhibition of HIV-antigen expression in human lymphotropic virus type I-positive MT-4 cells (hydrolyzable tannins); Activity
against Helicobacter pylori (hydrolyzable tannins). Marín et al., 2015 Nile and Park, 2014 Sieniawska, 2015 de Jesus, 2012 Anti-nutrient Inhibition of gastrointestinal enzymes (Proanthocyanidins); Reducing capacity on Cr., Fe and Cu with alteration of their absorption (Proanthocyanidins); Modulation of chronic inflammatory bowl diseases (Procyanidin B3)
Nile and Park, 2014 Sieniawska, 2015 Li et al., 2016 Cardioprotective Hypocholesterolemic effects (Proanthocyanidins); Preventing myocardial ischaemic injury in adult rats (Proanthocyanidins); Preventing myocardial ischaemic injury injury injury injury injury injury inj
differentiation of monocyte to macrophages (Oligomeric proanthocyanidins); Protective effect on doxorubicin-induced electrocardiographic and biochemical changes (Grape-seed proanthocyanidins); Protection against acute
ischaemic brain damage in rats (Proanthocyanidins); Vascular protective effects (Procyanidins); Vascular protective protein and decreased systolic and diastolic blood pressure (Grape-wine proanthocyanidins). Blumberg et al., 2013 Wang et al.,
2014 Holt et al., 2012 Guler et al., 2011 Mohana et al., 2013 Yunoki et al., 2013 Yunoki et al., 2013 Yunoki et al., 2014 Yang et al., 2014 Yang et al., 2014 Yang et al., 2015 Ammar et al., 2016 Ammar et al., 2016 Ammar et al., 2017 Yunoki et al., 2018 Yunoki et al
and proanthocyanidins); Reduced plasmatic insulin and improved homeostatic model assessment (HOMA) index (hydrolyzable tannins and proanthocyanidins); Hypocholesterolemic effect (tannin-rich fibre); Acute effects on postprandial lipaemia,
vascular function and blood pressure (Pomegranate ellagitannins); Insulinomimetic properties (Grape seed proanthocyanidins); Insulinomimetic properties (Grape
induction of metal chelation activity, reduced resistin formation, and inhibition or activation of transcriptional factors such as NF-kB and PPARx (Proanthocyanidins). Gonzalez-Abuin et al., 2015 Cock, 2015 Stohs and Ray, 2015 Salvadó et al., 2017 Cock, 2017 Cock,
2015 Most activities of the proanthocyanidins and hydrolyzable tannins, including antioxidant and free radical-scavenging capacity, largely depend on their structure; for example, an increase in anti-radical effects was observed with an increase in the degree of polymerization (Sieniawska, 2015). Proanthocyanidins are known to inhibit lipid peroxidation
and lipoxygenases in vitro, and several studies have demonstrated their ability to scavenge hydroxyl, superoxide and peroxyl radicals, helping to restore the oxidative balance of the body (Georgiev et al., 2014). In some instances, some procyanidin B1 and procyanidin B2 have been recognized to be stronger antioxidants than ascorbic
acid or α-tocopherol (Iglesias et al., 2012). These results observed in vitro have also been confirmed by several in vivo studies on animal models (Kancheva and Kasaikina, 2013; Nile and Park, 2014; Sieniawska, 2015; Skrovankova et al., 2015). Fushimi et al. (2015) have investigated the antioxidant effects of unripe and mature persimmon in rats. Results
showed that plasma phosphatidylcholine hydroperoxide levels, a biomarker of membrane lipid peroxidation, were significantly lower in the unripe persimmon group than in the control group. The authors suggested that soluble tannins, found more in
unripe fruits, could contribute to the difference in the antioxidant effect observed (Fushimi et al., 2015). A few years earlier, another study had shown that several proanthocyanidin-type dimers, from peanut skins and persimmon pulp, possess high dose-dependent antioxidant potency. B-type dimers showed the highest radical scavenging activity in
 aqueous systems while A and B-type dimers showed similar antioxidant potency in tissue or lipid systems highlighting the importance of the food matrix effect (Dong et al., 2013). Protection against lipid peroxidation has also been observed in several tannin-rich plants. For example, the ethanolic extract of Nigella sativa L. was found to counteract in vivo
Fe(II)-induced lipid peroxidation (Hassan et al., 2016). Also, Centella asiatica L. and its fractions were found to reduce lipid peroxidation induced by quinolinic acid and sodium nitroprusside in the rat brain (Marques et al., 2015). Free radical-scavenging activity of OPCs from Rhodiola rosea L. has been evaluated in mice serum, heart, liver and brain
tissues, These compounds enhanced SOD and GSH peroxidase (GPx) activity by reducing malondialdehyde (MDA) content (Zhou et al., 2014), Another interesting and recent study has evaluated the protective effect of grape seed proanthocyanidins (GSPs) on cadmium-induced renal toxicity (Nazima et al., 2015). Proanthocyanidins were also found able to
improve lead-induced cognitive impairments by blocking endoplasmic reticulum stress and NF -kB-mediated inflammatory pathways in rats (Liu et al., 2014). A meta-analysis of experimental studies regarding the efficacy of proanthocyanidins against oxidative damage has recently been performed (Li et al., 2015a). Compared with the control group,
proanthocyanidins significantly improved total antioxidative capacity, SOD, GSH, GPx and catalase (CAT) and reduced the MDA levels. Proanthocyanidins therefore effectively antagonize oxidative damage and enhance antioxidant capacity, but the antagonistic effect may be related to intervention method and biological sample from
 which the indexes are estimated. The authors observed, in fact, significant differences in the effects of proanthocyanidins in relation to themode of administration (gavage vs. feeding) and dependent on the biological matrix analysed (Li et al., 2015a). At present, there is only limited clinical evidence available about the antioxidant properties of hydrolyzable
tannins and proanthocyanidins. Three pilot studies on human volunteers have recently been carried out using a French oak wood (Quercus robur L.) extract rich in roburin (a dimeric tannin), known with the brand name of Robuvit®. The first examined the pharmacokinetics and effects at transcriptome level of this formulation in healthy volunteers and
showed that Robuvit® metabolites affected ribosomes, cell cycle and spliceosome pathways (Natella et al., 2014). The second study, which analysed the effect of 1 month intake of Robuvit® (300 mg·day-1) on oxidative stress markers in the plasma of healthy volunteers, demonstrated a decrease of the advanced oxidation protein products and lipid
peroxides, an increased SOD and CAT activity and total antioxidant capacity (Horvathova et al., 2014). The third study, which was the most recent, showed Robuvit® to have no significant influence on GSH levels and paraoxonase (an antioxidant enzyme) activity, although homocysteine and cysteine levels decreased significantly (Deáková et al., 2015).
 Finally, a double-blind crossover trial was performed on 18 volunteers to evaluate the effects of procyanidin-rich chocolate for two 4 week periods separated by a 4 week washout period. The authors observed a decreased free radical production
in fecal water with respect to control group, suggesting that chocolate proanthocyanidins, have identified several molecular targets potentially useful for the prevention and treatment of cancer. It should be
stated, however, that knowledge in this area is still at an embryonic stage, and further studies are needed to better clarify the anti-cancer properties of these compounds. Proanthocyanidins have been extensively studied on a wide range of cancer cells. GSPs induced p53-dependent apoptosis on JB6 C141 mouse skin epidermal cells, through involvement of
Bax/Bcl-2 proteins and caspase-3 activation (Gollucke et al., 2013). Furthermore, inhibition of the phosphorylation of NF-kB and its related genes were observed in normal human epidermal keratinocytes (Gollucke et al., 2013). The same molecular mechanisms were found to be involved in the
inhibition of cell growth and in the down-regulation of MMP-2 and -9 in both androgen-insensitive (DU145) and in androgen-insensitive (but and in the down-regulation of MMP-2 and -9 in both androgen-insensitive (DU145) and in androgen-insensitive (but and in the down-regulation of MMP-2 and -9 in both androgen-insensitive (but and in the down-regulation of MMP-2 and -9 in both androgen-insensitive (but and in the down-regulation of MMP-2 and -9 in both androgen-insensitive (but and in the down-regulation of MMP-2 and -9 in both androgen-insensitive (but and in the down-regulation of MMP-2 and -9 in both androgen-insensitive (but and in the down-regulation of MMP-2 and -9 in both androgen-insensitive (but and in the down-regulation of MMP-2 and -9 in both androgen-insensitive (but and in the down-regulation of MMP-2 and -9 in both androgen-insensitive (but and in the down-regulation of MMP-2 and -9 in both androgen-insensitive (but and in the down-regulation of MMP-2 and -9 in both androgen-insensitive (but and in the down-regulation of MMP-2 and -9 in both androgen-insensitive (but and in the down-regulation of MMP-2 and -9 in both androgen-insensitive (but and in the down-regulation of MMP-2 and -9 in both androgen-insensitive (but and in the down-regulation of MMP-2 and -9 in both and in the down-regulation of MMP-2 and -9 in both a
The down-regulation of these MMPs, involved in tumour development and metastasis, was also observed on mouse mammary tumour 4T1 and colorectal cancer HT29 and LoVo cell lines (Sieniawska,
```

2015). GSPs interfered with normal regulation of cell-cycle progression inducing an up-regulation of Cip1/p21 and Kip1/p27 protein levels together with a down-regulation of cyclins (D1, D2 and E) and cyclin-dependent kinases (CDK2, CDK4 and CDK6) leading to Go/G1 phase arrest (Prasad and Katiyar, 2014). Concentration-dependent effects of GSPs

```
were observed on breast and lung cancer and gastric adenocarcinoma cells (Gollucke et al., 2013). Besides GSPs, grapes and pine bark procyanidin-rich fraction, arresting the cell cycle in G2 phase and inducing apoptosis, as observed
in HT29 human colorectal cancer cells (Ouédraogo et al., 2011). In vitro anti-proliferative and pro-apoptotic effects were also observed with several berry proanthocyanidin-rich extracts on human oral (KB, CAL-27), breast (MCF-7), colon (HT-29, HCT116) and prostate (LNCaP) cancer cells (Nile and Park, 2014; Skrovankova et al., 2015). The in vitro anti-proliferative and pro-apoptotic effects were also observed with several berry proanthocyanidin-rich extracts on human oral (KB, CAL-27), breast (MCF-7), colon (HT-29, HCT116) and prostate (LNCaP) cancer cells (Nile and Park, 2014; Skrovankova et al., 2015).
