BIOACTIVE SUBSTANCES IN TREES AND SHRUBS OF CENTRAL EUROPE

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Abstract: Plants produce specific structures constituting a barrier hindering penetration of pathogens, while they also produce substances inhibiting pathogen growth . These compounds are secondary metabolites, such as phenolics, terpenoids, sesquiterpenoids, resins, tannins and alkaloids. Bioactive compounds are secendary metabolities from trees and shrubs are used in medicine, herbal medicine and cosmetology. To date fruits and flowers of exotic trees and shrubs have been primarily used as sources of bioactive compounds. In turn, search for new sources of bioactive compounds is currently focused on native plant species due to its availability. Application of such raw material needs to be based on knowledge of their chemical composition, particularly health-promoting or therapeutic compounds. Research conducted to date on European trees and shrubs has been scarce. This paper presents results of literature studies conducted to systematise knowledge on bioactive compounds found in trees and shrubs native to central Europe.
The aim of this review providing available information on the subject is to indicate gaps in the present knowledge.

Keywords: bioactive compounds from European trees and shrubs, gallic and cinnamic acids,
quercetin, pinosylvin, β–sitosterol, alfa- and β-pinene

1. Biosynthesis of active substances

Tree stands are exposed to the action of stress factors, both abiotic and biotic. The former include weather anomalies, UV radiation, intensive lighting, water deficit, substrate salinity, high temperature amplitudes and the presence of heavy metals. In turn, biotic factors include pest insects, pathogenic fungi, bacteria and viruses. Trees counter stressors by initiating defence mechanisms to minimise or eliminate disturbances in growth and development. They are related with the consumption of energy and assimilates, limited production of biomass, its disadvantageous allocation as well as reduced reproduction. The action of biotic stressors is mainly connected with trees and woody plants entering into symbiosis with antagonists of pathogens, insects, etc.

Plants produce specific structures constituting a barrier hindering penetration of pathogens, e.g. resin canals, the presence of waxes and resins on their surface, while they also produce substances inhibiting pathogen growth and reducing attractiveness of needles, etc. These compounds are secondary metabolites, such as phenolics, terpenoids, sesquiterpenoids, resins, tannins and alkaloids. A considerable number of secondary metabolites protect against the adverse effect of herbivorous insects [1,2], pathogenic fungi [3-6] and bacteria [7,8]. These compounds differ in their chemical structure and are found both on the surface of plants and inside their tissues. Most of them are located in vacuoles and cell walls of peripheral tissues. They are also contained in resins secreted from bark and fruits. Secondary metabolites are most frequently synthesised via three metabolic pathways: terpenoid (mevalonate), phenolic (shikimate) and nitrogen metabolism (amino acids). For woody plants the derivatives of the shikimate pathways are of greatest importance, e.g. phenolic compounds (phenols, alcohols and phenolic acids, phenylpropanoids, flavonoids, coumarins, tannins), hydroxamic acids and indole alkaloids [9-11].

1.1 The mevalonate pathway

The mevalonate pathway is initiated in the cytosol of plant cells, producing sterols, sesquiterpenes and triterpenes. It leads to the formation of active isoprene, being the primary structural unit of terpenoids [12]. Products of this pathway belong to the class of terpenoids and are formed as a result of condensation of 3 acetyl-CoA molecules. This process includes also the synthesis of isopentenyl pyrophosphate and 3,3-dimethylallyl pyrophosphate, which are recondensed to form the above-mentioned terpenoids [13, 14]. The other pathway for the synthesis of isopentenyl pyrophosphate takes place in plastids, where carotenoids are produced (Figure 1) [15].

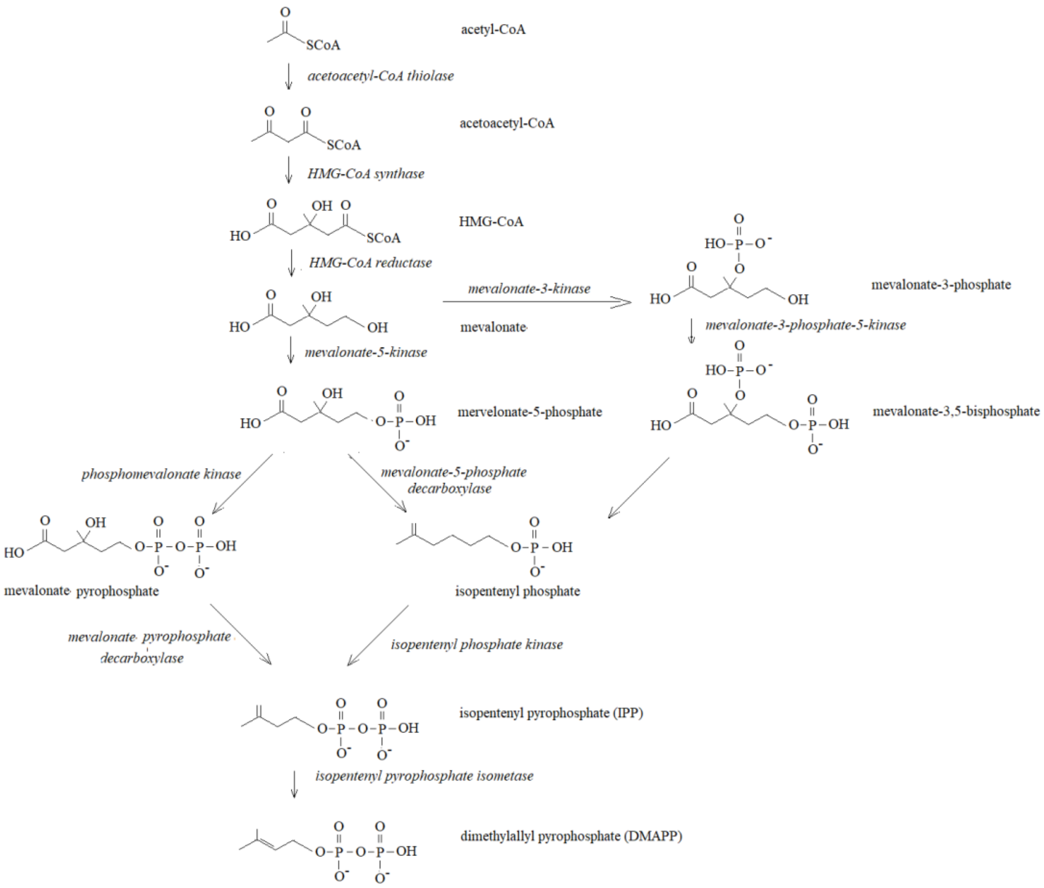


Figure 1. The mevalonate pathway

1.2 The shikimate pathway

This pathway plays an important role in the synthesis of many aromatic compounds in plants. In this pathway aromatic amino acids are formed, i.e. phenylalanine, tyrosine and tryptophan, used by higher plants as structural components of proteins and as precursors of secondary metabolites. In this process aromatic phenolic acids are produced, contained in complex structures of secondary metabolites, e.g. lignins [16, 17]. (Figure 2) They are synthesised in the reaction of phosphoenolpyruvate with erythrose-4-phosphate.

