Chemical composition and biologic activities of different preparations of Japanese quince

(Chaenomeles japonica)

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Abstract: The hectic pace of life and growing threat of cardiovascular, metabolic and neoplastic diseases highlight the demand for products with natural origin that could simultaneously be part of the balanced diet and improve human’s health. A promising finding in this respect is the Japanese quince – Chaenomeles japonica. It is an ancient plant with eastern origin, but the scientific knowledge about it has only recently started to build up.

The aim of this review is to gather scientific data about chemical composition and biologic activities of Chaenomeles japonica and to provide an insight into the possible prophylactic and therapeutic applications of the plant. The gathered and summarized information concerning Japanese quince shows that preparations of different parts of the plant, especially fruits and leaves, possess biologic properties that could be of exceptional nutritional and medicinal value. Antiinflammatory, antiproliferative, antimicrobial, carbohydrate metabolism-modulating activities in in vitro studies as well as safety profile, influence on neuropsychology and behavior in animal models are discussed.

This review outlines the prophylactic and therapeutic effects of Chaenomeles japonica, as well as the chemical composition that stands behind them, and aims to serve as a basis for further investigations of the medicinal plant’s potential.

Keywords: Functional food, Chaenomeles japonica, Japanese quince, medicinal plants
Introduction

*Chaenomeles* sp. is a type of deciduous shrub belonging to the family Rosaceae [1] and subfamily Maloideae, tribe Maleae. Parts of plants belonging to the genus *Chaenomeles*, also known as Mugua in Chinese (meaning papaya), have been used in traditional eastern medicine for thousands of years. *Chaenomeles* sp. has been reported to be used for treatment of cramps, anemia, rheumatism, gout, cardiovascular diseases, cholera, beriberi, stomach and intestinal pains, sunstroke, and as a sedative and excitant [1]. There is limited scientific validation of this data till now. The genus naturally occurs in Asia, although in the last centuries *Chaenomeles* sp. have been introduced to all the continents on Earth except for Antarctica [1]. Its massive expansion and flexibility to climate differences point out the increasing importance of finding out which of the numerous reported uses over the centuries could turn out to be actual therapeutic applications.

The genus name *Chaenomeles* originates from the Greek words *chaino* (“to gape”) and *melon* (“an apple”). Out of the four main species belonging to the genus, the Japanese quince – *Chaenomeles japonica* (Thunb.) Lindl, also known as Maule’s quince, is the one that was introduced to Europe by Messrs Maule, nursery workers in Bristol, England [2]. In Bulgaria it is known as Mountain lemon, “jabalche”, etc. Its height varies, being 120-130 cm on average with beautiful pink-colored flowers and apple-shaped fruits.

In recent years, there has been a growing scientific interest in natural plants used in traditional eastern medicine, particularly in the *Chaenomeles species*. Concurrently, there has also been an increase in interest in so called “functional foods” [3], which are defined as foods with health benefits that exceed their nutritional value. *Chaenomeles japonica* appears to be a suitable candidate for this category, as it possesses various beneficial properties. Furthermore, no-waste production technologies are becoming increasingly popular with Japanese quince waste products showing potential for use in cosmetics and other industries [4]. This review aims to summarize the current data on the biochemical composition, organoleptic properties and biological activities of *Chaenomeles japonica*.

Results and Discussion

Fruits

*Chaenomeles japonica* fruits are usually apple-shaped, although lemon-like or pear-like shapes are also present, with yellow to green color. They are the smallest in the genus *Chaenomeles* – their size is up to 4 cm in diameter and their weight is usually up to 50 g [5]. The fruits of *Chaenomeles japonica* seem to be a valuable source of ascorbic acid, fibers, phenolic compounds, macro- and microelements, including Mg, Fe, Zn and Cu. They are rich in vitamin A, vitamin E and essential amino acids.
Organoleptic properties

*Chaenomeles japonica* has a rich aroma profile. The flavour is described as having floral, fruity, balsamic and woody notes. The major volatile compounds isolated from its fruits and fruit juice contributing to this fragrance are methanol, ethanol, 1-penten-3-ol, α-terpineol, acetone, ethyl-vinyl-ketone, valeraldehyde, (E)-2-hexenal, ethyl acetate, linalyl acetate, geranyl acetate and ethyl anthranilate [6]. Based on this aroma profile, *Chaenomeles japonica* could extend its use in the food, perfume, cosmetic and pharmaceutical industries.