cancer properties of proanthocyanidins have been confirmed by several animal studies. Dietary feeding of GSPs was found to inhibit UVB-induced photocarcinogenesis in SKH-1 hairless mice. This event seems to be correlated with the ability of these compounds to decrease UVB-induced immune suppression in mice, by enhancing the production of IL-12
and reducing the expression of IL-10 (Gollucke et al., 2013; Sieniawska, 2015). A study performed in immunocompetent Balb/c mice fed with GSPs showed tumour-growth inhibition with an increase in the survival period and inhibition of metastatic status (Gollucke et al., 2013). Similar results were observed in other in vivo cancer models (Gollucke et al.,
2013). Moreover, it has been demonstrated that GSPs inhibit the spontaneous development of prostate cancer in male TRAMP mice (Sieniawska, 2015). Although a number of experimental studies have been published, few clinical trials on the anti-cancer properties of proanthocyanidins are available, to date. A double-blind, placebo-controlled, randomized
phase II trial was planned to elucidate the effects of supplementation with GSP extract (300 mg·day−1 for 6 months) in patients affected by radiation-induced breast induration in 29.5% of GSPs extract treated patients was recorded, while no significant
difference between treatment and control groups in terms of external assessments of tissue hardness, breast appearance or patient self-assessments of breast hardness, pain or tenderness was recorded (Sieniawska, 2015). Proanthocyanidins have been also evaluated for their potential to attenuate the adverse effects of cancer radiotherapy. A randomized
double blind, placebo-controlled, pilot study was conducted using standardized cranberry capsules, containing 72 mg of proanthocyanidins, for the prevention and treatment of radiation cystitis in control group double blind, placebo-controlled, pilot study was conducted using standardized cranberry capsules, containing 72 mg of proanthocyanidins, for the prevention and treatment of radiation cystitis in cidence in treated patients (65%) compared with control group
(90%); severe cystitis was reported in 30% of treated patients and 45% in the control group. Moreover, the incidence of pain and burning was significantly lower in treated group. The results demonstrate that patients who receive radiation therapy for prostate cancer, particularly those on low hydration regimens or with baseline urinary symptoms, may
benefit from cranberry supplementation (Hamilton et al., 2015). The antimicrobial properties of proanthocyanidins and HTs present in many medicinal plants and foods are well documented. These phytochemicals seem to affect bacterial growth via several mechanisms such as inhibition of extracellular enzymes, deprivation of microbial essential
substrates (for example by complexing metal ions), disintegration of bacterial outer membrane with cytoplasm leak or by direct action on microbial metabolism. Furthermore, these compounds can interfere with microbial cell wall polypeptides reacting with sulfhydryl groups, often leading to loss of function of the membrane proteins (Marín et al., 2015).
The anti-adhesion properties of berry fruits and derived products have long been known. Cranberry juice, for example, inhibits E. coli adherence to uroepithelium. However, the molecular structure of proanthocyanidins, seems to play a major role in conferring bacterial anti-adhesion activity to each matrix. In fact, cranberry proanthocyanidins,
characterized by a series of catechin oligomers with one or more A-type linkages - and therefore structurally quite different with respect to proanthocyanidins from other sources like grape and apple- have been confirmed by
several animal studies, which suggest that cranberry proanthocyanidins and/or their metabolites are able to inhibit bacterial adhesion to uroepithelium (Micali et al., 2014). Cloudberry, raspberry and strawberry extracts, rich in ellagitannins, were found to be the best inhibitors against Campylobacter jejuni and Candida albicans (Lipińska et al., 2014).
Bilberry and blueberry extracts showed bacteriostatic activity on Gram-positive bacteria (Listeria monocytogenes, Staphylococcus aureus, Bacillus subtilis and Enterococcus fecalis) and Gram-negative bacteria (Citrobacterfreundii, E. coli, Pseudomonas aeruginosa and Salmonella enteric ser. Typhimurium) (Nile and Park, 2014). The bacteria most
sensitive to berry extracts were Helicobacter pylori and Bacillus cereus, while yeasts were found to be resistant to the extracts (Lipińska et al., 2014). Several ellagitannin-rich plants have shown antibacterial properties. For example, Pteleopsis hylodendron Mildbr. extracts, containing mainly ellagic acid, were active against Klebsiella pneumoniae, B
cereus, E. coli and Salmonella typhi (Marín et al., 2015). Pomegranate peel extract has also been observed to be active against S. aureus, including themethicillin-resistant strains, and E. coli, as well as by the fungal pathogen C. albicans (Bakkiyara
et al., 2013). Antifungal properties against C. albicans, C. neoformans and Aspergillus fumigates have been shown by this compound as well as by punicalagin, punicalin and gallagic acids (Marín et al., 2015). Antimalarial activity against chloroquine-resistant Plasmodium falciparum has been reported for ellagic acid, which showed synergy
when combined with conventional antimalarial drugs (Marín et al., 2015). Antiviral activity has also been described and seems to be strictly related to the tannins may interfere with Herpes simplex virus absorption as well as the absorption of
HIV and its cytopathic effects (Lipińska et al., 2014; Ekambaram et al., 2016). This mechanism seems to be related to the capacity of tannins to bind the viral envelope components. Furthermore, ellagitannins and several proanthocyanidins have been demonstrated to be potent reverse transcriptase inhibitors (Ekambaram et al., 2016). One hydrolyzable
tannin, ellagic acid, also shows specific antiviral activity against hepatitis B virus (HBV) by inhibiting HBeAg secretion in HBV-infected cells (Marín et al., 2015). There are several clinical studies on dietary supplements containing ellagitannins or proanthocyanidins and their antimicrobial properties and the most recent are discussed below. A randomized
double-blind, placebo-controlled, acute study was performed to evaluate the E. coli anti-adhesion activity following administration of several cranberry extracts, containing a standardized level of 36 mg proanthocyanidins, in healthy subjects. The authors observed, for all formulations studied, a significantly anti-adhesion effect after intake of a single dose
of cranberry extracts compared with the control group (Howell et al., 2015). Another randomized, placebo-controlled study was carried out in order to clarify how cranberry fruit powder (500 mg·per day for 6 months), with a standardized 0.56% proanthocyanidin content, could prevent recurrent urinary tract infection (UTI) in 182 women with two or more
UTI episodes in the previous year. Results showed a much longer latency period before developing a new UTI episode than the placebo group (Vostalova et al., 2015). It should be mentioned, however, that the
ability of cranberry to prevent UTIs has been recently questioned (Jepson et al., 2013; Izzo et al., 2016). The health benefits of pomegranate consumption are attributed, as reported above, to ellagitannins and their metabolite content. In a recent study, performed on 20 healthy volunteers consuming 1000 mg·day-1 of pomegranate extract for 4 weeks,
three different behaviours - based on urinary and fecal content of the pomegranate metabolite urolithin A - were observed: 1) in nine subjects baseline urolithin A formation was present and enhanced by pomegranate extract
consumption; and 3) in six subjects there was no baseline urolithin A producers with respect to baseline values. After 4 weeks, Enterobacteria and Verrucomicrobia phyla and a decrease of Firmicutes in urolithin A producers with respect to baseline values. After 4 weeks, Enterobacteria and Veillonella, Serratia and Veillonella, S
genders also increased, in urolithin A producers compared with baseline values, while Collinsella decreased significantly. On this basis, the authors suggested that health benefits may be induced by pomegranate extract consumption due to changes in the microbiota (Li et al., 2015b). Tannins, known to be astringent compounds due to their ability to
complex and precipitate proteins, particularly proline-rich proteins, are present in the human saliva through hydrophobic interactions. Recently, a study was performed to elucidate the interactions, responsible for the onset of celiac
disease (CD). This study identified several soluble B3-peptide complexes containing immunoreactive peptides, of different sizes and diversity in CD epitopes, demonstrating the potential beneficial effects of proanthocyanidins can also
inhibit enzymes (pectinase, amylase, lipase, protease and β-galactosidase) and may interfere with absorption of other compounds like proteins and carbohydrates. Several in vitro studies have supported this claim. However, the in vivo studies have supported this claim.