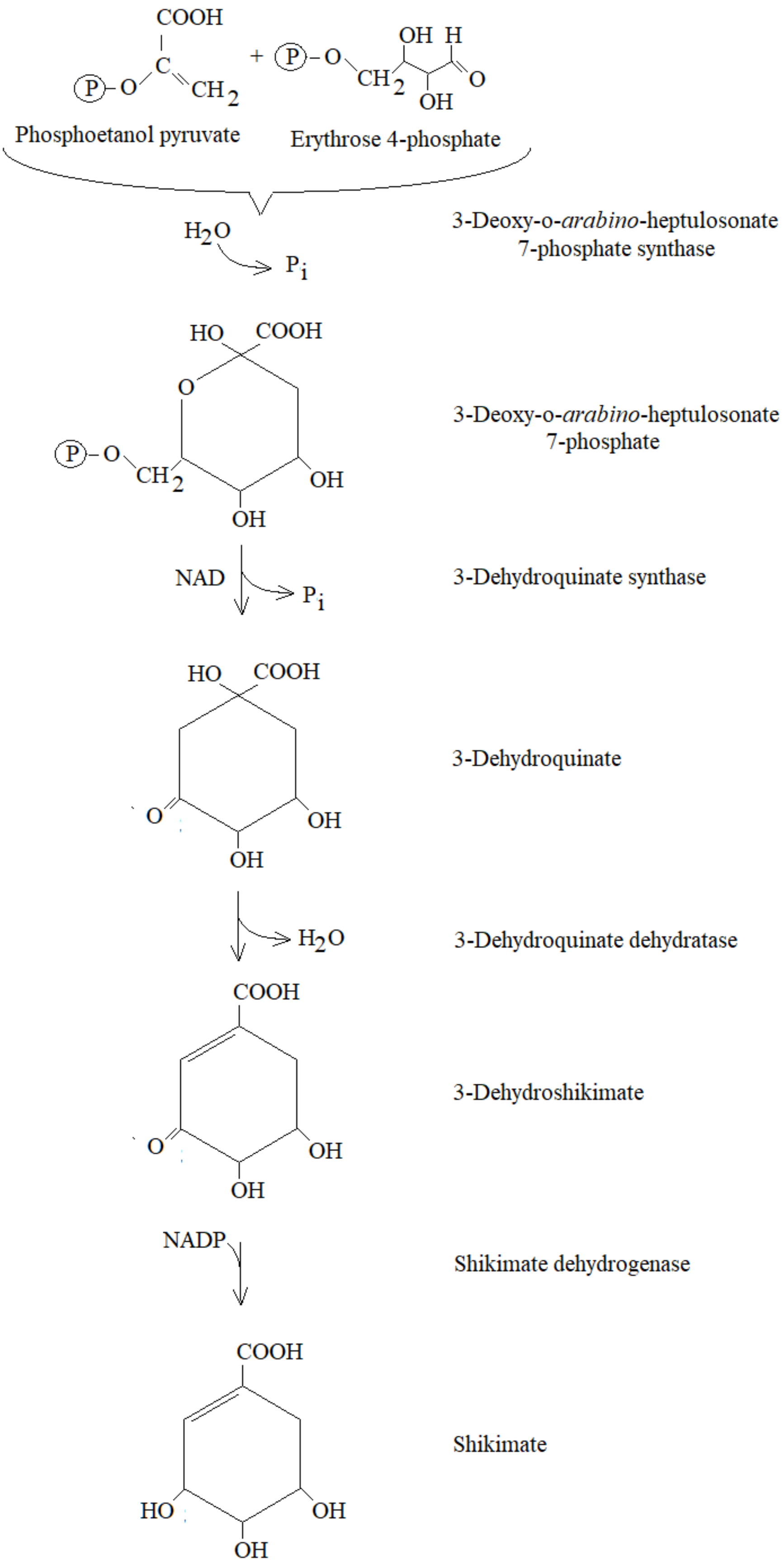


Figure 2. The shikimate pathway

1.3 The nitrogen metabolism pathway

Biosynthesis of amino acids begins with the assimilation of nitrogen ions occurring in several stages within the cytoplasm and plastids. Nitrates(V) absorbed inside the cell are transformed to nitrites(III) by nitrate reductase present in the cytoplasm and thus formed NO_2^- ions, toxic for the cell, are transported to plastids, in which thanks to the action of nitrite reductase NO_2^- ions are reduced to ammonium ions. The last stage in this process consists in the incorporation of NH_4^+ into the structures of carbon skeletons and the formation of amino acids in the glutamine synthetase-glutamate synthase (GS-GOGAT) pathway [18, 19]. Thus formed ammonium ions are transformed to glutamines by glutamine synthetase (GS1) and next to asparagine and glutamic acid by asparagine synthetase [19, 20, 21]. A significant role in the biosynthesis of amino acids is played by glutamate and glutamine. The former is synthesised from NH_4^+ and α-ketoglutarate with the participation of glutamate dehydrogenase. The ammonium ion (NH_4^+) was introduced to glutamine in the action of glutamine synthetase on glutamate. Amidation is dependent on the hydrolysis of ATP. The amino acid biosynthesis pathways vary in this respect (Figure 3) [22]. Their common characteristic is the fact that carbon skeletons originate from the intermediate compounds of glycolysis, the pentose phosphate pathway or the citric acid cycle.