Because of their high acidity and hard pulp, the raw fruits are not appropriate for direct consumption. A diverse range of Chaenomeles products has been developed and continues to expand, including juice, puree, wine, vinegar, syrup, liqueur, carbonated soft drinks, marmalades, flavoured sweets, ice cream, jam, curd [7] and even innovative food powder [8]. In the past century, there have been industrial experiments to produce pectic substances from the fruits, similar to those of apples. A study among the Swedish population reports a positive response to the flavour of *Chaenomeles* in several of these products [9].

Japanese quince wine is a very rich source of polyphenols, surpassing grape wines, some other fruit wines and ciders. The Japanese quince wine is characterized by high antioxidant capacity and good results obtained in sensory assessment tests. Therefore, the product shows promising commercial potential [10].

The enrichment of different products with *Chaenomeles* fruit extract improves their quality. Tarko et al. reported that the antioxidant activity of apple chips supplemented with Japanese quince extract was 62% higher than the control one. At the same time the total polyphenol content in both samples did not differ significantly, which shows that other non-polyphenolic compounds contribute for the antioxidant properties [11]. Same authors have examined the antioxidant activity and polyphenolic content in *Chaenomeles*-enriched apple, orange and grapefruit beverages, and noticed an elevation in both parameters as well as improved organoleptic properties reported by consumers [12].
Biologically active substances in fresh and dried fruits

Chaenomeles japonica fruits are characterized by a high content of ascorbic acid [13, 14], which is the main biologically active form of vitamin C. As a natural antioxidant, ascorbic acid could be helpful in the prevention of various chronic diseases. Japanese quince fruits are a great source of polyphenols, chlorogenic acid being the predominant one. Chlorogenic acid has been reported to produce a number of beneficial effects, including antidiabetic, neuroprotective, antioxidant, antiviral, hepatoprotective and anticancer activities [15] as well as antinociceptive [16] and anxiolytic [17] properties in animal models. The most abundant flavonoids, detected in the fruits, are catechin, epicatechin and quercetin. The antioxidant properties of these substances are well established. Quercetin has been shown to also possess lipid-lowering, antihypertensive, antihyperglycemic, anti-inflammatory, antimicrobial, antineoplastic, neuro- and cardioprotective effects. In addition, it seems to interfere with the level of some adipokines, such as adiponectin and leptin, suggesting another underlying mechanism of its beneficial effects in metabolic syndrome and associated conditions [18]. Procyanidins, mainly procyanidin B2 were identified in the fruits, too [19, 20]. The dietary consumption of procyanidins favours weight loss, adipose tissue reduction and might be involved in regulation of gene expression.
expression, concerning glucose and lipid metabolism [21]. Having in mind that direct raw fruit consumption is not appropriate, it is important to note that ascorbic acid and phenolic compounds are preserved in some edible forms of *Chaenomeles*, such as candied quince slices and syrup [22].

