

## CHAENOMELES – HEALTH PROMOTING BENEFITS

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### ABSTRACT

*Chaenomeles* is a genus of deciduous spiny in the family of *Rosaceae* (*Pomoideae* subfamily). For centuries, the plant was used for a treatment of anemia, rheumatism, gout and cardiovascular diseases. The chemical composition studies of *Chaenomeles* showed the presence of many biologically active compounds, such as: phenolic compounds, organic acids, terpenoids, alcohols, ketones or aldehydes. Fruit of *Chaenomeles* has the largest applying potential due to extensive use of medicinal and high concentration of vitamin C. Recent *in vivo* and *in vitro* studies suggest that *Chaenomeles* fruit can help in the healing process of diabetes, tumor, allergies and liver diseases. Furthermore the plant has many positive qualities, like: hepatoprotective effect, anti-inflammatory properties, antioxidant action, antimicrobial and neuroprotective effect. *Chaenomeles* fruit may promote the growth of beneficial intestinal microflora and contribute to the regulation of body weight. The aim of this review was to summarize the information and data on the chemical composition and therapeutic properties of *Chaenomeles*.

**Key words:** *Chaenomeles*, antioxidants, chemical composition, properties

### STRESZCZENIE

*Chaenomeles* należą do roślin, które od wieków wykorzystuje się w medycynie ludowej między innymi w przypadku anemii, reumatyzmu, artretyzmu czy w chorobach układu krążenia. Badania nad składem chemicznym poszczególnych części morfotycznych pigwowca wykazały obecność między innymi związków fenolowych, kwasów organicznych, terpenoidów, alkoholi, ketonów czy aldehydów. Największe zastosowanie znajdują owoce pigwowca, bogate w witaminę C, którym przypisuje się szerokie działanie lecznicze. W literaturze dostępne są zarówno wyniki badań na hodowlach komórkowych jak i na zwierzętach, sugerujące że mogą być one stosowane w przypadku cukrzycy, chorób nowotworowych i w alergiach. Udowodniono także ich działanie hepatoprotekcyjne, przeciwzapalne, antyoksydacyjne, neuroprotektoryjne i przeciwdrobnoustrojowe. Owoce pigwowca mogą też powodować rozwój korzystnej mikroflory jelitowej, korzystnie wpływać na wydolność sportową, a także wspomagać regulację masy ciała. Celem artykułu było przedstawienie aktualnych informacji i danych dotyczących składu chemicznego oraz właściwości leczniczych pigwowca.

**Słowa kluczowe:** *Chaenomeles*, antyoksydanty, skład chemiczny, właściwości

### SYSTEMATIC CLASSIFICATION

*Chaenomeles* is a type of shrub belonging to the family *Rosaceae* and subfamily *Pomoideae* [26, 30]. The plant comes from eastern Asia – China and Japan [30], but has found a wide recognition in temperate zones, where it is widely grown. *Chaenomeles japonica* was brought to Europe in XVI century [30,36]. There are following species of *Chaenomeles*: *C. japonica* Lidl., *C. sinensis* Kochne, *C. Cathayensis* Schn. and *C. Speciosa* Nakai [30, 36]. There are also some hybrid species, such as: *Chaenomeles Superba* (*C. speciosa* × *C. japonica*) and *Chaenomeles Californica* (*C. cathayensis* x *C. japonica*) [30, 36]. Some authors also

mention *C. thibetica* [36, 54]. *C. speciosa* Nakai, *C. japonica* and *C. superba* are the most common species occurring in Poland. *Chaenomeles speciosa* Nakai can reach 2 - 3 m in height [30, 36]. Its stems are bare, straight and covered in thorns. The leaves are oval or elongated, sharply serrated, with a shiny top and their size is 3-9 x 1.5-5 cm. It is flowering in late April and May. Flowers appear on shoots individually or in clusters on older stems. Their colour is bright red, rarely pinkish or white. The fruits of *Chaenomeles speciosa* Nakai are yellowish green 4 – 6 cm pomes (apple like shapes) [30, 36]. *Chaenomeles japonica* Lindl. is a slightly shorter shrub, not exceeding 1 m in height. Its branches are thorny, while the young shoots

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have felt-like coating. Leaves of *C. japonica* are 3 - 5 cm long, ovate or obovate, with widely serrated edges, they are bare and round-ended. The shrub blooms in late April and May. Its flowers are scarlet red, going through pink and onto white. Fruits resemble the shape of a small, very aromatic apple; their average size is 4 cm in diameter and the weight does not exceed 50 g. *Chaenomeles Superba* is a two-species hybrid bred from *C. japonica* and *C. speciosa*. Its branches look similar to *C. speciosa*, but leaves resemble the shape of *C. japonica*. Flowers are dark red. *Chaenomeles* shrubs grow well on the moist soil and pH range between 5.6 to 7.8. They tolerate both sunny and partial shady spots [30, 36].