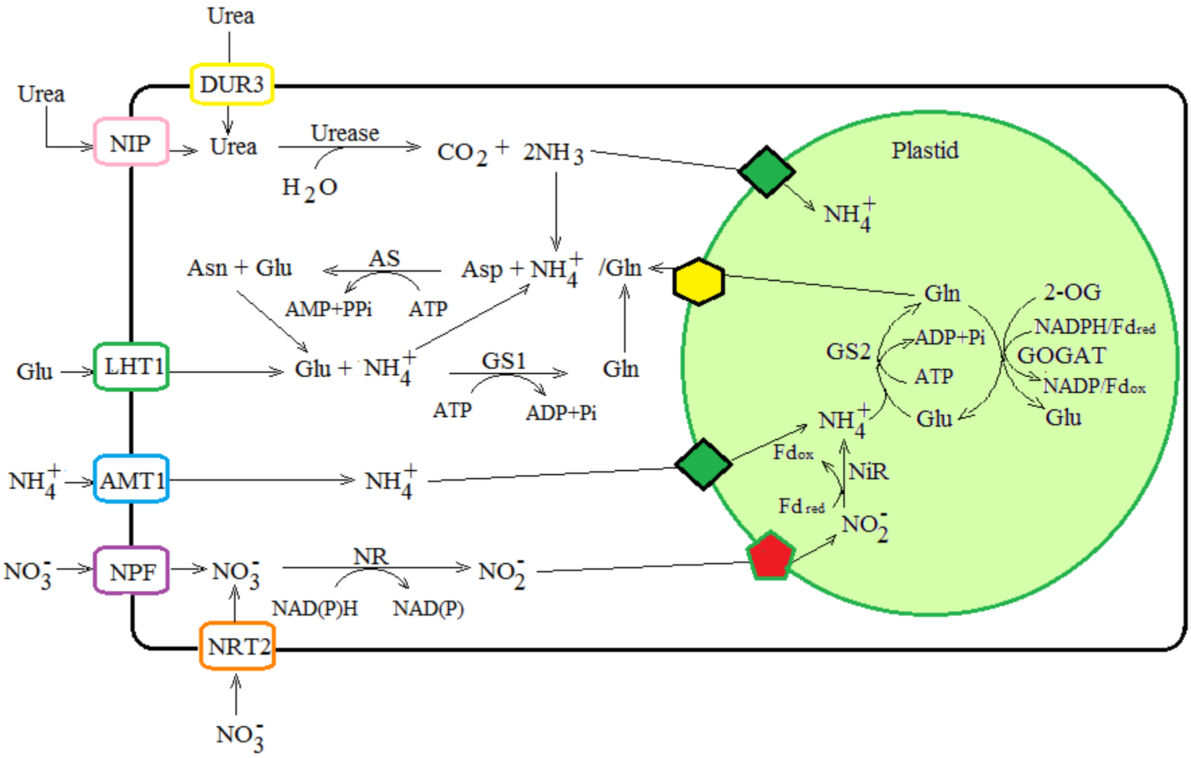


Figure 3. The nitrogen metabolism pathway

Endogenous amino acids such as e.g. alanine and asparagine, are synthesised in single-stage reactions from pyruvate and oxalacetate. Each of them obtains an amino group from glutamate in the reaction of transamination, in which pyridoxal phosphate acts as a co-enzyme. Asparagine is formed from asparaginate through its amidation.

The rate of amino acid synthesis depends on the number of enzymes and on their activity. Stress to which plant cells are exposed causes an increase in the production of enzymes, which triggers enzymatic defence mechanisms in plants and contributes e.g. to enhanced biosynthesis of endogenous amino acids [23].

Bioactive compounds from trees and shrubs are used in medicine, herbal medicine and cosmetology [24-32]. To date fruits and flowers of exotic trees and shrubs have been primarily used as sources of bioactive compounds. In turn, search for new sources of bioactive compounds is currently focused on native plant species due to its availability. Application of such raw material needs to be based on knowledge of their chemical composition, particularly health-promoting or therapeutic compounds. Research conducted to date on European trees and shrubs has been scarce. This paper presents results of literature studies conducted to systematise knowledge on bioactive compounds found in trees and shrubs native to central Europe.

The aim of this review providing available information on the subject is to indicate gaps in the present knowledge.

2. Chemical defence of trees and shrubs

Chemical defence mounted by plants requires considerable energy expenditure, which may have a negative effect on their growth and development. Thus a considerable body of research has been based on the growth−differentiation balance hypothesis and the trade−off principle. According to this approach, differentiation is understood as increased production of secondary metabolites involved in plant defence at the expense of primary metabolites directly related with plant growth and development [33, 34]. In this respect plant species are divided into those characterised by considerable and rapid growth, thus to a limited extent investing in chemical defence, and plants with limited, slow growth, but investing in secondary metabolites at a level ensuring effective protection against pathogens. Typically only one type of compounds predominates in plants: it is alkaloids, phenolic compounds or terpenoids. For example the main defence compounds in oak leaves are condensed tannins [35], while in coniferous trees it is terpenoids [36].

According to the dynamic stress concept, the action of stressors destabilises vital structures and functions of the organism leading to the so-called alarm phase, in which the intensity of vital functions is reduced (stress responses). In this phase if the organism's resistance is too low, it may lead to permanent damage. In contrast, at that moment in resistant organisms the resistance phase starts, in which they acquire enhanced resistance to stress factors (overcompensation). Next the organism returns to the normal operating level (adaptation). Plant organisms exposed to permanent stress enter the depletion stage leading to chronic damage.

Pathogen attack is one of the stress factors affecting plants. Among pathogens causing diseases in trees a special role is played by microscopic fungi. Tree seedlings are highly susceptible to fungal infections. They are attacked by fungi from the genera *Fusarium*, *Rhizoctonia* and *Pythium*, which may cause complete seedling dieback. Buds are attacked rarely, while frequent infections affect needles (e.g. needle cast of pine caused by *Lophodermium* spp.), leaves (e.g. powdery mildew of oak caused by *Erysiphe alphitoides*) and shoots (e.g. Brunchorstia disease resulting in pine shoot withering, caused e.g. by *Gremmeniella abietina* (Lagerb.) leading to considerably reduced growth and death of individual trees). Moreover, fruits and seeds may also be infected. The most dangerous infections are root diseases and trunk rot, whereas bark infections, although very frequent and affecting large areas, generally do not pose a significant threat to trees. The most frequent fungal diseases causing losses in stands in Poland include *Armillaria* root rot, root rot caused by *Fomes annosus* and needle cast of pine [37-40].

2.1. Biotic stress

Studies on plant response to the action of various abiotic and biotic stresses clearly show that that they are processes related to the uncontrolled increase in levels of reactive oxygen species (ROS), also referred to as free radicals, and H_2O_2 [41, 42]. When found in excessive amounts they readily enter chemical reactions with cellular components.

During exposure to the action of stressors one of the most important defence mechanisms is connected with the production of chemical compounds. This phenomenon involves two types of mechanisms: non-enzymatic and enzymatic. In the case of the former we observe the action of free radical scavenges, which when reacting with free radicals protect cells against adverse reactions. These include ascorbic acid (vitamin C), A-tocopherol (vitamin E), b-carotene and flavonoids. The former type comprises mechanisms related with the formation of specialised enzymes eliminating free radicals and preventing their formation. The enzymatic system includes superoxide dismutase (SOD E.C.), catalysing dismutation of the superoxide anion radical, and catalase (CAT E.C.), degrading hydrogen peroxide to water [43].

The penetration of a pathogen in the plant triggers defence mechanisms connected with the production of secondary metabolites (phytoalexins), defence proteins, i.e. glycine and serine rich proteins, GSRP, being structural components of plant cell walls, pathogenesis-related proteins (PR) as well as the accumulation of phenols [44-47].

Enhanced biosynthesis of the above-mentioned bioactive compounds is an advantageous side effect of the action of stressors. Trees in their anatomical parts most exposed to the action of pathogens accumulate greatest amounts of bioactive compounds, thanks to which shoots, fruits, leaves, needles and bark have become valuable sources of biologically active compounds.