The content of dietary fibre in *Chaenomeles japonica* fruits is high – on average 32 g/100 g dry fruit [23]. Dietary fibres are known to be a very important constituent of a healthy eating lifestyle with protective properties against cardiovascular diseases, diabetes, obesity, colon cancer, etc. Therefore, it is important to consider adequate fiber consumption in metabolic syndrome. Japanese quince fruits are rich in pectin. The immature fruits serve as a main source, since pectin is partly transformed into monosaccharides during the ripening process. The average content varies between 0.65-1.08% of fresh fruit in different genotypes [24], and the dry fruits contain 11 g pectin per 100 g [25]. The levels are comparable with these of apples. According to Hellin et al., the addition of *Chaenomeles* pectin to baked goods improves their quality [7]. Pectin is a structural polysaccharide – a component of the plant cells walls. It cleans intestinal villi, thus improving absorption of biologically active substances, and stimulates gut motility. The relationship between pectin intake and cholesterol levels has been studied. Gunnes and Gidli suggest three possible mechanisms for the lipid-lowering effect of pectin consumption: i) prevention of bile salt reabsorption from the small intestine; ii) reduced glycemic response leading to lower insulin stimulation of hepatic cholesterol synthesis; and iii) inhibition of cholesterol synthesis in the liver by pectin fermentation products (mainly propionate) [26]. Immunomodulatory, hypoglycemic, antioxidant, antibacterial, anticancer and anti-inflammatory activities have also been established [27]. Based on this data, high content of pectin in the Japanese quince fruits suggests a potential beneficial effect of their consumption in dyslipidemia, hyperglycemia, metabolic syndrome and related conditions.

*Chaenomeles japonica* fruits contain several carotenoid and chlorophyll compounds, vitamin A, vitamin E and ten aminoacids, three of them being essential ones [28]. Based on these findings, Japanese quince could be defined as a balanced source of nutritional elements.

The process of fertilization with organic and mineral fertilizers influences the chemical composition of Japanese quince fruits affecting the amount of dry matter, total sugars, sucrose, ascorbic acid and tanning substances [29], so it seems that the potential benefits of *Chaenomeles* fruits can increase even further.

**Fruit juice – content and biological activity**

The sour taste and the low pH of the *Chaenomeles* fruit juice are due to the high content of organic acids [30]. Three organic acids have been discovered in *Chaenomeles japonica* fruit juice by Hellin et al: malic acid, quinic acid and succinic acid [31]. Additional organic acids have been identified by Valcheva-Kuzmanova et al. in fruit juice of Japanese quince. These are citric acid, shikimic acid, ascorbic acid and oxalic acid [30]. *Chaenomeles* fruit juice is extremely rich in polyphenolic substances, with vanillic, caffeic...
and chlorogenic acid dominating among the phenolic acids and epicatechin, catechin and quercetin-3-β-glucoside being the most abundant flavonoids [30]. Several studies suggest a strong correlation between the phenolic content and the antioxidant capacity of *Chaenomeles* fruits [32]. Seven monosaccharides have been found in the juice – glucose, fructose, galactose, sucrose, xylose, rhamnose and arabinose [30].

In animal models, *Chaenomeles* fruit juice has demonstrated important effects on the central nervous system, probably related to its high content of polyphenolic substances. It has antagonized the reserpine-induced hypokinesia, likely through modulation of monoaminergic neurotransmission [33]. Subchronic administration of the fruit juice has also improved the locomotor activity in healthy animals [34]. The behavior of rats treated with *Chaenomeles* fruit juice in an open field test has revealed a psychomotor stimulating and anxiolytic-like activity [35]. The treatment of healthy rodents with *Chaenomeles* fruit juice decreased also the immobility time in the forced swim test that is used for assessment of depression-like behavior in animals. These results might be attributed either to the increased locomotor activity due to psychomotor stimulation or to antidepressant-like effect [36]. Antidepressant-like and anxiolytic-like effects were also observed in a model of mild stress due to impaired circadian rhythm [37]. In a study focused on the safety profile of *Chaenomeles maulei*, Borisova et al. found lack of liver and kidney toxicity in subchronic administration. What is more, the highest dose used demonstrated a potential hepatoprotective effect [38].

**Biological activity of fruit extracts**

For the purpose of further exploring Japanese quince fruit potential, different extracts have been prepared and investigated.

In a toxicological *in vitro* study, no evidence of apoptosis in hepatocytes or increased reactive oxygen species (ROS) formation in their mitochondria was found after incubation with the extract of quince at any concentration used. No signs of apoptosis or necrosis were found microscopically. What is more, a dose-dependent decrease in the lipid peroxides concentration was observed, which indicated potential hepatoprotective properties [13].