secretion in the gut and increase of proline-rich salivary proteins (Brandão et al., 2014). The limited absorption through the gut barrier of proanthocyanidins with a high degree of polymerization and the relatively weak affinity of those with a low polymerization degree, for proteins, have led to the hypothesis that non-specific binding of proanthocyanidins
to proteins is involved in the biological properties exerted by these compounds in inner tissues (Sieniawska, 2015). On the contrary, greater affinity to the shortest human saliva peptides has been observed (procyanidins C2 > B1 > B3) (Cala et al., 2012). Tannins have also been found to possess reductive capacity for some metals, for example Cr, Fe and
Cu, thereby reducing their absorption (Sieniawska, 2015; Li et al., 2012). No data are available from human studies about tannins and their anti-nutritional effects. The links between proanthocyanidin intake and cardioprotective properties have been extensively reviewed (Kay et al., 2012; Wang et al., 2014; Sieniawska, 2015; Bladé et al., 2016). A number
of in vitro and animal studies have recently been performed to elucidate the role of proanthocyanidins as promising molecules that could prevent the development of several coronary syndromes by inhibiting the atherogenic process and balancing blood pressure and lipid homeostasis (Hort et al., 2012; Pons et al., 2014; Quifer-Rada et al., 2016). Recently,
other mechanisms of action have been proposed. For example, an in vitro and in vivo study showed inhibition of monocyte to macrophages differentiation in atherosclerosis, by OPC isolated from Crataegus oxyacantha L. In summary, the OPCs decreased vascular cell adhesion protein 1 and chemokine CCL2 levels, down-regulating the inflammatory
pathway and macrophage markers, MMP 2 and 9 and PPARy. These results highlight the potential role of these phytochemicals in the initial stages of atherosclerosis development and in overt disease. dependent on macrophage function (Mohana et al., 2015). Another animal study evaluated the cardio-protective effect of GSPs on doxorubicin-induced
cardiac toxicity in rats. Administration of proanthocyanidins significantly suppressed doxorubicin-induced electrocardiographic changes and normalized the aconitine dose producing ventricular tachycardia. Furthermore, proanthocyanidins significantly suppressed the biochemical changes induced by doxorubicin on creatine kinase-myocardial band, LDH,
MDA, SOD, CAT and reduced GSH (Ammar et al., 2013). GSPs have also been found to possess antioxidant, anti-inflammatory and antiapoptotic effects through which they are able to protect the liver against ischaemia/reperfusion injury by attenuating endoplasmic reticulum stress (Xu et al., 2015). In addition, there is evidence that a proanthocyanidin-
rich diet protects against acute ischaemic brain damage in rats, improving motor function, reducing cerebral infarction volume and decreasing both peroxidative markers such as CCL2, ionized calcium-binding adapter molecule-1 and
TNF-α (Yunoki et al., 2014). Finally, another recent study investigation of NLRP3 inflammasome in HUVECs followed by an inhibition of caspase-1 activation and IL-1β secretion in response to LPS. In addition, procyanidin B2 reduced
LPS-induced formation of ROS and down-regulated the transcriptional activity of activator protein-1 (Yang et al., 2014). A cross-sectional study has recently demonstrated the potential role of dietary antioxidants, including proanthocyanidins, in the prevention of cardiovascular diseases because they are able to improve serum antioxidants status and
decrease serum C-reactive protein and plasma homocysteine concentrations (Yang et al., 2013). In a double-blind, placebo-controlled crossover study, the effect of two grape extracts (grape-red wine and grape alone) on blood pressure and vascular function was assessed in mildly hypertensive subjects. Results showed that only the grape wine extract, rich and plasma homocysteine concentrations (Yang et al., 2013).
disease (Draijer et al., 2015). Also, a randomized, double-blind, placebo-controlled study performed in women affected by menopausal symptoms (Terauchi et al., 2014). In conclusion, while several in vitro and animal studies are available, clinical trials are
sparse and have yielded controversial results. Further human studies are needed to confirm the preliminary findings obtained so far. A number of reviews and systematic reviews have recently been published about the in vitro and animal studies available, elucidating the role of proanthocyanidin-rich plant extract in the treatment of diabetes, diabetic
complications and other metabolic disorders like obesity (Bertoia et al., 2015; Gonzalez-Abuin et al., 2016). They highlight the main pharmacological mechanisms by which tannins may act on metabolic disorders. Several molecular mechanisms and molecular targets have been proposed to explain the
role of proanthocyanidins and hydrolyzable tannins in metabolic disorders. These phytochemicals have been found able to: (i) stimulate glucose uptake and glycogen and lipid synthesis by activation of insulin receptors, PKB, p44/42 and p38 MAPKs signalling pathways and translocation of glucose transporter type 4 (GLUT4) to the plasma membrane; (ii)
exert insulin-like effect on insulin-sensitive tissues; (iii) delay the onset of insulin receptor substrate 1 in mesenteric white
adipose tissue (WAT); (v) modulate active glucagon-like peptide-1 levels; (vi) inhibit intestinal enzymes like α-amylase (proanthocyanidins) and α-glucosidase (hydrolyzable tannins); (vii) inhibit intestinal enzymes like α-amylase; and (viii) induce triglyceride turnover (Banihani et al., 2013; Cascaes et al., 2015; Gonzalez-Abuin et al., 2015;
Salvadó et al., 2015; Stohs and Ray, 2015; Kooti et al., 2016). Despite the wealth of experimental evidence available regarding tannins and metabolic disorders, human studies are still scarce, and findings to date are controversial. A randomized, double-blind, placebo-controlled trial, which investigated the hypocholesterolemic effects of persimmon fruit.
tannin-rich fibre, showed a significant decrease of total plasma tholesterol levels as well as of LDL cholesterol levels were observed (Gato et al., 2013). Another randomized, controlled crossover trial was conducted on 19 young, healthy men with an energy drink (containing
ellagitannin-rich pomegranate extract). Results showed no significant differences in terms of capillary plasma triacylglycerol (TAG) between treated groups and control group while systolic blood pressure was found to be higher in treated groups and control group. No appreciable differences were observed for reflection and stiffness indices or
diastolic blood pressure (Mathew et al., 2012). When discussing t safety, it is important to make a distinction between biofunctional constituents in foods and the same molecules as purified or semi-purified compounds, and their contribution to overall dietary
intake of tannins needs to be taken into account. The dangers of diets containing very high levels of these compounds together with food-based polyphenol enrichment and supplements with purified agents or mixtures have not been studied in detail (Margină et al., 2015). This fact makes polyphenol consumption potentially problematic in terms of
alterations in bioavailability and the consequent possible occurrence of side effects due to pharmacokinetic interactions. In theory, there are encouraging results from some epidemiological studies reporting a dietary intake of more than
1 g·day-1 (i.e. related to eating habits) (Kumari and Jain, 2012) to be associated with a reduced onset of many chronic diseases (Sieniawska, 2015). However, further studies on the potential adverse events that might be associated with high intakes of these constituents are needed. Tannin toxicity is based essentially on three mechanisms: (i) microbial
enzyme inhibition (i.e. cellulases, pectinases, xylanases, GPx, laccase and glycosyltransferase) and substrates for decreased microbial growth (polysaccharides such as pectins, hemicelulose or polygalacturonic acid and less frequently peptides or aminoacids probably due to the lower affinity of tannins for these small molecules with respect to polymers),
closely related to tannin-protein interactions; (ii) action on membranes (inactivation of membrane-bound proteins; inhibition of electron transport system); and (iii) chelation of metal ions (e.g. iron and zinc) (Guil-Guerrero et al., 2016). Toxicology studies on tannic acid have so far been limited to
the evaluation of genotoxicity, short-term repeat-dose toxicity and carcinogenicity. For example, a subchronic toxicity study, in female rats, demonstrated that a dietary intake of 2.5% grape seed or grape skin extract produced a no-observed-adverse effect level (NOAEL) (Serrano et al., 2016). Subchronic oral toxicity of GSE was also examined in another
study on rats; the NOAEL of dietary GSE was found equal to 1.4 g·kg-1 body weight·day-1 in females (Fiume et al., 2014). Furthermore, the LD50, after grape seed and skin extract ingestion in rats, was found to be higher than 5 g·kg-1 body weight. Although numerous studies on the mutagenicity/genotoxicity
are available (Kaur et al., 2000; Lehmann et al., 2000; Lehmann et al., 2000; Fuentes et al., 2000; Fuentes et al., 2000; Fuentes et al., 2000; Lehmann et al., 2000; Lehmann et al., 2000; Fuentes et al., 2000; Lehmann et al., 2000; Lehmann et al., 2000; Lehmann et al., 2000; Fuentes et al., 2000; Fuentes et al., 2000; Fuentes et al., 2000; Lehmann et al., 2000; Lehmann et al., 2000; Fuentes et
Furthermore, no studies on reproductive toxicology are available. What can be said is that hydrolysable tannins are poorly absorbed per se by the gut lumen because they are extensively degraded in the gastrointestinal tract. Furthermore, their metabolites in target species, experimental animals and humans are very similar and appear to be efficiently
excreted, so the expected lack of residues in foods of animal origin suggests that it is unlikely that consumers will receive an appreciable amount of the parent compound or its metabolites such as to exert a potentially toxic effect (EFSA, 2014). Although many in vitro and in vivo studies on tannins, and in particular proanthocyanidins, have provided
important information with respect to the potential health effects of dietary intake of these compounds, to date, only 35 clinical trials are available, of which 27 are complete, five ongoing and three with unknown status (www.clinicaltrials.gov) (Table 4). Very few of these studies have been performed on potentially more susceptible subjects such as
postmenopausal women, and there are even fewer or no studies at all relating to other vulnerable groups, including pregnant and lactating women (Smeriglio et al., 2014b), children and the elderly. Information regarding potential adverse events cannot be more comprehensively assessed until this data becomes available. Current available list of