Available literature on the subject focuses mainly on studies concerning bioactive compounds in plant origin raw materials in terms of their application in herbal medicine, pharmacology and broadly understood health-promoting food. However, these compounds are found in tissues of all plants and they serve similar functions. Increasingly often new reports are being published on the application of various components of trees and shrubs in branches of industry other than the wood industry. This is connected with studies on bioactive compounds in leaves, bark, fruits and essential oils collected from trees, shrubs or their fruit. More valuable woody plants exhibiting health-promoting properties include e.g. Cornelian cherry, also called Cornelian cherry dogwood (*Cornus mas* L.), hawthorn, black elder, bark of buckthorn as well as common trees such as birch, pine, linden, oak and willow. The presence of bioactive compounds in those plants has contributed to their use in detoxicants, vitamin preparations, preparations enhancing resistance and adjuvant drugs in treatment of various diseases both in the elderly and children [32, 48-52].

3. Bioactive compounds

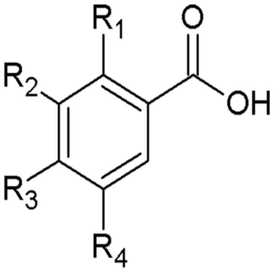
To date literature on the subject has focused on trees of the equatorial and tropical zones, i.e. exotic trees. However, trees of the temperate climatic zone are also rich sources of bioactive compounds such as phenolic compounds, sterols, organic volatile compounds, fatty acids, etc.

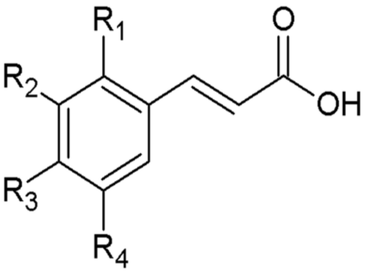
3.1 Phenolic compounds

Polyphenolics are secondary plant metabolites varying greatly in terms of their structure, molecular mass as well as physical, biological and chemical properties. They are found in all plant parts, i.e. flowers, fruits, seeds, leaves, roots, bark and lignified parts [53, 54]. Phenolic compounds in terms of the structure of the basic carbon skeleton may be divided into phenolic acids, flavonoids, proanthocyanidins and stilbenes [55].

3.1.1 Phenolic acids

Phenolic acids in their structure contain a hydroxyl and a carboxyl group. Hydroxyl derivatives of benzoic and cinnamic acids are common in the plant world (Figure. 4).





Hydroxybenzoic acids

	R_1	R_2	R_3	R_4
3-hydroxybenzoic acid	H	OH	H	H
4-hydroxybenzoic acid	H	H	OH	H
salicylic acid	OH	H	H	H
pyrocatechuic acid	OH	OH	H	H
genistic acid	OH	H	H	OH
α-resorcylic acid	H	OH	H	OH
β-resorcylic acid	OH	H	OH	H
protocatechuic acid	H	OH	OH	H
vanillic acid	H	OCH_3	OH	H
isovanillic acid	H	OH	OCH_3	H
gallic acid	H	OH	OH	OH
syringic acid	H	OH	OH	OH

Hydroxycinnamic acids

	R_1	R_2	R_3	R_4
cinnamic acid	H	H	H	H
2-coumaric acid	OH	H	H	H
3-coumaric acid	H	OH	H	H
4-coumaric acid	H	H	OH	H
caffeic acid	H	OH	OH	H
4-methoxycinnamic acid	H	H	OCH_3	H
3,4-dimethoxycinnamic acid	H	OCH_3	OCH_3	H
ferulic acid	H	H	OH	OCH_3
isoferulic acid	H	H	OCH_3	OH
sinapic acid	H	OCH_3	OH	OCH_3

Figure 4. The structures of phenolic acids [56, 57]

In plants phenolic acids are mostly found in the bound form as esters and glycosides, contained in lignins and hydrolysed tannins. Examples in this respect may be provided by hydroxycinnamic acids found in ester complexes with carboxylic acids or with glucose. They appear in ester complexes with the following acids: malonic, tartaric, α-hydroxy-hydrocaffeic, hydroxycinnamic, tartronic, shikimic, galacturonic, glucaric (as caffeic acid glucuronide), gluconic (as feruloylgluconic acid, which main isomer is 2-O-feruloyl gluconic acid) and 4-methoxyaldaric (as 2-O-feruloyl-4-methoxyaldaric acid). In turn, hydroxybenzoic acids are primarily found as glycosides. In plant tissues other complexes of phenolic acids were also identified, e.g. complexes with flavonoids, fatty acids, sterols and polymers of cell walls. Phenolic acids may also be components of anthocyanins or flavones [56, 57]. A separate group is composed of depsides, being a complex of two or more molecules of phenolic acids. In plant organisms, including trees, they are formed mainly in the reaction of the so-called shikimate pathway or malate acid (Figure 1, 2) .

Tyrosine and phenylalanine are precursors of most phenolic acids, from which as a result of deamination cinnamic acid and its hydroxy derivatives are formed [58].

A particularly interesting active compound from the group of hydroxybenzoic acids is ellagic acid, a dimer of gallic acid, in plants found in the free form and (more frequently) in the ester complex with glucose, forming hydrolysing tannins (ellagotannins) [59,60]. It is found in wood of oak, walnut and sweet chestnut, as well as berry fruits, in strawberries and raspberries [61, 62], in the loosestrife family (*Lythraceae*), particularly pomegranate [24, 35, 42], in certain nut seeds [63] and *Muscadine* grapes [64]. Ellagic acid exhibits e.g. anti-cancer properties, thanks to which it may inhibit cell division and induce apoptosis in cancer cells [65, 66]. Moreover, its anti-inflammatory and antioxidant action [67, 68] were investigated and confirmed. Ellagic acid found in Cornelian cherry fruit exhibits immunostimulatory, immunomodulatory, antimicrobial, antioxidative and anti-cancer action. It inhibits the adverse effect of UVB radiation, protects skin against degradation and exhibits anti-inflammatory action [69-71]. Ellagic acid is also found in the ester form bound with glucose forming hydrolysing tannins, the so-called ellagitannins.

Salicylic acid, i.e. 2-hydrobexybenzoic acid, which natural source is willow, is another compound of particular interest. Willow bark contains a biologically active substance referred to as salicin [72]. Salicin is β-glucoside of saligenin [73], which *in vivo* undergoes two-stage transformation consisting in deglycolisation and oxidation to salicylic acid [74, 75]. Thanks to the rapid development of chemical synthesis in the late 19th century this acid has become a direct precursor of other drugs of similar structure, the so-called salicylates, and non-steroid anti-inflammatory drugs. They include e.g. non-acetylated derivatives of salicylic acid such as sodium salicylate, methyl salicylate, diflunisal, phenyl salicylate (salol), choline salicylate, ethylene glycol salicylate, salicylamide, salsalate, benorylate and diethylamine salicylate [76, 77]. In turn, the acetylated derivative of this acid, i.e. aspirin, is an anti-inflammatory, analgesic, antipyretic and antirheumatic drug. Phenolic acids found in the trees and shrubs are shown in Table 1.