In another *in vitro* study, Japanese quince fruit extract demonstrated a growth inhibitory effect on human colorectal adenocarcinoma Caco-2 cells. Gorlach et al. observed that the incubation of Caco-2 cells with 50 μg extract/mL increased the number of apoptotic cells by 52.1% versus control, as assessed by flow and image cytometry after 72-hour incubation [39]. These cells are characterized by high malignancy and are known to be resistant to a number of conventional cytostatic drugs. According to the authors, the growth inhibitory and pro-apoptotic effects of the Japanese quince fruit extract could be attributed to the presence of oligomeric and polymeric procyanidins. The suggested mechanisms might involve inhibition of tyrosine kinase ErbB2 expression, inhibition of polyamine biosynthesis, inhibition of protein kinase C activity, alteration of membrane fluidity. A flavanol extract from *Chaenomeles japonica* fruits is reported to suppress
expression of cyclooxygenase-2, metalloproteinase-9 and nuclear factor-kappaB in human colon cancer cells [40]. The flavanol preparation is also observed to have an antiproliferative effect against human prostate and breast cancer cells. The fruit flavanols inhibited the invasiveness of the cells and decreased the expression of several genes involved in apoptosis, angiogenesis and metastasis [41].

Japanese quince fruit extract has also shown potent concentration-dependent antimicrobial activity against gram-positive and gram-negative bacteria, with highest effect on Enterococcus faecalis [42].

Zakłos-Szyda and Pawlik evaluated the in vitro activity of polyphenolic extract from Japanese quince on carbohydrate metabolism. For this purpose, HepG2 cell line was cultivated either in normal, metabolically unchanged conditions, or in hyperglycemic conditions. Pretreatment of the cells with the extract decreased the production of free oxygen radicals and influenced polarization of mitochondrial membrane, which seemed to lead to activation of 5-adenosine monophosphate activated protein-kinase (AMPK) – one of the most important regulators of lipid and glucose metabolism with expression in liver, brain, skeletal muscles and fat tissue. AMPK activation is one of the mechanisms of action of the antidiabetic drug metformin. In addition, elevation of glucose uptake and glycogen content, and alleviation of gluconeogenesis through modulation of gene expression were observed. Based on these results, the authors suggest that polyphenolic extract of Japanese quince could be useful for prevention of prediabetes, diabetes type 2 and metabolic syndrome [43].

Another potentially beneficial effect of Japanese quince in diabetes is related to its ability to inhibit pancreatic alpha-amylase and intestinal alpha-glucosidase. Alpha-glucosidase is an enzyme located on intestinal mucosal cells that converts starch and disaccharides to glucose. Its inhibition leads to delayed intestinal absorption of glucose and therefore to reduction of postprandial hyperglycemia. Some of the approved medications for diabetes type 2, such as acarbose, produce their effects through the same mechanism of action. Turkiewicz et al. reported values of IC50 between 16.11–17.45 mg dried fruit/ml for alpha-amylase and 6.09–15.19 mg dried fruit/ml for alpha-glucosidase [24].

**Essential oil**

Current data on Chaenomeles japonica essential oil composition varies significantly according to the environmental conditions and method of destillation. The oil is rich in monoterpenes, the main components being carvacrol, limonene, p-cymene and γ-terpinene [44]. Carvacrol, the most abundant component, is a phenolic monoterpenoid known for its antimicrobial, antioxidant and anticancer activities [45]. The oil also contains sesquiterpenes and nonterpenoids, including aldehydes, acids and esters. Essential oils find use as food additives, in aromatherapy, in cosmetics, etc. As far as we know, potential uses of Chaenomeles japonica essential oil have not been studied yet, so it is one more possible direction for future research.
Seeds and seed oil

The seeds represent 5-9% of the fresh fruit weight. The content of seed oil is reported to be on average 8.2% of the dry weight of the fruit [46]. Like the fruits, Japanese quince seeds serve as a valuable source of phenolic compounds, such as protocatechuic acid, chlorogenic acid, vanilla acid, syringic acid, p-coumaric acid, gallic acid and coffee acid [19].