### CHEMICAL COMPOSITION OF THE MORPHOLOGICAL COMPONENTS OF CHAENOMELES

#### *Chaenomeles* fruits

The content of the main nutrients of *Chaenomeles* fruits are presented in Table 1.

Table 1. The content of the main nutrients of *Chaenomeles* fruits

	<i>C. speciosa</i> [59, 62]	<i>C. sinensis</i> [5]
Water content	87.6-89.6%	71.03%
Proteins	0.19-0.25%	1.3%
Carbohydrates		
• Sugars	1.85-2.27%	15.02%
• Fibre	1.21-1.53%	6.69%
Fats	0.13-0.8%	1.8%

*Chaenomeles japonica* fruits contain about 1.2 - 3.1% of sugars (including 0.5% of fructose, 1.62% of glucose, the rest are sorbitol and sucrose), and 1.3 -

1.4% of pectin (including 80% of protopectin, most pectin is in the flesh of the fruit) [48, 51, 52]. From all sugars, fructose occurs in the largest quantities in *Chaenomeles japonica* fruits (3609 mg/100 g of the fruit). The content of glucose, sorbose, and sucrose in the fruits was also determined [5]. The total content of fibre occurring in *C. japonica* is 3.9 g/100 g of the fresh fruit, and calculated on the base of dry weight is 35 g/100 g (including 8.8g of soluble fibre and 26.6g of insoluble fibre). The main components of the soluble fraction of fibres are: galacturonate (56%), arabinose (10%), galactose (4%) and mannose (7%), and they form pectin, and in the insoluble fraction dominate glucose (38%) and xylose (11%), and they are the parts of the cellulose and hemicellulose.

The content of vitamin C in the fruits of *C. speciosa* has been determined in an amount of 68.8 – 159.3 mg/10 g [62], and in the fruits of *C. sinensis* the content is 154.5 mg% [5]. The amount of this vitamin increases as the fruit ripens [53]. *C. speciosa* has a high content of amino acids, which may reach 0.26 - 0.5 g/100 g of the fruit. It is rich in aspartic acid and glutamic acid, while methionine is not present in fruits [62]. Amino acids occurring in the fruits of *C. sinensis*, in a free form and the largest quantities, are: asparagine, valine, and  $\gamma$ -aminobutyric acid. Cysteine, methionine and tryptophan are among protein building amino acids, which do not occur in fruits of *C. sinensis* [5].

Minerals content in the fruits of *Chaenomeles* are shown in Table 2. *Chaenomeles* fruits are a rich source of potassium, but have a low sodium content, and therefore may serve as a useful food ingredient in the diet of people having high blood pressure. The concentration of calcium, iron, magnesium, zinc, manganese and copper has also been determined. The content of above elements varies according to the species.

Table 2. Minerals in *Chaenomeles* fruits

Minerals	<i>C. speciosa</i> [mg/100 g] [62]	<i>C. japonica</i> [mg/100 g] [28]	<i>C. sinensis</i> [mg/100 g] [5]
Potassium	84.7 – 147.0	249	n/d
Sodium	5.7 – 13.7	4	n/d
Calcium	7.1 – 26.5	22.6	25.3 – 26.8
Magnesium	6.1 – 11.6	16.3	1.1 – 6.6
Iron	0.33 – 0.64	1.8	2.6
Zinc	0.096 – 0.25	0.38	0.4 – 0.7
Manganese	0.031 – 0.43	0.18	1.4 – 3.1
Copper	0.03 – 0.12	0.3	0.1

n/d- no data

The organic acids content in the fruits of *C. speciosa* is 2.09 - 3.47% [54]. Among them the most concentrated are malic acid (70% of all organic acids) and citric acid (22% of all organic acids) [11]. Organic acids, which were identified in *C. sinensis*

fruits, in the largest quantities are tartaric acid (122.9 mg/100 g of the fruit) and  $\alpha$ -glutaric acid (108.6 mg/100 g of the fruit), but also the concentrations of malic, palmitic and stearic acids were determined [5]. Oleanolic, ursolic and pomolic acids belong to

the group of triterpenoids and they were determined in all three species [58]. A new triterpenoid called a speciosaperoxide, and the sesquiterpenoids [45], one of which is a new compound called speciosaoside A, were also determined in *C. speciosa*. [19]. The amount

of tannins in the fruits of *C. sinensis* is 0.4 g/100 g of the fruit. They are condensed tannins or, in other words, proanthocyanidins [32].

Phenolic compounds, occurring in the *Chaenomeles* fruits, are listed in Table 3.