completed clinical trials provided by U.S. National Institutes of Health (www.clinicaltrials.gov) Number ID Title Subjects enrolled NCT01688154 Ability of Grape Seed Proanthocyanidins to Reduce Postprandial Triglycerides in Humans Both (20-40 years) NCT00742287 Cardiovascular Effects of Oligomeric Procyanidins (OPCs) in Smokers Male (30-40 years) NCT00742287 Cardiovascular Effects of Oligomeric Procyanidins (OPCs) in Smokers Male (30-40 years) NCT00742287 Cardiovascular Effects of Oligomeric Procyanidins (OPCs) in Smokers Male (30-40 years) NCT00742287 Cardiovascular Effects of Oligomeric Procyanidins (OPCs) in Smokers Male (30-40 years) NCT00742287 Cardiovascular Effects of Oligomeric Procyanidins (OPCs) in Smokers Male (30-40 years) NCT00742287 Cardiovascular Effects of Oligomeric Procyanidins (OPCs) in Smokers Male (30-40 years) NCT00742287 Cardiovascular Effects of Oligomeric Procyanidins (OPCs) in Smokers Male (30-40 years) NCT00742287 Cardiovascular Effects of Oligomeric Procyanidins (OPCs) in Smokers Male (30-40 years) NCT00742287 Cardiovascular Effects of Oligomeric Procyanidins (OPCs) in Smokers Male (30-40 years) NCT00742287 Cardiovascular Effects of Oligomeric Procyanidins (OPCs) in Smokers Male (30-40 years) NCT00742287 Cardiovascular Effects of Oligomeric Procyanidins (OPCs) in Smokers Male (30-40 years) NCT00742287 Cardiovascular Effects of Oligomeric Procyanidins (OPCs) in Smokers Male (30-40 years) NCT00742287 Cardiovascular Effects of Oligomeric Procyanidins (OPCs) in Smokers Male (30-40 years) NCT00742287 Cardiovascular Effects of Oligomeric Procyanidins (OPCs) in Smokers Male (30-40 years) NCT00742287 Cardiovascular Effects of Oligomeric Procyanidins (OPCs) NCT00742287 Cardiovascular Effects (30-40 years) NCT00742287 Cardiovascular Effects (30-40 years
60 years) NCT01483508 Absorption and Metabolism of Dietary Cocoa Procyanidins in Humans Both (18-70 years) NCT02515929 Prospective Double-Blind Randomized Controlled Clinical Trial in the Gingivitis Prevention With
OPCs Both (18-50 years) NCT01707615 Beneficial Effects of Grape Seed Proanthocyanidin Extrat on Progression of Atherosclerotic Plaques in Clinical Use Both (43-75 years) NCT02039648 The Influence of Rumex Acetosa L on the Intraoral Colonization With
Porphyromonas Gingivalis Both (>18 years) NCT01219595 Cranberry Proanthocyanidins for Modification of Intestinal E. Coli Flora and Prevention of Urinary Tract Infections in UTI-Susceptible Women Female (18-65 years) NCT01669317 Mechanisms Underlying the Sleep Promoting Effect of Cherry Juice Standardized to Its Proanthocyanidin Content
Both (>65 years) NCT01099150 Dark Chocolate and Platelet Function in Humans Both (18-70 years) NCT00100893 IH636 Grape Seed Extract in Preventing Breast Cancer Female (40-75 years) NCT02087735 Measurement of Urinary Catabolites of PACs as Biomarkers of Consumption of
Cranberry Extracts Female (18-40 years) NCT01969994 Absorption, Metabolism, and Excretion of (-)-[2-14C]Epicatechin in Humans Male (18-50 years) NCT01010841 Trial of Two Dietary Programs on Cardiometabolic Risk Factors in Subjects With Metabolic
Syndrome Female (20-75 years) NCT01289860 Investigating the Acute Effects of Flavonoids in Blueberries on Cognitive Function. Both (18-75 years) NCT00568152 Effect of Oligopin® on Blood Pressure. Both (>18 years) NCT00713167 The Efficacy of Red
Grape Seed Extract on Lipid Profile and Oxidized Low-Density Lipoprotein (OX-LDL) Both (21-64 years) NCT01398150 Cranberry Enhances Human Immune Function and Reduces Illness Both (18-50 years) NCT00740077 Bioavailability of Flavonoids and Phenolic Acids From Cranberry Juice Cocktail in Healthy Older Adults Both (50-70 years)
NCT01691430 A Trial of Cranberry Capsules for Urinary Tract Infection Prevention in Nursing Home Residents Female (>65 years) NCT02333461 Evaluation of Botanicals for Mechanisms Related to Appetite and Fat Metabolism Both (18-70 years) NCT01346774 Preventing Urinary
Tract Infection Post-Surgery Female (>18 years) NCT01681394 Effect of the Administration of a Polyphenol-rich Cocoa Extract on Peripheral Blood Mononuclear Cells Gene Expression Male (18-40 years) Tannins are bioactive compounds that are widely found in nature, and commonly present in edible and medicinal plants. Nowadays, most of the interest
in this field derives from the possible implications of tannin intake for disease prevention, and, to this end, significant advances in understanding the biological properties of these bioactive compounds have been made. Current epidemiological and clinical data have shown a very preliminary correlation between tannin intake and health benefits in humans
although further studies are necessary to better investigate the effect of tannins in particular categories of the population. However, there are still numerous issues to be addressed. One of these is the lack of scientific rigour, especially as far as experimental design is concerned. The common use of non-standardized food or plant extracts generates results
that are often controversial and difficult to interpret. Further studies on the pharmacological targets and toxicological features should be performed to gain a better understanding of bioavailability
metabolism, tissue distribution and behaviour of these complex molecules, also in relation to other bioactive compounds in order to identify possible interactions and adverse effects that may arise from the co-administration or by use of dietary supplements. In some cases, polyphenol intake can easily reach very high levels normally not encountered in the
typical diet. Given the peculiar pharmacokinetics of tannins, there are other aspects that should not be overlooked, that is the food matrix constituents which could exert their effects in the intestinal lumen. Also, the genetic aspects of individuals that could affect gut cell uptake. Finally, individual variations in microbiota can affect the metabolism and,
thus, the ultimate health effect in some cases. In our opinion, all these aspects should be taken into account, and an appropriate risk-benefit assessment should be made before making claims about the health effects in humans. The authors declare no conflicts of interest. Smeriglio, A., Barreca, D., Bellocco, E., and Trombetta, D. (2017)
to PHARMACOLOGY 2015/16: G Protein-Coupled Receptors. Br J Pharmacol 172: 5744-5869. [DOI] [PMC free article] [PubMed] [Google Scholar] Alexander SPH, Cidlowski JA, Kelly E, Marrion N, Peters JA, Benson HE et al. (2015c). The Concise Guide to PHARMACOLOGY 2015/16: Nuclear hormone receptors. Br J Pharmacol 172: 5956-5978. [DOI] [PMC
free article] [PubMed] [Google Scholar] Ammar el-SM, Said SA, El-Damarawy SL, Suddek GM (2013). Cardioprotective effect of grape-seed proanthocyanidins on doxorubicin-induced cardiac toxicity in rats. Pharm Biol 51: 339-344. [DOI] [PubMed] [Google Scholar] Bakkiyaraj D, Nandhini JR, Malathy B, Pandian SK (2013). The anti-biofilm potential of
(2011). Evaluation of the antioxidant and cytoprotective properties of the exotic fruit Annona cherimola Mill. (Annonaceae. Food Res Int 44: 2302-2310. [Google Scholar] Berry AC, Nakshabendi R, Abidali H, Atchaneeyasakul K, Dholaria K, Johnson C et al. (2016). Adverse Effects of Grape Seed Extract Supplement: A Clinical Case and Long-Term Follow-
Up. J Diet Suppl 13: 232-235. [DOI] [PubMed] [Google Scholar] Bertoia ML, Rimm EB, Mukamal KJ, Hu FB, Willett WC, Cassidy A (2015). Dietary flavonoid intake and weight maintenance: three prospective cohorts of 124,086 US men and women followed for up to 24 years. Br Med J 352: i17. [DOI] [PMC free article] [PubMed] [Google Scholar] Bittner K,
Kemme T, Peters K, Kersten S, Dänicke S, Humpf HU (2014). Systemic absorption and metabolism of dietary procyanidin B4 in pigs. Molecular Nutrition and. Food Res 58: 2261-2273. [DOI] [PubMed] [Google Scholar] Bladé C, Aragonès G, Arola-Arnal A, Muguerza B, Bravo FI, Salvadó MJ et al. (2016). Proanthocyanidins in health and disease. Biofactors
42: 5-12. [DOI] [PubMed] [Google Scholar] Blumberg JB, Camesano TA, Cassidy A, Kris-Etherton P, Howell A, Manach C et al. (2013). Cranberries and their bioactive constituents in human health. Advance in. Nutrition 4: 618-632. [DOI] [PMC free article] [PubMed] [Google Scholar] Brandão E, Soares S, Mateus N, de Freitas V (2014). In vivo interactions
between procyanidins and human saliva proteins: effect of repeated exposures to procyanidins solution. J Agric Food Chem 62: 9562-9568. [DOI] [PubMed] [Google Scholar] Brenes A, Viveros A, Chamorro S, Arija I (2016). Use of polyphenol-rich grape by-products in monogastric nutrition. A review. Anim Feed Sci Technol 211: 1-17. [Google Scholar] Cala
O, Dufourc EJ, Fouquet E, Manigand C, Laguerre M, Pianet I (2012). The colloidal state of tannins impacts the nature of their interaction with proteins: the case of salivary proline-rich protein/procyanidins binding. Langmuir 28: 17410-17418. [DOI] [PubMed] [Google Scholar] Cascaes MM, Guilhon GM, Andrade EH, Zoghbi M, Santos LS (2015).
Constituents and Pharmacological Activities of Myrcia (Myrtaceae): A Review of an Aromatic and Medicinal Group of Plants. Int J Mol Sci 16: 23881-23904. [DOI] [PMC free article] [PubMed] [Google Scholar] Chung YC, Huang CC, Chen CH, Chiang HC, Chen KB, Chen YJ et al. (2012). Grape-seed procyanidins inhibit the in vitro growth and invasion of the control of the con
pancreatic carcinoma cells. Pancreas 41: 447-454. [DOI] [PubMed] [Google Scholar] Cock IE (2015). The medicinal properties and phytochemistry of plants of the genus Terminalia (Combretaceae. Inflammopharmacology 23: 203-229. [DOI] [PubMed] [Google Scholar] Coppo E, Marchese A (2014). Antibacterial activity of polyphenols. Curr Pharm
Biotechnol 15: 380-390. [DOI] [PubMed] [Google Scholar] de Jesus NZ, de Souza Falcão H, Gomes IF, de Almeida Leite TJ, de Morais Lima GR, Barbosa-Filho JM et al. (2012). Tannins, peptic ulcers and related mechanisms. Int J Mol Sci 13: 3203-3228. [DOI] [PMC free article] [PubMed] [Google Scholar] Déprez S, Brézillon C, Rabot S, Philippe C, Mila I
Lapierre C et al. (2000). Polymeric proanthocyanidins are catabolized by a human colonic microflora into low molecular weight phenolic acids. J Nutr 130: 2733-2738. [DOI] [PubMed] [Google Scholar] de Rezende AA, Graf U, Guterres Zda R, Kerr WE, Spanó MA (2009). Protective effects of proanthocyanidins of grape (Vitis vinifera L.) seeds on DNA
damage induced by Doxorubicin in somatic cells of Drosophila melanogaster. Food Chem Toxicol 47: 1466-1472. [DOI] [PubMed] [Google Scholar] Deáková Z, Andrezálová L, Slezák P, Lehotay J, Muchová J (2015). Influence of oak wood polyphenols on cysteine, homocysteine and glutathione total levels and PON1 activities in human adultations.
volunteers - a pilot study. Gen Physiol Biophys 34: 73-80. [DOI] [PubMed] [Google Scholar] Dias R, Perez-Gregorio MR, Mateus N, De Freitas V (2016). Interaction study between wheat-derived peptides and procyanidin B3 by mass spectrometry. Food Chem 194: 1304-1312. [DOI] [PubMed] [Google Scholar] Dias R, Perez-Gregorio MR, Mateus N, De Freitas V (2016). Interaction study between wheat-derived peptides and procyanidin B3 by mass spectrometry.