A detailed analysis of metabolism of phenolic compounds synthesised in infected plants showed L-phenylalanine and chorismic acid to be the primary precursors of salicylic acid. These compounds undergo enzymatic transformation to trans-cinnamic acid due to the action of an enzyme, phenylalanine ammonia lyase (PAL), orto-iso-chorismic acid [78].

Table 1. Phenolic acids found in trees and shrubs

Trees and shrubs	Phenolic acids	Literature
Scots pine *Pinus sylvestris* L.	Caffeic acid, ferulic acid	[79, 80]

Spruce *Picea abies* H.Karst	Shikimic acid, galusic acid, *p*-coumaric acid, protocatechuic acid, quinic acid	[79, 81]
European beech *Fagus sylvatica* L. - leaves	Caffeic acid, ferulic acid, p−hydroxybenzoic acid	[79, 82]
Oak *Quercus robus* L.	Ellagic acid, gallic acid, gentisic acid, *p*-hydroxybenzoic acid, protocatechuic acid syringic acid vanillic acid, *p*-coumaric acid, caffeic acid, ferulic acid sinapic acid	[79, 82-85]
Walnut *Juglans regia* L.	Ellagic acid, caffeic acid, *p*-coumaric acid, galusic acid	[79, 82]
Willow *Salix* spp.	Ferulic, caffeic, salicylic, vanillic, syringic, α-resorcylic, m and p-hydroxybenzoic, p-coumaric, cinnamic acids	[82, 86]
Salix alba L.	Salicylic and p-coumaric acid	[87]
Salix babylonica L. - leaves	Caffeic and p-coumaric acids	[88]
Salix capitata L. - leaves	Protocatechuic acid	[89, 90]
Silver birch *Betula pendula* Roth - leaves	Chlorogenic, p-hydroxybenzoic, caffeic, gallic, coumaric, p-hydroxycinnamic acids	[82, 91]
Hawthorn *Crataegus* L.	Chlorogenic, caffeic acid	[82, 92]
Rowan *Sorbus aucuparia* L.	Neochlorogenic, chlorogenic, protocatechuic, caffeic and p-hydroxybenzoic acids	[93]
White poplar *Populus alba* L. - buds	Benzoic, ferulic, caffeic acids, cinnamic, *cis*-*p*-coumaric and *trans*-*p*-coumaric acids	[82, 94]
Bird cherry *Prunus padus* L.	Caffeic acid, chlorogenic acids	[82]

Summing up, phenolic acids protects plants against the action of microorganisms and insects, while in combination with polysaccharides they make cell walls more rigid. In the human organism they exhibit diverse biological activity, e.g. scavenging free radicals, chelating metal ions, modifying enzyme activity and protein availability. They prevent cardiovascular disease, cancer and diabetes. Additionally, they protect against photooxidative skin damage

[95].

3.1.2 Flavonoids

The greatest and most diverse group of phenolic compounds found in plants is composed of flavonoids. Chalcone formed via biosynthesis from phenylalanine is a precursor of flavonoids. Synthesis starts with shikimic acid. These compounds are found not only as free molecules, i.e. aglycones, but rather - much more frequently - in the bound form with sugars, i.e. as glycosides. All flavonoids are based on the 2-phenylchromate skeleton, while most types of flavonoids (apart from catechins and anthocyanidins) contain the flavone skeleton, with the ketone group in position 4 (Figure 5) [96, 97].

Chemically all flavonoids are based on the hydrocarbon skeleton of flavone. They differ in the number and type of substituents, while differences between these compounds result primarily from the different structure in only one extreme ring. To date over 7000 various flavonoids have been identified, which in terms of their chemical structure are divided into flavones, flavonols (3-hydroxyflavones), flavanones, flavanols (flavan-3-oles, flavanonoles), anthocyanidins, isoflavones and neoflavonoids (Figure. 5). Thanks to their unique structure flavonoids may protect the cell against reactive oxygen species (ROS) generated in the organism [98, 99].

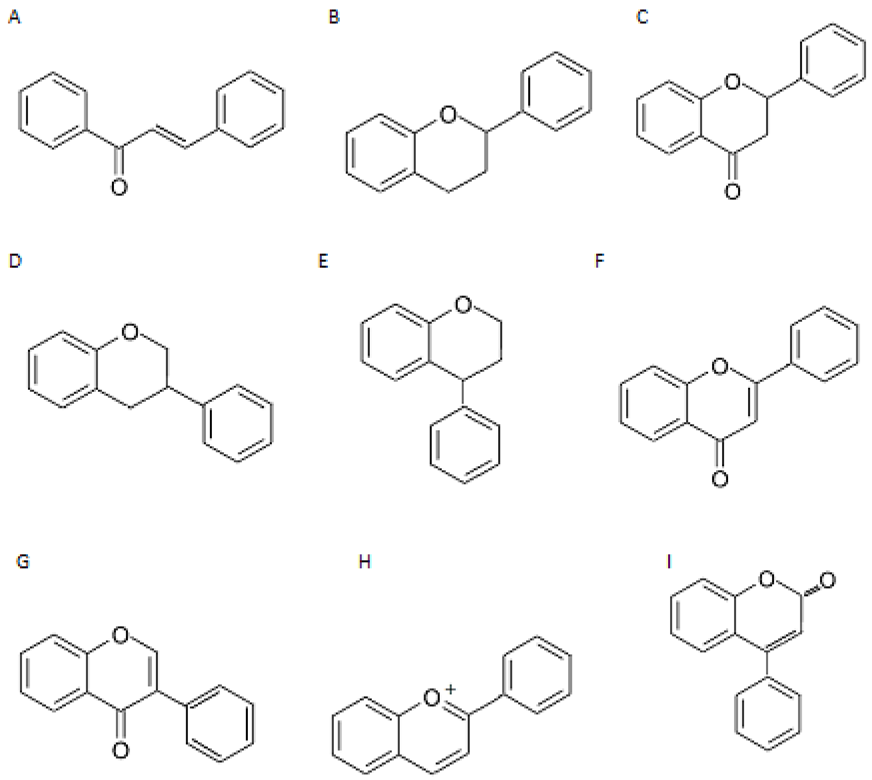


Figure 5. Structural formulas of individual flavonoid groups: A. chalcone, a precursor of

flavonoids; B. flavane; C. flavanones; D. isoflavanes; E. neoflavanes; F. flavones; G. isoflavones; H. flavylium ion; I. neoflavones (nomenclature according to IUPAC).