Table 3. Phenolic compounds in *Chaenomeles* fruits

Phenolic compounds	<i>C. speciosa</i> [33, 65]	<i>C. japonica</i> [9, 16]	<i>C. sinensis</i> [9, 27, 33]
Phenolic acids	gallic, protocatechuic, hydroxybenzoic, chlorogenic, cinnamic, caffeic, ferulic, p-cumaric, vanillic, polylactic, 4-hydroksy-3-methoxybenzoic, 2'-methoxyaucuparin	chlorogenic	gallic, chlorogenic, vanillic, ferulic, p-cumaric,
Flavonoids	quercetin, rutin, catechin, epicatechin	catechin, epicatechin, quercetin,	catechina, epicatechin, rutin, maesopsin, luteolin, quercetin, genistein, tricetin, apigenin
Tannins	Procyanidins	procyanidins	Procyanidins

The amount of polyphenols, in fruits of *C. japonica*, is at the level of 924 mg catechin/100 g, but it tends to decrease as the fruits ripen [49, 53]. The content of flavonoids, in *C. japonica* fruits extract, was determined at the level of 0.091 - 0.618 mg/g. These values varied depending on the solvent used [15]. *Sancheti* et al. calculated the content of polyphenols in the fruits of *C. sinensis*, which was 97 mg of gallic acid equivalents/g of dry weight, and the content of flavonoids, which was 35 mg of quercetin equivalents/g of dry weight [40]. However, the research conducted by *Miao* et al. (2016) showed the higher quantities and also a strong correlation between the antioxidant potential and the polyphenols content of these compounds [33]. Analyses were made in the different parts of the fruits of *C. sinensis* and *C. speciosa* (Table 4).

Table 4. Polyphenols and flavonoids content in various parts of the fruits of *C. sinensis* and *C. speciosa* [33]

	Content of polyphenols [mg gallic acid/g dry weight]	Content of flavonoids [mg rutin /g dry weight]
<i>C. sinensis</i>		
• Skin	345	42
• Flesh	430	47
• Endocarp	590	52
<i>C. speciosa</i>		
• Skin	356	26
• Flesh	380	26
• Endocarp	404	51

There have been forty different compounds determined in the fruits of *C. speciosa*, of which the most numerous were  $\beta$ -caryophyllene (12.52%),  $\alpha$ -terpineol (5.41%), terpinene-4-ol (4.56%) 1,8-cineol (4.31%),  $\alpha$ -kadinol (4.23%) and  $\gamma$ -eudesmol (4.12%) [2]. 35 compounds were isolated from the essential oil

of *C. japonica* fruits. The oil in 88% consisted of monoterpenes (of which carvacrol was the most numerous), sesquiterpenes (eg.  $\gamma$ -Cadinene) and non-terpenes compounds, the latter included aldehydes (eg. n-decanal), acids (eg. decanoic acid) and esters (eg. ethyl ester of capric acid) [15]. The essential oil of *C. sinensis* consisted primarily of esters. The following compounds, among others, were established in that oil: ethyl butyrate, butyric acid, ethyl ester, 2-methyl ester, ethyl caproate, hexanal, linalool and menthol. Essential oil content varied depending on whether it came from the skin or the flesh of the fruit. The concentration of terpenes in the oil was low [69]. Aromatic compounds, responsible for the *Chaenomeles* fruit flavours, are shown in Table 5.

Table 5. Aromatic compounds in fruits of *Chaenomeles*

Compounds	<i>C. sinensis</i> [35]
Alcohols	hexanol, diacetone alcohol, (Z)-3-hexenol, (E)-2-hexenol, octanol, $\beta$ -dihydroionol, propanol, 2-methylpropanol, butanol, 1-penten-3-ol, 3-methylbutanol, pentanol, cyclopentanol, benzyl alcohol, 2-phenylethyl alcohol
Aldehydes	hexanal, heptanal, (E)-2-hexenal, (E)-2-heptenal, nonanal, (E,E)-2,4-decadienal, benzaldehyde
Ketons	Methyl isobutyl ketone, $\alpha$ -ionone, $\beta$ -ionone, acetone, diisopropylketone, carvone
Esters	isobutyl octanoate, butyl 7-octanoate, isobutyl 7-octanoate, hexyl hexanoate, ethyl hexanoate, heksyl ethanoate, ethyl 5-hexenoate, ethyl (Z)-4-hexanoate, (Z)-3-hexenyl acetate, 5-heksyl acetate, (E)-2-heksyl acetate, heksyl isobutyrate, isobutyl hexanoate, (Z)-3-hexenyl isobutyrate
Terpenes	Limonene