(2013). Preparation of A-type proanthocyanidin dimers from peanut skins and persimmon pulp and comparison of the antioxidant activity of A-type and B-type dimers. Fitoterapia 91: 128-139. [DOI] [PubMed] [Google Scholar] Draijer R, de Graaf Y, Slettenaar M, de Groot E, Wright CI (2015). Consumption of a polyphenol-rich grape-wine extract lowers
ambulatory blood pressure in mildly hypertensive subjects. Nutrients 7: 3138-3153. [DOI] [PMC free article] [PubMed] [Google Scholar] EFSA (2014). Scientific Opinion on the safety and efficacy of tannic acid when used as feed flavouring for all animal species. EFSA J 12: 3828. [Google Scholar] Ekambaram SP, Perumal SS, Balakrishnan A (2016). Scope
of Hydrolysable Tannins as Possible Antimicrobial Agent. Phytother Res 30: 1035-1045. [DOI] [PubMed] [Google Scholar] Ellam S, Williamson G (2013). Cocoa and human health. Annu Rev Nutr 33: 105-128. [DOI] [PubMed] [Google Scholar] Ellam S, Williamson G (2013). Cocoa and human health. Annu Rev Nutr 33: 105-128. [DOI] [PubMed] [Google Scholar] Ellam S, Williamson G (2013). Cocoa and human health. Annu Rev Nutr 33: 105-128. [DOI] [PubMed] [Google Scholar] Ellam S, Williamson G (2013). Cocoa and human health. Annu Rev Nutr 33: 105-128. [DOI] [PubMed] [Google Scholar] Ellam S, Williamson G (2013). Cocoa and human health. Annu Rev Nutr 33: 105-128. [DOI] [PubMed] [Google Scholar] Ellam S, Williamson G (2013). Cocoa and human health. Annu Rev Nutr 33: 105-128. [DOI] [PubMed] [Google Scholar] Ellam S, Williamson G (2013). Ellam S, Williamson 
Microbial Ellagic Acid-Derived Metabolites: The Evidence So Far. Evid Based Complement Alternat Med 2013: 270418. [DOI] [PMC free article] [PubMed] [Google Scholar] Fiume MM, Bergfeld WF, Belsito DV, Hill RA, Klaassen CD, Liebler DC (2014). Safety assessment of Vitis vinifera (grape)-derived ingredients as used in cosmetics. Int J Toxicol 33: 48S-
83S. [DOI] [PubMed] [Google Scholar] Fuentes JL, Vernhe M, Cuetara EB, Sánchez-Lamar A, Santana JL, Llagostera M (2006). Tannins from barks of Pinus caribaea protect Escherichia coli cells against DNA damage induced by gamma-rays. Fitoterapia 77: 116-120. [DOI] [PubMed] [Google Scholar] Fuentes JL, Vernhe M, Cuetara EB, Sánchez-Lamar A, Santana JL, Llagostera M (2006). Tannins from barks of Pinus caribaea protect Escherichia coli cells against DNA damage induced by gamma-rays.
Miyazawa T (2015). Young persimmon ingestion suppresses lipid oxidation in rats. J Nutr Sci Vitaminol (Tokyo) 61: 90-95. [DOI] [PubMed] [Google Scholar] Gato N, Kadowaki A, Hashimoto N, Yokoyama S, Matsumoto K (2013). Persimmon fruit tannin-rich fiber reduces cholesterol levels in humans. Ann Nutr Metab 62: 1-6. [DOI] [PubMed] [Google Scholar]
Scholar] Georgiev V, Ananga A, Tsolova V (2014). Recent advances and uses of grape flavonoids as nutraceuticals. Nutrients 6: 391-415. [DOI] [PMC free article] [PubMed] [Google Scholar] Gollucke AP, Aguiar O Jr, Barbisan LF, Ribeiro DA (2013). Use of grape polyphenols against carcinogenesis: putative molecular mechanisms of action using in vitro
and in vivo test systems. J Med Food 16: 199-205. [DOI] [PubMed] [Google Scholar] Gonzalez-Abuin N, Pinent M, Casanova-Marti A, Arola L, Blay M, Ardevol A (2015). Procyanidins and their healthy protective effects against type 2 diabetes. Curr Med Chem 22: 39-50. [DOI] [PubMed] [Google Scholar] Goodrich KM, Smithson AT, Ickes AK, Neilson AP
(2015). Pan-colonic pharmacokinetics of catechins and procyanidins in male Sprague-Dawley rats. J Nutr Biochem 26: 1007-1014. [DOI] [PubMed] [Google Scholar] Guil-Guerrero JL, Ramos L, Moreno C, Zúñiga-Paredes JC, Carlosama-Yepez M, Ruales P (2016). Antimicrobialactivityofplant-foodby-products: Areviewfocusing on thetropics. Livest Sci 189: 32-
49. [Google Scholar] Guler A, Sahin MA, Yucel O, Yokusoglu M, Gamsizkan M, Ozal E et al. (2011). Proanthocyanidin prevents myocardial ischemic injury in adult rats. Med Sci Monit 17: BR326-BR331. [DOI] [PMC free article] [PubMed] [Google Scholar] Hamilton K, Bennett NC, Purdie G, Herst PM (2015). Standardized cranberry capsules for radiation
cystitis in prostate cancer patients in New Zealand: a randomized double blinded, placebo controlled pilot study. Support Care Cancer 23: 95-102. [DOI] [PubMed] [Google Scholar] Hassan W, Noreen H, Khalil S, Hussain A, Rehman S, Sajjad S et al. (2016). Ethanolic extract of Nigella sativa protects Fe(II) induced lipid peroxidation in rat's brain, kidney
and liver homogenates. Pak J Pharm Sci 29: 231-237. [PubMed] [Google Scholar] Holt RR, Heiss C, Kelm M, Keen CL (2012). The potential of flavanol and procyanidin intake to influence age-related vascular disease. J Nutr Gerontol Geriatr 31: 290-323. [DOI] [PubMed] [Google Scholar] Hort MA, Straliotto MR, Duz MS, Netto PM, Souza CB, Schulz Tanana (1998).
(2012). Cardioprotective effects of a proanthocyanidin-rich fraction from Croton celtidifolius Baill: focus on atherosclerosis. Food Chem Toxicol 50: 3769-3775. [DOI] [PubMed] [Google Scholar] Horvathova M, Orszaghova Z, Laubertova L, Vavakova M, Sabaka P, Rohdewald P et al. (2014). Effect of the French oak wood extract Robuvit on markers of
oxidative stress and activity of antioxidant enzymes in healthy volunteers: a pilot study. Oxid Med Cell Longev 2014: 639868. [DOI] [PMC free article] [PubMed] [Google Scholar] Howell A, Souza D, Roller M, Fromentin E (2015). Comparison of the Anti-Adhesion Activity of Three Different Cranberry Extracts on Uropathogenic P-fimbriated Escherichia coli
a Randomized, Double-blind, Placebo Controlled, Ex Vivo, Acute Study. Nat Prod Commun 10: 1215–1218. [PubMed] [Google Scholar] Iglesias J, Pazos M, Torres JL, Medina I (2012). Antioxidant mechanism of grape procyanidins in muscle tissues: redox interactions with endogenous ascorbic acid and α-tocopherol. Food Chem 134: 1767–1774. [DOI]
[PubMed] [Google Scholar] Izzo AA, Hoon-Kim S, Radhakrishnan R, Williamson EM (2016). A critical Approach to Evaluating Clinical Efficacy, Adverse Events and Drug Interactions of Herbal Remedies. Phytother Res 30: 691-700. [DOI] [PubMed] [Google Scholar] Jepson R, Craig J, Williamson EM (2013). Cranberry products and prevention of urinary tractions of Herbal Remedies.
infections. JAMA 310: 1395-1396. [DOI] [PubMed] [Google Scholar] Jiménez N, Esteban-Torres M, Mancheño JM, de las Rivas B, Muñoz R (2014). Tannin Degradation by a Novel Tannase Enzyme Present in Some Lactobacillus plantarum Strains. Appl Environ Microbiol 80: 2991-2997. [DOI] [PMC free article] [PubMed] [Google Scholar] Kamiloglu S,
Capanoglu E, Bilen FD, Gonzales GB, Grootaert C, Van de Wiele T et al. (2016). Journal of Agricoltural and. Food Chem 64: 2450-2458. [DOI] [PubMed] [Google Scholar] Kancheva VD, Kasaikina OT (2013). Bio-antioxidants a chemical base of their antioxidants a chemical base of their antioxidant activity and beneficial effect on human health. Curr Med Chem 20: 4784-4805. [DOI] [PubMed]
[Google Scholar] Katiyar SK (2015). Proanthocyanidins from grape seeds inhibit UV-radiation-induced immune suppression in mice: detection and analysis of molecular and cellular targets. Photochem Photobiol 91: 156–162. [DOI] [PMC free article] [PubMed] [Google Scholar] Kaur SJ, Grover IS, Kumar S (2000). Modulatory effects of a tannin fraction
isolated from Terminalia arjuna on the genotoxicity of mutagens in Salmonella typhimurium. Food Chem Toxicol 38: 1113-1119. [DOI] [PubMed] [Google Scholar] Kay CD, Hooper L, Kroon PA, Rimm EB, Cassidy A (2012). Relative impact of flavonoid composition, dose and structure on vascular function: a systematic review of randomised controlled trials
of flavonoid-rich food products. Mol Nutr Food Res 56: 1605-1616. [DOI] [PubMed] [Google Scholar] Kim J, Kim J, Shim J, Lee CY, Lee KW, Lee HJ (2014). Cocoa phytochemicals: recent advances in molecular mechanisms on health. Critical Review Food Scince. Nutrition 54: 1458-1472. [DOI] [PubMed] [Google Scholar] Kooti W, Farokhipour M, Asadzadeh
Z, Ashtary-Larky D, Asadi-Samani M (2016). The role of medicinal plants in the treatment of diabetes: a systematic review. Electron Physician J 8: 1832-1842. [DOI] [PMC free article] [PubMed] [Google Scholar] Kumari M, Jain S (2012). Tannins: An Antinutrient with Positive Effect to Manage Diabetes. Research Journal of Recent. Sciences 1: 70-73.