Table 2. Division of flavonoids depending on their chemical structure [100]

Flavonoids	Representatives
Flavonol	(containing solely OH groups) quercetin, kaempferol, myricetin, morin and others
Flavone	(containing also CHO groups): luteolin, apigenin
Flavonone	flavonones: (containing C=O groups): hesperidin, naringenin, eriodictyol
Flavan-3-ol	catechin, theaflavin and derivatives
Isoflavones	daidzein, genistein, glycitein
Anthocyanidin	anthocyanins: cyanidin, delphinidin, malvidin, pelargonidin, peonidin, petunidin, neoflavonoids (4-phenylcoumarin or 4-phenylchromen-2-one): dalbergin, dalbergichromene, nivetin

Flavonoids are phytoalexins, i.e. substances serving protective functions, formed as a result of the plant's contact with a pathogen, frequently inducing expression of several genes encoding enzymes of the phenolic biosynthesis pathway [101]. Isoflavonoids are highly toxic towards fungal pathogens, which is particularly evident in such compounds as pterocarpanes, isoflavanes, isoflavones and isoflavonones. The mechanism of their action consists in the inhibition of spore development and mycelium growth as well as the damage of fungal cell membrane structure [102-104].

Flavonoids are extensively used in woody plants of our climatic zone. They are found in the bark of common oak *Quercus robur Linne*, sessile oak *Quercus petrea Lieblein* or downy oak *Quercus pubescens Willdenow* = *Quercus lanuginosa Thuillier.*, in inflorescences of hawthorn *(Inflorescentia Crataegi)*, leaves of birch *(Betulae Folium)*, flowers of elderberry *(Sambuci flos)*, as well as linden inflorescences (Table 3). Flavonoids introduced to the human organism may serve a similar role as vitamins. They seal blood vessel walls, as well as exhibit antiviral, antibacterial and antifungal action [105], while in oral medicine flavonoids show considerable efficacy in prevention of periodontitis. An inhibitory effect of flavonoids on cancer cell growth was also observed [106-109].

Table 3 Flavonoids found in trees and shrubs

Tree and shrub species	Flavonoids	Literature
Scots pine *Pinus sylvestris* L. needles	Prodelphinidin and lacks taxifolin, quercetin and taxifolin taxifolin, taxifolin 3′-O-glucoside, quercetin as well as quercetin 3-O-glucoside and 3′-O-glucoside	[82, 110] [111]
Oak *Quercus robus* L.	Tannins - derivatives of pirocatechin and pyrogallol, epikatechina flawan-3-oli, katechina, quercetin	[79, 112, 113]
European beech *Fagus sylvatica* L. - leaves	Catechin,kempferol, gallocatechin, kaempferol 3-glucoside, naringenin, quercetin, quercetin-3-glucoside, mirycetyna, quercetin, taxifolin	[79, 82]
Spruce *Picea abies* H. Karst - needle	Catechin, kaempferol, kaempferol 3-glucoside, naringenin, quercetin, quercetin 3-glucoside, quercitrin	[79, 82]
Salix purpurea L.	Salipuroside, isosalipuroside. naringenin, naringenin 5-O-glucoside, naringenin 7-O-glucoside, chalcone isosalipurposide, flavan-3-ol, catechina	[114, 115]
Salix spp: *S. alba* *S. viminalis*	Amentoflavone, isoquercetin, quercetin, rutin, quercimeritrin, apigenin, 3-O-glucoside rhamnasine, izosalipurpurozyd, hiperozyd, catechin naringenin, luteolin, eriodycerol, naringin, kaempferol, apigenin-7-O-glucoside, astralgin, quercimeritrin and quercetin-3,7-di-O-glucoside	[79, 88, 94, 116-120]
Hawthorn *Crataegus* L.	Catechin, epicatechin, hyperoside, quercetin, witexin, isovitexin, apigenin, rutin and kemferol	[79, 82, 121]
Black elder *Sambucus nigra*	rutin, quercetin, astragalin and isoquercetin	[79, 82, 122,

L. - flowers		123]
Birch - leaves	hyperoside, myricetin and luteolin, catechin tannins	[79, 82, 124]
Rowan *Sorbus aucuparia* L.	quercetin, rutin, hyperoside, isoquercetin and quercetin-3-O-sophoroside	[125]
Common yew *Taxus baccata* L.	3-O-rutinosides quercetin, myricetin, kaempferol, 7-O-glucosides	[126]
Black locust *Robinia pseudoacacia* L.	dihydrorobinetin robinetin, butein dihydromyricetin, fisetin, fustin, isoliquiritigenin, myricetin liquiritigenin	[127]

3.1.3 Anthocyanins

Anthocyanins constitute another class of the discussed compounds. They are the largest group of water soluble phytopigments widely distributed in the plant kingdom. They are mainly found in flowers and fruits providing them with colour, while they are also contained in seeds, leaves, stems and roots. The chemical structure of anthocyanins is based on the anthocyanidin skeleton, to which various substituents are attached (Figure 6). Most proantocyanidins are compounds containing in their structure epicatechin units, referred to as procyanidins [128]. The polyphenol structure and numerous -OH groups in proanthocyanidin molecules are responsible for their high antioxidant activity. Chemically anthocyanins are glycosides; glycosilation makes them more stable and more water soluble. These polyphenols are also found in the non-glycosiled form (aglycones) as anthocyanidins. The presence of various chemical groups as substituents determines the considerable biological activity of these compounds, including anti-inflammatory, antioxidant, antibacterial or even anti-cancer activity. These compounds are found in such vegetables as beets, red cabbage, red onion, radish, red lettuce and almost all fruits, primarily berries, in their skin and flesh. An example may here be provided also by pelargonidin present in the skin of radish and potatoes, or derivatives of delphinidin found in aubergine skin [128]. Proanthocyanidins (also called condensed or non-hydrolysing tannins) are also found in leaves, lignified parts of plants, as well as flowers and fruits [129]. Inflorescences of hawthorn (*Crataegi inflorescentia*, *Crataegus* sp. *Rosaceae*) are a well-known source of proanthocyanidin used in herbal medicine for years [130, 131]. Recently intensive studies have been conducted on the extract from bark of maritime pine *Pinus pinaster* (*Pinaceae*), patented as Pycnogenol, which proanthocyanidin content is 85%. This preparation exhibits e.g. strong antioxidant properties (Table 4) [132, 133].

A considerable body of data indicates that a diet rich in anthocyanins plays a significant role in the prevention of cardiovascular disease and cancer [134]. It was shown that plant extracts rich in anthocyanins may exert a protective effect on the function of blood vessel walls, preventing endothelium dysfunction and loss of its regulatory activity [135, 136]. Antioxidant properties of these compounds may be used in the prevention of cancer both of the alimentary tract and internal organs [137]. They also prevent oxidation of the LDL cholesterol fraction [138].