### Juice of *Chaenomeles* fruits

The juice content in the fresh fruits is 42 - 50%. The fruit juice has a very low pH of 2.5 to 2.8, which correlates with the high acidity of 2.8 - 4.2%. The amounts of nutrients in the juice provide the following values: 45 - 109 mg vitamin C/100 ml of juice and 210 - 592 mg of phenols in 100 ml of juice. Malic acid was a major acid present in the juice (3.06 - 5.09 g/100 ml). The presence of quinic acid (0.62 - 2.27 g/100 ml), and succinic acid (8 - 174 mg/100 ml) were also identified [18]. The juice contained some amino acids, from which the most numerous were glutamic acid (8 - 14 mg/100 ml), phosphoserine (3 - 9 mg/100 ml) and aspartic acid (2 - 6 mg/100 ml). Other amino acids, with the concentration of less than 2 mg/100 ml of juice, include threonine, serine, asparagine, alanine, phenylalanine,  $\gamma$ -aminobutyric acid and lysine [18]. Among the minerals the greatest concentration have potassium (161 - 241 mg/100 ml), fluorine (43 - 139 mg/100 ml) and chlorine (3.5 - 9 mg/100 ml). Sodium, magnesium and calcium have also been identified. Among the carbohydrates the greatest content have fructose (0.7 - 2.3 g/100 ml), glucose (0.3 - 1.1 g/100 ml), sorbitol (0.1 - 0.5 g/100 ml) and sucrose (0.01 - 0.1 g/100 ml), but there are also stachyose, raffinose, sucrose, xylose, rhamnose and inositol present in the juice [18].

### *Chaenomeles* seeds

Seeds, containing about 42% water, make between 5 and 9% of weight of the fruit [18]. The oil content in the seeds of *C. japonica* is between 6.1 and 10.1%. The iodine value of the oil was 94 - 106, and acid value was 2.2 - 2.5. The following fatty acids were found in the seed oil: linoleic acid (44 - 53%), oleic acid (36 - 44%), palmitic acid (9%), stearic acid (1%), arachidonic acid (0.5 - 1%), cis-11-eicosenoic acid (0.5%), linolenic acid (0.5%), behenic acid (0.25%) and erucic acid. It has been shown, that 11% were saturated acids, 37 - 45% monounsaturated fatty acids and 44 - 52% polyunsaturated fatty acids. Behind the strong smell of bitter almond oil of the seeds of *Chaenomeles*, stands benzaldehyde [14]. The seeds of *C. japonica* contained the following phenolic compounds: protocatechuic acid, chlorogenic acid, vanilla acid, syringic acid, p-coumaric acid, gallic acid and coffee acid [34]. The total polyphenol content, in the seed oil of *C. japonica*, was 64 mg/kg (mainly syringic acid),  $\beta$ -carotene - 11 mg/kg, and the antioxidant capacity measured by the DPPH method was determined at the level of 84.5%. The seed oil contained also tocopherols:  $\alpha$ -,  $\beta$ - and  $\gamma$ -tocopherol with amounts respectively to: 69.71 mg/100g, 0.64mg/100g and 2.22 mg/100g, which can be calculated to a total content of all tocopherols in the amount of 72.62 mg/100g [13].

### *Chaenomeles* root

Following substances: daukosterol, three terpenoids (ursolic acid, oleanolic acid and polmoic acid), prunasin and epicatechin have been isolated from the roots of *C. japonica* [57].

### *Chaenomeles* branches

The following substances were isolated from branches of *C. speciosa*: five new oksylipins, chaenomic acid A-E, as well as six previously known compounds which were: pinellic acid, methyl (9S, 12S, 13S)-9,12,13-trihydroksy-10E-octadecanoate, corchorifatty acid, methyl 9,12,13-trihydroksyoctadeca-10E,15Z-dienoate and 9-hydroksynonanoic acid [22]. Biphenyl compounds, which were identified in this part of the *C. sinensis* shrub, include chaenomin, berbekorin A, aukuparyna, 2'-hydroksyaukuparyna, 2',4'-dimetoksyaukuparyna and  $\epsilon$ -cotonefuran [24]. Lignin glycosides, which occur in the branches of this species, are six new compounds named chaenomisine A-F, as well as the five already known glycosides, including aviculin [23].

### *Chaenomeles* leaves

The leaves of different species of *Chaenomeles* have been tested for the content of phenolic compounds. Glycoside naringenin, flavonols (quercetin and kaempferol) and isochlorogenic acid were isolated from *C. speciosa* leaves. Large amount of epicatechin and flavonols (quercetin and kaempferol) and trace amounts of glycoside naringenin were determined in the leaves of *C. japonica*. In the leaves of *C. sinensis*, 7-ramnozyloglikozyd luteolin and epicatechin were the most frequently occurring phenolic compounds [1].