[Google Scholar] Lamy E, Pinheiro C, Rodrigues L, Capela e Silva F, Lopes OS, Tavares S et al. (2016). Determinants of Tannins: Biochemistry, Food Sources and Nutritional Properties. Nova Science Publishers Inc: New York, USA, pp. 29-58.
[Google Scholar] Landete JM (2011). Ellagitannins, ellagic acid and their derived metabolites: A review about source, metabolism, functions and health. Food Res Int 44: 1150-1160. [Google Scholar] Lehmann M, Graf U, Reguly ML, Rodrigues De Andrade HH (2000). Interference of tannic acid on the genotoxicity of mitomycin C, methylmethanesulfonate
and nitrogen mustard in somatic cells of Drosophila melanogaster. Environ Mol Mutagen 36: 195-200. [DOI] [PubMed] [Google Scholar] Li M, Jia X, Yang J, Deng J, Zhao G (2012). Effect of tannic acid on properties of soybean (Glycine max) seed ferritin: a model for interaction between naturally occurring components in foodstuffs. Food Chem 133: 410-
415. [DOI] [PubMed] [Google Scholar] Li S, Xu M, Niu Q, Xu S, Ding Y, Yan Y et al. (2013a). Efficacy of Procyanidins against In Vivo Cellular Oxidative Damage: A Systematic Review and Meta-Analysis. PLoS One 10: e0139455. [DOI] [PMC free article] [PubMed] [Google Scholar] Li S, Xu M, Niu Q, Xu S, Ding Y, Yan Y et al. (2013a). Absorption and urinary
excretion of A-type procyanidin oligomers from Litchi chinensis pericarp in rats by selected ion monitoring liquid chromatography-mass spectrometry. Food Chem 138: 1536-1542. [DOI] [PubMed] [Google Scholar] Li Z, Henning SM, Lee RP, Lu QY, Summanen PH, Thames G et al. (2015b). Pomegranate extract induces ellagitannin metabolite formation
and changes stool microbiota in healthy volunteers. Food Funct 6: 2487-2495. [DOI] [PubMed] [Google Scholar] Liu CM, Ma JQ, Liu SS, Zheng GH, Feng GH, Feng GH, Feng CH, Feng 
ZJ, Sun JM (2014). Proanthocyanidins improves lead-induced cognitive impairments by blocking endoplasmic reticulum stress and nuclear factor-kB-mediated inflammatory pathways in rats. Food Chem Toxicol 72: 295-302. [DOI] [PubMed] [Google Scholar] Lluís L, Muñoz M, Nogués MR, Sánchez-Martos V, Romeu M, Giralt M et al. (2011). Toxicology
evaluation of a procyanidin-rich extract from grape skins and seeds. Food Chem Toxicol 49: 1450-1454. [DOI] [PubMed] [Google Scholar] Lu C, Luo X, Lu L, Li H, Chen X, Ji Y (2013). Preliminary extract using macroporous resins. J Sep Sci 36: 959-
964. [DOI] [PubMed] [Google Scholar] Margină D, Ilie M, Grădinaru D, Androutsopoulos VP, Kouretas D, Tsatsakis AM (2015). Natural products-friends or foes? Toxicol Lett 236: 154-167. [DOI] [PubMed] [Google Scholar] Margină D, Ilie M, Grădinaru D, Androutsopoulos VP, Kouretas D, Tsatsakis AM (2015). Natural products-friends or foes? Toxicol Lett 236: 154-167. [DOI] [PubMed] [Google Scholar] Margină D, Ilie M, Grădinaru D, Androutsopoulos VP, Kouretas D, Tsatsakis AM (2015). Natural products-friends or foes? Toxicol Lett 236: 154-167. [DOI] [PubMed] [Google Scholar] Margină D, Ilie M, Grădinaru D, Androutsopoulos VP, Kouretas D, Tsatsakis AM (2015). Natural products-friends or foes? Toxicol Lett 236: 154-167. [DOI] [PubMed] [Google Scholar] Margină D, Ilie M, Grădinaru D, Androutsopoulos VP, Kouretas D, Tsatsakis AM (2015). Natural products-friends or foes? Toxicol Lett 236: 154-167. [DOI] [PubMed] [Google Scholar] Margină D, Ilie M, Grădinaru D, Androutsopoulos VP, Kouretas D, Tsatsakis AM (2015). Natural products-friends or foes? Toxicol Lett 236: 154-167. [DOI] [PubMed] [Google Scholar] Margină D, Ilie M, Grădinaru D, Androutsopoulos VP, Kouretas D, Tsatsakis AM (2015). Natural products-friends or foes? Toxicol Lett 236: 154-167. [DOI] [PubMed] [Google Scholar] Margină D, Ilie M, Grădinaru D, Androutsopoulos VP, Kouretas D, Tsatsakis AM (2015). [Doi: 10.000] [PubMed] [Google Scholar] [PubMed] [Goog
properties. Biomed Res Int 2015: 905215. [DOI] [PMC free article] [PubMed] [Google Scholar] Marques NF, Stefanello ST, Froeder AL, Busanello A, Boligon AA, Athayde ML et al. (2015). Centella asiatica and Its Fractions Reduces Lipid Peroxidation Induced by Quinolinic Acid and Sodium Nitroprusside in Rat Brain Regions. Neurochem Res 40: 1197-
1210. [DOI] [PubMed] [Google Scholar] Masci A, Coccia A, Lendaro E, Mosca L, Paolicelli P, Cesa S (2016). Evaluation of different extraction methods from pomegranate whole fruit or peels and the antioxidant and antiproliferative activity of the polyphenolic fraction. Food Chem 202: 59-69. [DOI] [PubMed] [Google Scholar] Mateos-Martín ML, Fuguet E,
Quero C, Pérez-Jiménez J, Torres JL (2012). New identification of proanthocyanidins in cinnamon (Cinnamomum zeylanicum L.) using MALDI-TOF/TOF mass spectrometry. Anal Bioanal Chem 402: 1327-1336. [DOI] [PubMed] [Google Scholar] Mathew AS, Capel-Williams GM, Berry SE, Hall WL (2012). Acute effects of pomegranate extract on postprandial
lipaemia, vascular function and blood pressure. Plant Foods Hum Nutr 67: 351-357. [DOI] [PubMed] [Google Scholar] Micali S, Isgro G, Bianchi G, Miceli N, Calapai G, Navarra M (2014). Cranberry and recurrent cystitis: more than marketing? Crit Rev Food Sci Nutr 54: 1063-1075. [DOI] [PubMed] [Google Scholar] Mohana T, Navin AV, Jamuna S,
Sakeena Sadullah MS, Niranjali Devaraj S (2015). Inhibition of differentiation of monocyte to macrophages in atherosclerosis by oligomeric proanthocyanidins -In-vivo and in-vitro study. Food Chem Toxicol 82: 96-105. [DOI] [PubMed] [Google Scholar] Natella F, Leoni G, Maldini M, Natarelli L, Comitato R, Schonlau F et al. (2014). Absorption, metabolism
and effects at transcriptome level of a standardized French oak wood extract, Robuvit, in healthy volunteers: pilot study. J Agric Food Chem 62: 443-453. [DOI] [PubMed] [Google Scholar] Nazima B, Manoharan V, Miltonprabu S (2015). Grape seed proanthocyanidins ameliorates cadmium-induced renal injury and oxidative stress in experimental rats
through the up-regulation of nuclear related factor 2 and antioxidant responsive elements. Biochem Cell Biol 93: 210-226. [DOI] [PubMed] [Google Scholar] Nuñez-Sánchez MA, García-Villalba R,
Monedero-Saiz T, García-Talavera NV, Gómez-Sánchez MB, Sánchez-Álvarez C et al. (2014). Targeted metabolic profiling of pomegranate polyphenols and urolithins in plasma, urine and colon tissues from colorectal cancer patients. Mol Nutr Food Res 58: 1199-1211. [DOI] [PubMed] [Google Scholar] Okuda T, Ito H (2011). Tannins of Constant Structures
in Medicinal and Food Plants—Hydrolyzable Tannins and Polyphenols Related to Tannins. Molecules 16: 2191-2217. [Google Scholar] Oliveira BG, Costa HB, Ventura JA, Kondratyuk TP, Barroso ME, Correia RM et al. (2016). Chemical profile of mango (Mangifera indica L.) using electrospray ionisation mass spectrometry (ESI-MS. Food Chem 204: 37-45.