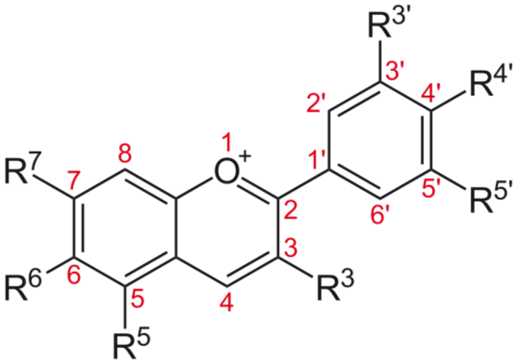


Figure. 6 The basic structure of anthocyanidins, aglycone components of anthocyanins. The numbers of the carbon skeleton and the position of naturally found substituents (R^x = H, OH, OCH_3) [139]

Table 4 Proanthocyanidins found in trees and shrubs

Tree and shrub species	Proanthocyanidins	Literature
Scots pine *Pinus sylvestris* L. *Pinus densiflora* L. needles	Proanthocyanidins (OPC) procyanidins, prodelphinidins and propelargonidins catechin derivatives, both dimers and trimers.	[140-143]
Quercus petraea L. and *Q. robur*	Proanthocyanidins	[144-146]
Hawthorn *Crataegus oxyacantha* L.	Procyanidin glycosides	[92,147,148]
Bird cherry *Prunus padus*	Cyanidin-3-rutinoside and cyaniding-3-glucoside	[149]
Salix purpurea L.	Cyanidin-3-glucoside, myrtillin (delphinidin-3-glucoside)	[150]

3.1.4 Stilbenes

Stilbenes are metabolites of the phenylpropanoid pathway activated under biotic and abiotic stress. They are compounds with the 1,2-diphenylethylene skeleton. Only some, unrelated plant species are capable of synthesising and accumulating stilbenes . The enzyme facilitating this synthesis of stilbene synthase (STS). In plants stilbenes serve several functions, among which the most significant is related to strong antimicrobial properties, thus they are classified as phytoalexins [151]. Other known functions include also their repellent action against herbivores as well as allelopathic and antioxidant properties. Stilbenes are produced in small amounts; however, biosynthesis is activated primarily post-infection, while it is also triggered by wounding, UV radiation, ozone and aluminum ions. Resveratrol (3,5,4'-trihydroxy-trans-stilbene) is one of the most extensively described stilbenes [152].

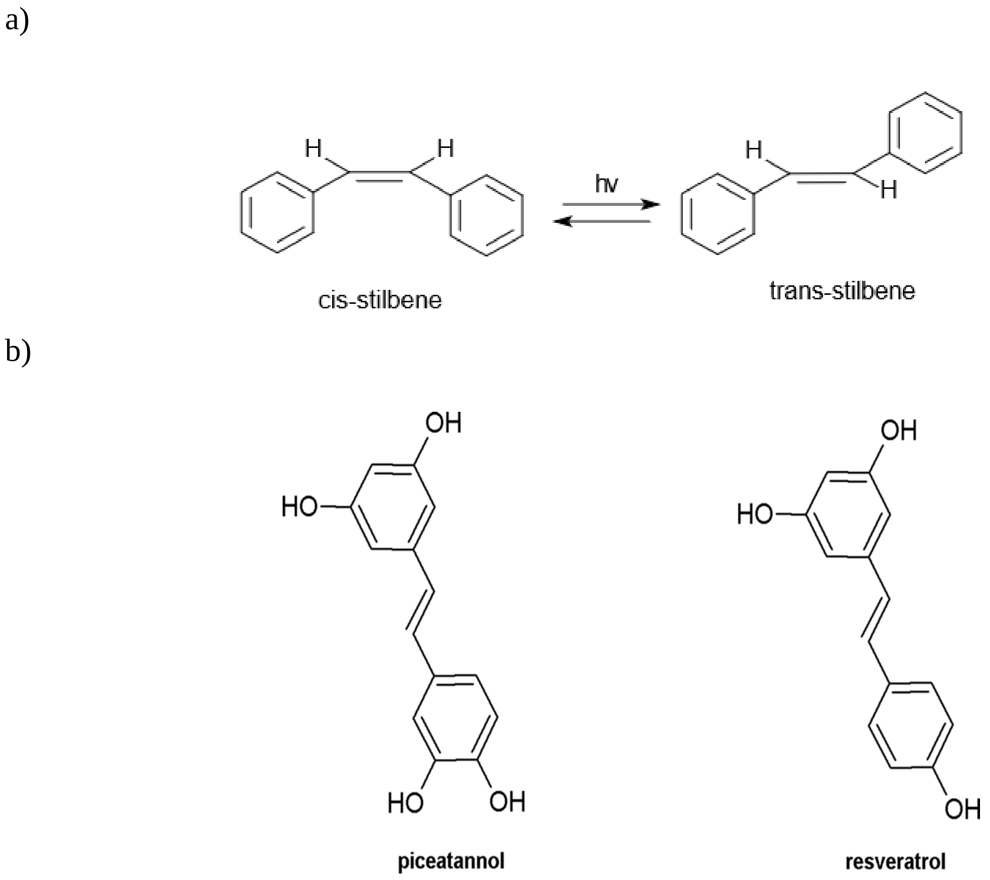


Figure. 7. The chemical structure of stilbenes: a) cis and trans b) piceatannol and resveratrol [153].

Resveratrol is found in the form of two isomeric forms: cis- and trans- (Figure 7). Transresveratrol is a phenol stilbene found in many plants, e.g. the grape family (Vitaceae), particularly common grape vine (*Vitis vinifera*). The other form of resveratrol, i.e. cis-, is formed as a result of isomerisation of trans-resveratrol and after decomposition of resveratrol

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polymer molecules during fermentation of grape skins, due to the action of UV radiation and at high pH [154]. Resveratrol was first isolated in 1940 from roots of *Veratum gradiflorum* [155]. Its highest concentration was recorded in roots of Japanese knotweed (*Polygonum cuspidatum*). In folk medicine this plant was successfully used to treat pyoderma, mycoses and venereal diseases [156]. Moreover, resveratrol has been applied in cancer prevention and treatment thanks to its ability to effectively inhibit each stage of neoplasia, i.e. initiation, promotion and progression of the disease [157].

Stilbenes are secondary metabolites relatively rarely found in nature. To date they have been reported in almost 70 unrelated plant species belonging to approx. 30 genera and 12 families. The greatest stilbene contents are detected in plants from the pine family (*Pinaceae*), the grape family (*Vitaceae*), the beech family (*Fagaceae*), the mulberry family (*Moraceae*) and the grass family (*Poaceae*) [151].