## HEALTH PROPERTIES OF *CHAENOMELES*

### *Use in traditional medicine*

*Chaenomeles* fruits are used as an energizing food supplement and a source of vitamins. They have beneficial effects on the cardiovascular system and provide relief in the case of leg oedema. Fruit juice increases the secretion of digestive acids, and thereafter stimulates an appetite, it is also recommended in the case of anaemia, rheumatism, gout, painful muscle contractions and as an antiemetic agent. Decoctions of *Chaenomeles* provide relief in case of haemorrhoids, used as a compress. Roasted fruits are supposed to help in the case of liver disease, and the slime from the soaked seeds has a protective effect, when used for skin irritation [30]. *C. speciosa* fruits have long been used in Chinese medicine against diarrhoea. Studies on mice have shown, that the *Chaenomeles* extract effectively blocks the effects of thermolabile enterotoxin *E. coli*, which is the most important factor causing so-called traveller's diarrhoea. The researchers suggest, that the compounds responsible for the antidiarrheal effect of

fruit *C. speciosa* are triterpenes: oleanolic, ursolic and betulinic acids. Another feature of the *Chaenomeles* fruits, which contributes to the diarrhoea prevention, is a high tannin content [2].

#### *Antioxidant and anti-inflammatory potentials*

Antioxidant properties of *Chaenomeles* fruits, measured by the method of DPPH, and their reducing properties, investigated using the method of FRAP, are shown in Table 6.

Table 6. Antioxidant and reducing properties of *Chaenomeles* fruits

Properties	<i>C. japonica</i> [37, 48]	<i>C. sinensis</i> [40]	<i>C. speciosa</i> [47]
Antioxidant properties (DPPH)	10512 $\mu\text{mol}$ Trolox equivalents/100 g fresh weight	97 mg gallic acid equivalents/100 g dry weight	236 $\mu\text{m}$ DPPH/g fresh weight
Reducing properties (FRAP)	6.12 $\mu\text{mol}$ $\text{Fe}^{3+}$ /g fresh weight	nd	55 $\mu\text{mol}$ $\text{Fe}^{3+}$ /g fresh weight

nd - no data

Studies on mice have shown, that antioxidant properties of powdered fruits of *C. speciosa* resulted in lower levels of LDL, total cholesterol and triglycerides, increased glutathione peroxidase activity and a reduction in atherosclerotic plaque in the aorta. The compounds responsible for the antioxidant properties are primarily polyphenols and vitamin C, and they are present in large quantities in the fruits [47].

Some of triterpenoids present in *C. speciosa*, eg. oleanolic acid, ursolic acid and maslinic acid, exhibit anti-inflammatory properties. Betulinic acid, also found in *C. speciosa*, has the potential inhibitory properties against inflammatory processes occurring in the blood vessels. Flavonoids and glycosides, in *Chaenomeles* fruits, have an analgesic effect, related to reduced production of inflammation relays in peripheral tissues [65]. Glucosides, separated from fruits of *C. speciosa*, in rats' studies, demonstrated the ability to inhibit the development of collagen-induced arthritis. Sick rats, which have been given the glucosides, resulted in a body mass gain and the increase of thymus and spleen weight. They reduced the proliferation of lymphocytes and synoviocytes, as well as production of IL-1, IL-2 and TNF- $\alpha$ . The effect of glucosides was also based on the inhibition of delayed-type skin hypersensitivity, occurring in rats with arthritis, most likely through the induction and/or activation of T-suppressor lymphocytes. As a result, bone defects have decreased and the inflammation has also been reduced [4]. Further studies have confirmed the beneficial effect of glucosides of *Chaenomeles* fruits in rats with a post-adjuvant arthritis. The administration of glucosides to rats resulted in the reduction of symptoms of disease, the reduction of A synoviocytes, and the production of pro-inflammatory cytokines: IL-1, TNF- $\alpha$  and PGE2 [7]. Therapeutic effect of glucosides on the collagen-induced arthritis has also been observed in

studies on mice [64]. Studies conducted by Strugała have shown, that the ethanol extract of the fruits of *C. japonica* has an antioxidant ability in correlation to liposomes composed of phosphatidylcholine, as well as to red blood cell membranes [46]. According to the researchers, the phenolic compounds present in fruits, including chlorogenic acid and epicatechin, are responsible for these properties. It was also observed, that the components of the extract from the fruit of *C. japonica* are capable of being incorporated in the lipid membrane, which enables them to protect the components of cell membranes and also to stabilize them [46]. The anti-inflammatory properties of *C. sinensis* fruits may be related to their ability to inhibit the mast cells migration and ability to reduce the inflammatory mediators release. The inhibitory effect of TNF- $\alpha$  production by HMC-1 cells was observed in vitro after use of an extract of the fruits. It has been proved, that the extract can also reduce the secretion of IL-6, IL-8 and MCP-1 by macrophages THP-1 and inhibit the release of IL-6 by keratinocytes HaCaT [25]. Leaves of *C. sinensis* have also been tested for their anti-inflammatory and antioxidant properties. The total content of polyphenols in the leave extract was 132 - 166 mg of gallic acid equivalents/g of extract, and the total flavonoids amount was 155 - 174 mg catechin equivalents/g of extract. Antioxidant capacity of the extract against the ABTS radical was determined at the level of 0.94 - 0.99 mmol Trolox equivalents/mg of extract, whereas the reduction potential level of 2.16 - 2.45 mmol equivalents of  $\text{FeSO}_4$ /mg of extract. Higher values of all parameters were determined in the aqueous extract, while lower in the ethanol extract [17]. The same in vitro studies have shown anti-inflammatory activity of *C. sinensis* extract, which was an effect of reducing the production of TNF- $\alpha$ , IL-6 and pro-IL-1 $\beta$  by macrophages, as well as excessive production of nitric oxide induced by endotoxin called lipopolysaccharide [17].