[DOI] [PubMed] [Google Scholar] Ou K, Gu L (2014). Absorption and metabolism of proanthocyanidins. J Funct Foods 7: 43-53. [Google Scholar] Ouédraogo M, Guissou IP, Stévigny C, Duez P (2011). An overview of cancer chemopreventive potential and safety of proanthocyanidins. Nutr Cancer 63: 1163-1173. [DOI] [PubMed]
[Google Scholar] Park SY, Lee YH, Choi KC, Seong AR, Choi HK, Lee OH et al. (2011). Hwang HJ, Yoon HG (2011). Grape seed extract regulates androgen receptor-mediated transcription in prostate cancer cells through potent anti-histone acetyltransferase activity. J Med Food 14: 9-16. [DOI] [PubMed] [Google Scholar] Pinent M, Cedó L, Montagut G,
Blay M, Ardévol A (2012). Procyanidins improve some disrupted glucose homoeostatic situations: an analysis of doses and treatments according to different animal models. Crit Rev Food Sci Nutr 52: 569-584. [DOI] [PubMed] [Google Scholar] Pons Z, Guerrero L, Margalef M, Arola L, Arola-Arnal A, Muguerza B (2014). Effect of low molecular grape seed
proanthocyanidins on blood pressure and lipid homeostasis in cafeteria diet-fed rats. J Physiol Biochem 70: 629-637. [DOI] [PubMed] [Google Scholar] Prasad R, Katiyar SK (2014). Down-regulation of miRNA-106b inhibits growth of melanoma cells by promoting G1-phase cell cycle arrest and reactivation of p21/WAF1/Cip1 protein. Oncotarget 5: 10636-
 10649. [DOI] [PMC free article] [PubMed] [Google Scholar] Quifer-Rada P, Choy YY, Calvert CC, Waterhouse AL, Lamuela-Raventos RM (2016). Use of metabolomics and lipidomics to evaluate the hypocholestreolemic effect of Proanthocyanidins from grape seed in a pig model. Mol Nutr Food Res 60: 2219-2227. [DOI] [PubMed] [Google Scholar] Salvadó
MJ, Casanova E, Fernández-Iglesias A, Arola L, Bladé C (2015). Roles of proanthocyanidin rich extracts in obesity. Food Funct 6: 1053-1071. [DOI] [PubMed] [Google Scholar] Sánchez-Moreno C, Cao G, Ou B, Prior RL (2003). Anthocyanidin rich extracts in obesity. Food Funct 6: 1053-1071. [DOI] [PubMed] [Google Scholar] Sánchez-Moreno C, Cao G, Ou B, Prior RL (2003). Anthocyanidin rich extracts in obesity.
nontraditional wines obtained from highbush blueberry. J Agric Food Chem 51: 4889-4896. [DOI] [PubMed] [Google Scholar] Serrano J, Casanova-Martí À, Gil-Cardoso K, Blay MT, Terra X, Pinent M et al. (2016). Acutely administered grape-seed proanthocyanidin extract acts as a satiating agent. Food Funct 7: 483-490. [DOI] [PubMed] [Google Scholar]
Serrano J, Puupponen-Pimiä R, Dauer A, Aura AM, Saura-Calixto F (2009). Tannins: current knowledge of food sources, intake, bioavailability and biological effects. Mol Nutr Food Res 2: S310-S329. [DOI] [PubMed] [Google Scholar] Sieniawska E (2015). Activities of Tannins:-From In Vitro Studies to Clinical Trials. Nat Prod Commun 10: 1877-1884.
[PubMed] [Google Scholar] Skrovankova S, Sumczynski D, Mlcek J, Jurikova T, Sochor J (2015). Bioactive Compounds and Antioxidant Activity in Different Types of Berries. Int J Mol Sci 16: 24673–24706. [DOI] [PMC free article] [PubMed] [Google Scholar] Smeriglio A, Monteleone D, Trombetta D (2014a). Health effects of Vaccinium myrtillus L.:
evaluation of efficacy and technological strategies for preservation of active ingredients. Mini Rev Med Chem 14: 567-584. [DOI] [PubMed] [Google Scholar] Smeriglio A, Trombetta D (2014b). Herbal products in pregnancy: experimental studies and clinical reports. Phytother Res 28: 1107-1116. [DOI] [PubMed] [Google Scholar] Southan C
Sharman JL, Benson E, Faccenda E, Pawson AJ, Alexander SP et al. (2016). The IUPHAR/BPS Guide to PHARMACOLOGY in 2016: towards curated quantitative interactions between 1300 protein targets and 6000 ligands. Nucleic Acids Res. 44 (D1): D1054-D1068. [DOI] [PMC free article] [PubMed] [Google Scholar] Stalmach A, Williamson G, Crozier A
(2014). Impact of dose on the bioavailability of coffee chlorogenic acids in humans. Food Funct 5: 1727-1737. [DOI] [PubMed] [Google Scholar] Terauchie of Salacia reticulata and Related Species. Phytother Res 29: 986-995. [DOI] [PubMed] [Google Scholar] Terauchie of Salacia reticulata and Related Species. Phytother Res 29: 986-995. [DOI] [PubMed] [Google Scholar] Terauchie of Salacia reticulata and Related Species. Phytother Res 29: 986-995. [DOI] [PubMed] [Google Scholar] Terauchie of Salacia reticulata and Related Species. Phytother Res 29: 986-995. [DOI] [PubMed] [Google Scholar] Terauchie of Salacia reticulata and Related Species. Phytother Res 29: 986-995. [DOI] [PubMed] [Google Scholar] Terauchie of Salacia reticulata and Related Species. Phytother Res 29: 986-995. [DOI] [PubMed] [Google Scholar] Terauchie of Salacia reticulata and Related Species. Phytother Res 29: 986-995. [DOI] [PubMed] [Google Scholar] Terauchie of Salacia reticulata and Related Species. Phytother Res 29: 986-995. [DOI] [PubMed] [Google Scholar] Terauchie of Salacia reticulata and Related Species. Phytother Res 29: 986-995. [DOI] [PubMed] [Google Scholar] Terauchie of Salacia reticulata and Related Species. Phytother Res 29: 986-995. [DOI] [PubMed] [Google Scholar] Terauchie of Salacia reticulata and Related Species. Phytother Res 29: 986-995. [DOI] [PubMed] [Google Scholar] Terauchie of Salacia reticulata and Related Species. Phytother Res 29: 986-995. [DOI] [PubMed] [Google Scholar] Terauchie of Salacia reticulata and Related Species. Phytother Res 29: 986-995. [DOI] [PubMed] [Google Scholar] Terauchie of Salacia reticulata and Related Species. Phytother Res 29: 986-995. [DOI] [PubMed] [Google Scholar] Terauchie of Salacia reticulata and Related Species. Phytother Res 29: 986-995. [DOI] [PubMed] [PubMed
M, Horiguchi N, Kajiyama A, Akiyoshi M, Owa Y, Kato K et al. (2014). Effects of grape seed proanthocyanidin extract on menopausal symptoms, body composition, and cardiovascular parameters in middle-aged women: a randomized, double-blind, placebo-controlled pilot study. Menopause 21: 990–996. [DOI] [PubMed] [Google Scholar] Turati F, Rossi M,
Pelucchi C, Levi F, La Vecchia C (2015). Fruit and vegetables and cancer risk: a review of southern European studies. Br J Nutr 113: S102-S110. [DOI] [PubMed] [Google Scholar] Velderrain-Rodríguez GR, Palafox-Carlos H, Wall-Medrano A, Ayala-Zavala JF, Chen CY, Robles-Sánchez M et al. (2014). Phenolic compounds: their journey after intake. Food
Proanthocyanidins Key to Cranberry Efficacy in the Prevention of Recurrent Urinary Tract Infection? Phytother Res 29: 1559-1567. [DOI] [PubMed] [Google Scholar] Wang X, Jun YY, Zhao G (2014). Flavonoid intake and risk of CVD: a systematic review and meta-analysis of prospective cohort studies. Br J Nutr 111: 1-11. [DOI] [PubMed] [Google Scholar]
Wiese S, Esatbeyoglu T, Winterhalter P, Kruse HP, Winkler S, Bub A et al. (2015). Comparative biokinetics and metabolism of pure monomeric, dimeric, and polymeric flavan-3-ols: a randomized cross-over study in humans. Mol Nutr Food Res 59: 610-621. [DOI] [PubMed] [Google Scholar] Xu ZC, Yin J, Zhou B, Liu YT, Yu Y, Li GQ (2015). Grape seed
proanthocyanidin protects liver against ischemia/reperfusion injury by attenuating endoplasmic reticulum stress. World J Gastroenterol 21: 7468-7477. [DOI] [PMC free article] [PubMed] [Google Scholar] Yang H, Xiao L, Yuan Y, Luo X, Jiang M, Ni J et al. (2014). Procyanidin B2 inhibits NLRP3 inflammasome activation in human vascular endothelial cells
Biochem Pharmacol 92: 599-606. [DOI] [PubMed] [Google Scholar] Yang M, Chung SJ, Floegel A, Song WO, Koo SI, Chun OK (2013). Dietary antioxidant status and decreased serum antioxidant status and decreased serum C-reactive protein and plasma homocysteine concentrations. Eur J Nutr 52: 1901-1911. [DOI] [PubMed] [Google Scholar] Yang M, Chung SJ, Floegel A, Song WO, Koo SI, Chun OK (2013). Dietary antioxidant status and decreased serum C-reactive protein and plasma homocysteine concentrations.