Table 5 Stilbenes found in trees and shrubs

Tree and shrub species	Stilbenes	Literature
Scots pine - *Pinus sylvestris* L. Eastern white pine - *Pinus strobus* Japanese red pine - *Pinus densiflora*	Pinosylvin, pinosylvin 3-o-methyl ether	[158-160]
Spruce *Picea abies* L. H.Karst	Cis and trans- astringin, trans-piceatannol, cis- and trans-piceid, trans-resveratrol	[159, 161-164]
Black locust *Robinia pseudoacacia* L.	Piceatannol and resveratrol	[165]
Morus spp. *Mulberry*	Resveratrol	[166]

For economic reasons the durability and resistance of softwood has been of considerable interest for many decades. In the 1980's and 1990's it was definitely shown that it is stilbenes that protect wood against pathogens [167]. It was confirmed in vitro that both pinosylvin and pinosylvin 3-O-methyl ether are very strong inhibitors of two main wood degrading fungi, i.e. *Coriolus versicolor* and *Gloephyllum trabeum* [168]. Additionally, also some nematode-resistant pine species in their bark and heartwood contain nematicidal compounds, among which pinolsylvin 3-O-methyl ether proved to be the most effective [169].

3.2 Sterols

Sterols constitute another group of compounds found in trees. They are widely distributed in the plant world. These compounds are classified as lipids, specifically to the non-saponifying fraction. Sterols are an important component of biological membranes. The nonpolar, hydrophobic part of the sterol molecule, by attaching to fatty acids of phospholipids, contributes to a reduction of membrane fluidity [170]. Sterols are organic chemical compounds, alcohols belonging to the group of steroids. They are formed by formal substitution of the carbon atom in position 3 in the steroid skeleton by the hydroxyl group. Phytosterols include sterols (unsaturated compounds) and stanols (saturated compounds). Phytosterols are chemical homologues of cholesterol differing in the saturation rate and chain configuration. Basic plant sterols found in vegetable oils differ in the structure of their side chain (Figure 8). Depending on their structure and biosynthesis, plant sterols were divided into the following groups: 4-dimethylsterols, 4α-monomethylsterols and 4,4-dimethylsterols, 4-dimethylsterols, including stigmasterol, β-sitosterol and campesterol, are most common plant sterols. Phytosterols are natural plant components, e.g. in soy, vegetable oils, rice and pine wood. They are also found in small amounts in nuts, vegetables and fruit. Research results indicate that certain lipid components such as polyunsaturated fatty acids, sterols and plant stanols may effectively lower blood cholesterol level. The content of the LDL cholesterol fraction is reduced not only by unrefined sterols, but also those subjected to hydrogenation or esterification. To date almost 40 forms of plant sterols have been identified, among which β-sitosterol, campesterol and stigmasterol are most common [171-173]. The most abundant source of phytosterols is presently provided by tall oil (the name originates from Finnish "tallolie", meaning pine oil), which is obtained as a result of wood conversion in the process of cellulose production.

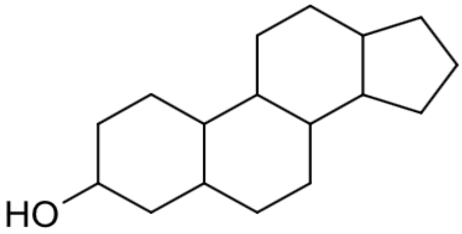

Figure 8. The sterol skeleton [170]

Table 6 Sterols found in trees and shrubs

Trees and shrubs	Sterols	Literature

Silver birch *Betula pendula* Roth L., Scots pine *Pinus sylvestris* L., Black locust *Robinia pseudoacacia* L.	Free sterols: β–sitosterol, β–sitostanol (stigmastanol), campesterol Esterified sterols: β–sitosterol, β–sitostanol (stigmastanol), campesterol, α-sitosterol, Cycloartenol, 24-methylenecycloartanol, squalene, betulaprenol-6, betulaprenol-7, betulaprenol-8, lupeol	[174-180]
Hawthorn fruits *Crataegus* L.	Stigmasterol, kaempesterol, β-sitosterol	[181]

3.3 Volatile compounds

Another group of plant origin active compounds comprises essential oils. They are volatile compounds most frequently found in special cells of secretory tissues of plants. These compounds are natural isoprene oligomers widely found in nature. Chemically they are complex, multicomponent mixtures of monoterpene and sesquiterpene compounds and their derivatives, including aromatic derivatives. These substances may be alcohols, ketones, aldehydes, esters or ethers. They occasionally contain also nitrogen or sulphur compounds. Their distinguishing characteristic is connected with the fact that one essential oil may contain more than ten or even several dozen compounds differing in their concentrations and properties [182,183]. Plants are considered as sources of essential oils if they contain over 0.01% oil. Essential oils are obtained from trees and shrubs from the family Pinaceae (genera Pinus, Abies, Picea, Larix) (Table 7). Pine oil exhibits antiseptic activity, it alleviates symptoms of the common cold, flu, tonsillitis, sinusitis, rhinitis and cough, while it also stimulates the circulatory system. Fir oil next to its expectorant and antiseptic action shows diuretic and antirheumatic action, whereas studies have confirmed that terpenes present in birch oil exhibit anti-inflammatory, anticancer, antibacterial and antiviral activity.

Table 7. Essential oils found in trees and shrubs

Trees and shrubs	Essential oil	Literature
Norway spruce *Picea abies* L., H. Karst	Spruce composition: camphor, limonene, camphene, borneol, α- and β-pinene	[184,185]
Scots pine *Pinus sylvestris* L.	Pine composition: pinenes, carenes, cadidene, (S)-(-)-limonene	[186, 187]

Black locust *Robinia pseudoacacia* L.	Flower extract: monoterpenes including linalool, geraniol, terpinen-4-ol and α-terpineol, cis- and trans-farnesol, nerolidol and β-bisabolol	[188]
Silver birch *Betula pendula* Roth	Birch composition: betuline, betulinic acid, betulin aldehyde, oleanolic acid	[189]
European siver fir *Abies alba* Mill.	Fir needle oil composition: santene, L-α limonene, L-bornyl acetate, lauric aldehyde	[190-191]
Juniper *Juniperus communis* L.	α-Pinene, camphene, limonene, cadinene, terpinen-4-ol, myrcene, β-pinene, sabinene	[192-195]

Presented literature sources indicate that active substances of plant origin, particularly those obtained from trees and shrubs growing in the temperate climate zone, exhibit a beneficial effect on human health. Thanks to the presence of bioactive compounds in those plants they have found applications as detoxicants, vitamin supplements, as well as preparations boosting immunity and adjunctive medication in treatment of various diseases. These is a considerable body of data indicating that the diet rich in bioactive compounds plays a significant role in prevention of cardiovascular diseases and cancer. In view of the fact that treatment of chronic pain, cancer, cardiovascular disease and a number of other diseases requires a combination of several therapeutic methods, alternative therapies using plant origin preparations are gaining popularity. It also needs to be stressed that molecular mechanisms of action in the case of active substances contained in plant preparations have not been fully elucidated and require further research.

The review of literature presented in this paper presents the potential of trees and shrubs native to the temperate zone as sources of bioactive compounds.

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