#### Anti-microorganism activity

The essential oil, derived from *C. speciosa*, demonstrated anti-microorganism activity, more effective against bacteria G (+). *Staphylococcus aureus* proved to be the most sensitive to the oil properties. The researchers suggest, that the oil anti-bacterial properties may result from the presence of  $\alpha$ -terpineol, terpinene-4-ol or p-cymene [55]. In vitro studies indicate the potential use of an extract from the fruit of *C. speciosa* against the influenza virus. The study by Zhang verified the ability of the compounds, isolated from an extract, for inhibiting the secretion of inflammatory mediators by macrophages, that are involved in the pathophysiological processes underlying influenza [69]. The compounds, such as 3,4-dihydroxybenzoic acid, methyl 3-hydroxy butanedioic ester and roseoside have shown the ability to lower TNF- $\alpha$ , and IL-6 secretion was inhibited by methyl 3-hydroxy butanedioic ester. Most of the tested compounds had the ability to inhibit the production of nitric oxide which is associated with post-influenza complications in lungs. Methyl 3-hydroxy butanedioic ester, 3,4-dihydroxybenzoic acid and vomifoliol were also involved in blocking of influenza virus replication [63]. *C. sinensis* fruits also indicate an antiviral activity. Properties of *Chaenomeles* fruits ethanolic extract are similar to the results obtained from the green tea leaves extract. Neutralization of influenza virus is primarily achieved by inhibition of viral hemagglutinin (which prevents the virus from penetration into human cells) and also blocking the replication of the virus. The high content of polyphenols is probably the most important feature responsible for antiviral activity of *C. sinensis*. Further studies showed more than two-fold reduction of individual cells infection in the case of using solution from the fruit of *C. sinensis*. Total infectivity of influenza virus, under the influence of the solution, is reduced to 1/100 as compared with the control group [43, 44]. *C. sinensis* fruits antiviral properties have also been observed in studies by Hamauzu from 2005. The authors suggested that these properties may be caused by the presence of procyanidins in the *chaenomeles* fruits [16].

#### Immunomodulatory and anticancer properties

Polysaccharides, extracted from *C. sinensis*, showed an indirect antitumor effect. The mechanism of action of these compounds was based primarily on enhancing the immune system response by the proliferation of lymphocytes and macrophages, as well as improving the ability of the latter to phagocytosis. At the same time, *Chaenomeles* extract showed the intensifying effect of type IV hypersensitivity reactions, which may confirm the role of polysaccharides in enhancing of cellular immune responses. Researchers have also tested the impact of *C. sinensis* polysaccharides on

the secretion of cytokines. It has been found, that the extract increased the secretion of IL-2, TNF- $\alpha$  and IFN- $\gamma$ . All the compounds, mentioned above, improve the immunity response of the human body [56]. Gao et al. conducted an in vitro study relating to the anticancer attributes of woody parts of *C. sinensis* [10]. The studies indicate that certain compounds, isolated from the branches of *C. sinensis*, inhibit the growth of colonies of epidermal cancer cells JB6 in mice. The compound with the highest potential, regarding above occurrence, was betulinic acid and its derivatives: caffeoyl and p-cinnamoyl [10]. Yao et al. showed, that the ethanol extract of *C. speciosa* has the ability of inhibiting the proliferation and inducing apoptosis in tumour cells in vitro [61]. The apoptosis was induced via the activation of endonucleases, as well as by the decrease in energy production in mitochondria. This effect was confirmed in the in vivo study using, as the model, the mouse liver cancer. The effectiveness of tumour cell colony growth inhibition was determined at 39%, while this percentage for a cisplatin (a drug used in cancer chemotherapy) was 58%. It has been also recorded, that mice, treated with the extract of *Chaenomeles*, had less severe side-effects of therapy compared to cisplatin and there was also the increase in lymphocyte proliferation and antibody production (the both parameters decreased while using the chemotherapeutic agent). In addition, the extract reduced the expression of the genes Foxp3, PD-L1 and TGF- $\beta$ , which adversely affects the functioning of the immune system [61]. Anti-cancer properties of the extract of the fruits of *C. japonica* have also been proved in vitro. In the experiment, using the cell colonies of human colon adenocarcinoma (Caco-2), the inhibition of the growth of tumour cells, while the increase of the cell numbers undergoing apoptosis, and also the number of dead cells, have been recorded. This effect was not observed against healthy small intestine epithelial cells (IEC-6) in rats. The researchers suggest the above effect is caused by the high content of procyanidins in fruit extract of *C. japonica* [12]. Lewandowska et al. [29] verified antitumor properties of the extract from the fruit of *C. japonica* on human breast tumour cells MDA-MB-231, prostate tumour DU 145 and healthy prostate cells PNT1A. The tested extract showed ant proliferative activity against cancer cells, breast tumour cells MDA-MB-231 were especially sensitive to its effect. This consequence was not observed in the case of healthy cells, on the contrary - their numbers were increased. The extract also reduced the invasiveness of tumour cells, probably by reducing the genes expression, whose products are involved in the angiogenesis and tumour metastasis. The increase in the susceptibility of cancer cells to apoptosis inducing factors has also been recorded [29].