Scholar] Yunoki T, Deguchi K, Omote Y, Liu N, Liu W, Hishikawa N (2014). Anti-oxidative nutrient-rich diet protects against acute ischemic brain damage in rats. Brain Res 1587: 33-39. [DOI] [PubMed] [Google Scholar] Zhang L, Wang Y, Li D, Ho CT, Li J, Wan X (2016). The absorption, distribution, metabolism and excretion of procyanidins. Food Funct 7
1273-1281. [DOI] [PubMed] [Google Scholar] Zhou Q, Yin ZP, Ma L, Zhao W, Hao HW, Li HL (2014). Free radical-scavenging activities of oligomeric proanthocyanidin from Rhodiolarosea L. and its antioxidant effects in vivo. Nat Prod Res 28: 2301-2303. [DOI] [PubMed] [Google Scholar] Zorenc Z, Veberic R, Stampar F, Koron D, Mikulic-Petkovsek M
(2016). White versus blue: Does the wild 'albino' bilberry (Vaccinium myrtillus L.) differ in fruit quality compared to the blue one? Food Chem 211: 876-882. [DOI] [PubMed] [Google Scholar] Zou Y, Guo J, Yin SW, Wang JM, Yang XQ (2015). Pickering Emulsion Gels Prepared by Hydrogen-Bonded Zein/Tannic Acid Complex Colloidal Particles. J Agric Food
Chem 63: 7405-7414. [DOI] [PubMed] [Google Scholar] Articles from British Journal of Pharmacology are provided here courtesy of The British Pharmacology are provided here.
against microbes, insects and vertebrate herbivores. Hydrolyzable tannins also impact soil nutrient dynamics and affect the germination, growth and development of other plant species. Besides impact soil nutrient dynamics and affect the germination, growth and development of other plant species.
biosynthesis using strawberry and pomegranate as model systems. Cloning of hydrolyzable tannin biosynthetic genes will facilitate modification of plant composition for improved protein utilization in forage crops. Underpinning hydrolyzable tannin biosynthesis using strawberry and pomegranate as model systems. Cloning of hydrolyzable tannin biosynthesis using strawberry and pomegranate as model systems.
plant (allelopathic) interactions. Broader Impacts In addition to the scientific impacts, various aspects of the research will be used to provide multidisciplinary training opportunities, encompassing molecular biology, biochemistry, and cell biology, to high school, undergraduate, and graduate students, and postdoctoral scholars. The educational activities at
the undergraduate level will be focused on three areas: providing research opportunities to new UC Davis transfer students, and retaining students from low-income families. Another major focus of the educational activities is to prepare graduate students and postdoctoral
scholars for their future independent careers in science. An outreach program is currently being developed to expose high school students to research activities and biotechnological applications through internships in the PI's laboratory. PUBLICATIONS PRODUCED AS A RESULT OF THIS RESEARCH Note: When clicking on a Digital Object Identifier
(DOI) number, you will be taken to an external site maintained by the publisher. Some full text articles may not yet be available without a charge during the embargo (administrative interval). Some links on this page may take you to non-federal websites. Their policies may differ from this site. Ono, N.N., Britton, M.T., Fass, J.N., Nicolet, C.M., Lin, D.W.
and Tian, L. "Exploring the transcriptome landscape of pomegranate (Punica granatum) fruit peel for natural product biosynthetic gene and SSR marker discovery." Journal of Integrative Plant Science, v.180, 2011, p.439 Ono, N.N., and Tian, L. "The multiplicity of hairy root cultures: prolific possibilities." Plant Science, v.180, 2011, p.439 Ono, N.N.,
Bandaranayake, P.G. and Tian, L. "Establishment of pomegranate (Punica granatum) hairy root cultures for genetic interrogation of the hydrolyzable tannin biosynthetic pathway." Planta, v.236, 2012, p.931-941 PROJECT OUTCOMES REPORT Disclaimer This Project Outcomes Report for the General Public is displayed verbatim as submitted by the
Principal Investigator (PI) for this award. Any opinions, findings, and conclusions or recommendations expressed in this Report are those of the PI and do not necessarily reflect the views of the National Science Foundation; NSF has not approved or endorsed its content. Plants synthesize specialized chemicals that play important roles in ensuring optimal
plant growth and effective defense against pathogens and predators; healthy plants can provide abundant food and medicine for human nutrition and health, as well as biomass for biofuel production. Our investigations centered on understanding how a group of specialized chemicals named hydrolyzable tannins are synthesized in plants. Although many
beneficial activities have been reported for hydrolyzable tannins in animals and humans, there is a gap in our understanding of their production in plants, knowledge that is necessary for dissecting the mechanistic basis of their production in plants, knowledge that is necessary for dissecting the mechanistic basis of their production in plants, knowledge that is necessary for dissecting the mechanistic basis of their production in plants, knowledge that is necessary for dissecting the mechanistic basis of their production in plants, knowledge that is necessary for dissecting the mechanistic basis of their production in plants, knowledge that is necessary for dissecting the mechanistic basis of their production in plants, knowledge that is necessary for dissecting the mechanistic basis of their production in plants, knowledge that is necessary for dissecting the mechanistic basis of their production in plants, knowledge that is necessary for dissecting the mechanistic basis of their production in plants, knowledge that is necessary for dissecting the mechanistic basis of their production in plants, knowledge that is necessary for dissecting the mechanistic basis of their production in plants, knowledge that is necessary for dissecting the mechanistic basis of the mechanism of t
and demonstrated for the first time their functions in plants. Isolation of hydrolyzable tannin biosynthetic genes provides critical molecular tools for modification of hydrolyzable tannin biosynthetic genes provides critical molecular tools for modification of hydrolyzable tannin biosynthetic genes provides critical molecular tools for modification of hydrolyzable tannin biosynthetic genes provides critical molecular tools for modification of hydrolyzable tannin biosynthetic genes provides critical molecular tools for modification of hydrolyzable tannin biosynthetic genes provides critical molecular tools for modification of hydrolyzable tannin biosynthetic genes provides critical molecular tools for modification of hydrolyzable tannin biosynthetic genes provides critical molecular tools for modification of hydrolyzable tannin biosynthetic genes provides critical molecular tools for modification of hydrolyzable tannin biosynthetic genes provides critical molecular tools for modification of hydrolyzable tannin biosynthetic genes provides critical molecular tools for modification of hydrolyzable tannin biosynthetic genes provides critical molecular tools for modification of hydrolyzable tannin biosynthetic genes provides critical molecular tools for modification of hydrolyzable tannin biosynthetic genes provides critical molecular tools for modification of hydrolyzable tannin biosynthetic genes provides critical molecular tools for modification of hydrolyzable tannin biosynthetic genes provides critical molecular tools for modification of hydrolyzable tannin biosynthetic genes provides critical molecular tools for modification of hydrolyzable tannin biosynthetic genes provides critical molecular tools for modification of hydrolyzable tannin biosynthetic genes provides critical molecular tools for modification of hydrolyzable tannin biosynthetic genes provides critical molecular tools for modification of hydrolyzable tannin biosynthetic genes provides critical molecular tools for modification of hydrolyzable tann
forage crops for animal consumption. Elucidation of hydrolyzable tannin biosynthesis will also broaden our understanding of general plant defense mechanisms, as well as plant-soil and plant-plant interactions. Various aspects of this research were used to provide multidisciplinary training opportunities, encompassing molecular biology, biochemistry and
cell biology, to high school, undergraduate and graduate students and postdoctoral researchers. In addition, we focused our educational activities on promoting graduate students and postdoctoral researchers for their future
independent careers in science. The PI has also incorporated topics on phytonutrients and human health into her classroom curriculum and developed an outreach program that exposed high school students to research activities and biotechnological applications through internships in the PI's laboratory. Last Modified: 07/17/2015 Modified by: Li Tian
Please report errors in award information by writing to: awardsearch@nsf.gov. NSF's Fiscal Year 2024 enacted budget Percent of budget supported by NSF across every state and U.S. territory Researchers, entrepreneurs, students and teachers supported by NSF Learn more about our
impacts Share — copy and redistribute the material in any purpose, even commercially. Adapt — remix, transform, and build upon the material for any purpose, even commercially. The licensor cannot revoke these freedoms as long as you follow the license terms. Attribution — You must give appropriate credit, provide a link to
the license, and indicate if changes were made. You may do so in any reasonable manner, but not in any way that suggests the license as the original. No additional restrictions — You may not apply
legal terms or technological measures that legally restrict others from doing anything the license permits. You do not have to comply with the license for elements of the material in the public domain or where your use is permitted by an applicable exception or limitation. No warranties are given. The license may not give you all of the permissions
necessary for your intended use. For example, other rights may limit how you use the material. Wikipedia 0.0 / 0 votes Hydrolyzable tannin or pyrogallol-type tannin is a type of tannin that, on heating with hydrochloric or sulfuric acids, yields gallic or ellagic acids. At the center of a hydrolyzable
tannin molecule, there is a carbohydrate (usually D-glucose but also cyclitols like quinic or shikimic acids). The hydroxyl groups of the carbohydrate are partially or totally esterified with phenolic groups such as gallic acid in gallotannins or ellagic acid in gallotannins are mixtures of polygalloyl glucoses and/or poly-galloyl quinic acid
derivatives containing in between 3 up to 12 gallic acid residues per molecule. Hydrolyzable tannins are the gallic acid esters of glucose in tannic acid (C76H52O46), found in the leaves and bark of many plant species. Hydrolysable tannins
can be extracted from different vegetable plants, such as chestnut wood (Castanea sativa), oak wood (Quercus infectoria and Rhus semialata), myrobalan (Terminalia chebula), sumac (Rhus coriaria) and Aleppo gallnuts (Andricus kollari). How to pronounce
hydrolysable tannin?How to say hydrolysable tannin in Sign language?NumerologyThe numerical value of hydrolysable tannin in Pythagorean Numerology is: 2 References Wikipedia - Select - 简体中文 (Chinese - Simplified) 繁體中文
(Chinese - Traditional) Español (Spanish) Esperanto (Esperanto) 日本語 (Japanese) Português (Português (Portuguêse) Deutsch (German) עברית (Hebrew) Gaeilge (Irish) Українська (Ukrainian) الدو (Urdu) Magyar (Hungarian) ПППП (Korean) المورة (Portuguêse) Portuguêse) (Indonesian) Italiano (Italian)
(Tamil) Türkçe (Turkish) מור (Telugu) [חחרות (Telugu) [חחרות (Telugu) [חחרות (Thai) Tiếng Việt (Vietnamese) Čeština (Czech) Polski (Polish) Bahasa Indonesian) Româneşte (Romanian) Nederlands (Dutch) Eλληνικά (Greek) Latinum (Latin) Svenska (Swedish) Dansk (Danish) Suomi (Finnish) שונישט (Persian) און ידיש (Yiddish) hujtptů (Armenian) Norsk (Norwegian) English (Engl
```