### Hepatoprotective property

A study has been conducted, to examine the effects of the drug Jiangzhi, which consists of thirteen plants, including fruit *C. speciosa*. The recipe has its roots in a traditional Chinese medicine and is used in cases of lipid disorders, which are causing the non-alcoholic fatty liver disease. The administration of the tested drug to rats, which were previously fed with fructose to induce the lipid disorder, significantly affected the reduction of triglycerides in the liver. It also resulted in a decrease in gene expression of SREBP-1c, ACC-1 and SCD-1, involved in the regulation of hepatic synthesis of fatty acids de novo [68]. Further studies recorded the hepatoprotective effect of the extract from the fruit of *C. tibetica* in rats, whose liver damage was induced by carbon tetrachloride (CCl<sub>4</sub>). The experiment has shown, that the use of an extract of *Chaenomeles* fruits resulted in the reduction of liver enzymes ALT, AST and ALP. There was also a recession of histopathological changes within the organ [31].

### Neuroprotective activity

The studies over *C. speciosa* recorded its impact on the regulation of the dopamine transporter (anti-parkinsonism effect). According to ex vivo studies, the extract of *Chaenomeles* fruits shows the inhibitory effect against the dopamine transporter (DAT) in Chinese hamster ovary cells (CHO). At the same time the extract had no effect on the functioning of GABA transporter and serotonin, and only a small effect on the norepinephrine transporter. It can conclude, that this effect is specific to the dopamine transporter. The extract also had no cytotoxic effect against cells with DAT expression, its neuroprotective effect is likely caused by the prevention of the toxic ligands transport by dopamine receptors. *Chaenomeles* fruits had a positive impact on the neurobehavioral functioning of rats with early stage of *Parkinson's* disease. Studies have also shown a reduction in neurons loss, containing tyrosine hydroxylase, in the substantia nigra [67]. The effect of the extracts of the fruit of *C. sinensis* on cognitive abilities has also been studied. Mice, having problems in this regard, showed a behavioural improvement after the administration of the ethanol extract of *Chaenomeles* fruits. The researchers suggest, that the substance responsible for this activity, may be a methyl ester of stearic acid. This compound has the ability to activate the choline acetyltransferase, the function of which is impaired in the case of dementia. It works also well in protecting nerve cells against the toxic compounds [26].

### Antidiabetic properties

In vitro studies have revealed, that the fraction of *C. sinensis* fruit extract, which is soluble in

ethyl acetate, shows inhibitory properties against  $\alpha$ -glucosidase,  $\beta$ -glucosidase [42],  $\alpha$ -amylase, lipase and acetylcholinesterase [41]. In the study by Sancheti et al. the *Chaenomeles* extract ability for lowering the glucose level in the blood of rats with the artificially induced diabetes, were researched [40]. The effect of orally administered solution of *C. sinensis*, at the concentration of 500 mg/kg, was comparable to glibenclamide (sulfonylurea derivative used to treat diabetes). The intervention also caused the increase of the level of haemoglobin in the blood of rats. Levels of total cholesterol, triglycerides, VLDL and LDL in the blood - the parameters which are usually disrupted in people with diabetes - after applying of the *Chaenomeles* solution have been restored to the levels before the diabetes was induced. The solution positively influenced the level of HDL, increased glycogen content in the liver, decreased levels of acetylcholinesterase (associated with a higher incidence of dementia and *Alzheimer's* disease in diabetic patients), and ALT and AST. *Chaenomeles* fruit extract, also helped to boost the activity of enzymes, such as superoxide dismutase, catalase and glutathione, in the tissues of sick rats, which activity decreased as a result of the development of diabetes. The markers of liver and kidney damage have also been improved [40]. In the experiment conducted on rats, by the same team of researchers, the tests of glucose and maltose were performed, and part of the test group was given the fraction of the solution soluble in ethyl acetate. The animals, which were given the solution of *C. sinensis*, had significantly lower increase in blood glucose level, and it also returned to baseline much faster when compared to rats given no solution [41]. All of above experiments indicate the potential use of the solution of *Chaenomeles* fruits to treat diabetes. The high content of polyphenols, flavonoids and the presence of quercetin, rutin, ursolic acid and oleanolic acid in fruits also have a beneficial effect on the improvement of diabetic parameters [6, 8, 20, 21].

### Antiallergic and antipruritic abilities

Glucosides, extracted from *C. speciosa*, reduce the immune response in the case of contact hypersensitivity in mice by reduction of the ratio in lymphocytes T CD4<sup>+</sup>/CD8<sup>+</sup> and the reduction of production of IL-2 and TGF- $\beta$ 1, and, at the same time, increase of the level of IL-4 in the thymus [30]. The study on rats examined the effectiveness of the compounds isolated from an extract of the fruits of *C. sinensis* to alleviate the pruritus induced by administration of the compound 48/80, which causes mast cells degranulation. It has been found, that the isolated compounds, such as 3-galactoside quercetin or protocatechuic acid, reduced the frequency of scratching in rats as much effective as ketanserin, but

significantly less than cimetidine. These compounds had no effects of reducing the animals' mobility. Based on this experiment, the researchers concluded, that the extract of the fruits of *C. sinensis* may lower the itching induced by 5-HT, however, have no effect on the pruritus induced by histamine [39].

#### *Effect on gastrointestinal microbiota*

The influence of extracts of *C. japonica* fruits, on normal bacterial flora, was tested by *Strugala et al*[46]. In vitro studies have demonstrated, that the ethanolic extract of *C. japonica* increased the bacterial culture numbers of *Lactobacillus casei* about 14-44%, and *Lactobacillus plantarum* about 1-23%, dependable on the dosage, against the control test. The researchers explain this effect by the high content of phenolic compounds in the extract, and their unique composition [46].

#### *The impact on the performance in sport*

Animal studies indicate that the aqueous extracts of the fruits of *C. sinensis* and *Schinsandra chinensis* affect the ability to exercise. These studies have found, that the mixture of extracts of both plants decreased accumulation of lactate and assisted in its removal from the blood circulation in rats, during and after a high intensity training, carried out on a treadmill. The second experiment, using the same extract, was carried out on mice. Physical performance of these animals was checked for the exercise performed in the water. It was observed that the group, which was administered the extract, could exercise for longer, and could better metabolize the lactate, the substance produced during exercising. The results of these studies indicate a potential use of the extract from the fruits of *Chaenomeles* in sport [38]. Studies on the powder obtained from the fruits of *C. speciosa* show, that it may be beneficial in the case of exhausting aerobic exercise. This powder lowered the reduction of the concentration of glucose in the blood of rats, as well as assisted in saving glycogen amounts in the muscles and liver. This effect allowed the exercise to be continued for a longer period of time. Other advantages, recorded after the ingestion of the extract of the fruits of *C. speciosa*, were, the reduction of the concentration in exercise-induced lactic acid and urea nitrogen (which are the sensitive indicators of physical exhaustion), reduction in the markers of inflammation, and an increase in the exogenous antioxidants activity. Most likely, the delay effect in the feeling of being exhausted, after using the fruits of *C. speciosa*, is obtained by a regulation in the Nrf2/ARE pathway [3].

#### *Effect on body weight*

Traditional Chinese medicine have recipes that help regulate body weight. One of these recipes is W-LHIT,

which consists of six plant materials, including *C. speciosa*. In order to verify its effectiveness, an experiment has been conducted. In this experiment the mice were on a high-fat diet, that caused them to be obese, and then divided into two groups: a one group was fed using the normal food and a second group additionally receiving a supplement of W-LHIT. The weight loss has been recorded in both groups, but in the supplemented group the decrease was faster. In the next experiment the tested drug was administered to the obese mice, which were on a high-fat diet. In comparison to the control group, not receiving the W-LHIT, the weight gain in the supplemented group was lower [60].

#### *Impact on metabolism of ethanol*

*Zhang et al.* [66] tested the effect of different fruit juices on the metabolism of ethanol. It has been recorded, that the juice from *C. japonica*, given after drinking alcohol, increased the ethanol concentration in the blood of rats, against the control group, which received distilled water. The researchers conclude, that the juice from the fruits of *C. sinensis* should not be drunk together with alcohol, as it may increase the toxicity of ethanol. At the same time, the juice reduced the activity of aldehyde dehydrogenase *in vitro*, which may be associated with worsening of the symptoms of alcohol poisoning [66].

## SUMMARY

Long-standing in folk medicine, the *Chaenomeles* fruit contains many ingredients, including vitamin C, minerals, amino acids, antioxidants and others which can exert beneficial effects on health and promote the treatment of many diseases. Numerous published experimental data on the *Chaenomeles* fruits show their therapeutic properties. Besides, the extracts of *Chaenomeles* fruits may be used as an energizing food supplement and a source of vitamins which indicates a potential use of the extract from the fruits of *Chaenomeles* in sport.

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