*Chaenomeles japonica* seed oil (CJSO) is liquid at 4°C. It is characterized by intense yellow color (due to the high number of carotenoids) and specific pleasant odor [47]. Its content includes seven carotenoids: beta-caroten, beta-cryptoxanthine, zeaxanthine, lutein, violaxanthin, trans- and cis-neoxanthin; the presence of one more carotenoid has been detected, but it remains unidentified. CJSO is a richer source of carotenoids than the common edible plant oils, such as linseed, grapeseed, peanut and sunflower, surpassing them more than 10 times [48]. The average carotenoid concentration is 2.68 mg/100 mg, with limited influence of the genotype over the concentration. This is an interesting and useful observation since *Chaenomeles* species are prone to spontaneous hybridization and cultivated genotypes of Japanese quince are numerous. The small variation in carotenoid concentration suggests a constant yield of carotenoids [49]. That is good news in the light of evidence for reduced incidence of various chronic diseases and reduced all-cause mortality associated with the dietary intake of carotenoids, but also existing concerns about their safety when administered in high doses [50].

A number of phytosterols have also been isolated from the seeds: campesterol, stigmasterol, beta-sitosterol, avenasterol, delta7-stigmasterol, cycloartenol. Their total amount in the oil is 3.86 mg/g. Phytosterols are natural bioactive substances, clinically recommended for reduction of cardiovascular disease risk, and represent promising anti-cancer agents [51]. In addition, they exert some healing effects on the skin and are, therefore, potentially useful in local rejuvenation therapy [52]. The natural triterpene squalene has also been detected in the seed oil at a concentration of 0.67 mg/g [53]. Due to its moisturizing and antioxidant activities, squalene is used in cosmetic dermatology. Another effect of the CJSO that could be useful in cosmetics is its ability to absorb harmful UV radiation.

Gornas et al. discovered that CJSO contained the highest number of tocopherols (vitamin E compounds), beta-carotene and total phenols, and presented the lowest level of chlorophyll and peroxide value in comparison to sesame, poppy, peanut, flaxseed, pumpkin, sunflower, almond, hazelnut and walnut oils [54]. Peroxide value is an indicator of oxidation being a major concern in the production of bio-oils. Low peroxide value of the product stands for good quality of the raw material and proper conditions during extraction process. Low chlorophyll content shows low tendency for oxidation under the influence of light. Authors identified also thirteen fatty acids, the palmitic, oleic and linoleic acid being the predominating ones. Amygdalin is not present in the CJSO, which allows its use in food industry [54]. In addition, CJSO has been
characterized by a high iodine index (98 on average) and low acid index (2.3% on average) [4]. The antioxidant properties of the seeds were reported also by Mierina et al., who found out that their extracts increase oxidative stability of vegetable oils up to 2 times [55]. The authors outline the potential use of CJSO for stabilization of other oils [56].

**Roots**

The roots of *Chaenomeles* sp. grow extensively and deeply into the soil, which allows them to absorb water and nutrients efficiently. They have been found to contain various bioactive compounds such as daukosterol, three terpenoids (ursolic acid, oleanolic acid and polmoic acid), prunasin, epicatechin and an acylated triterpene [57]. Pentacyclic triterpenes represent an interesting topic. Oleanolic acid and its isomer ursolic acid are known with their anti-inflammatory, hepatoprotective and lipid-lowering effects in the traditional eastern medicine [58]. Recently, their antiviral, antimicrobial and anticancer properties are being investigated [59].

**Leaves**

Leaves are smooth, soft, green, with an ovoid shape and a length of 3-5 cm [60]. They are a rich source of polyphenols, the major polyphenol group being proanthocyanidins according to some authors [61] and phenolic acids according to others [62]. Total phenolic acid and flavonoid content in leaves of Japanese quince was evaluated by Grygorieva et al., estimating their antioxidant activities and suggesting that they could be a promising source of antioxidants useful in medical practice [63]. Large amount of epicatechin and flavonols (quercetin and kaempferol) and trace amounts of the glycoside naringenin were determined in the leaves of *Chaenomeles japonica* by Challice [64]. The most abundant triterpene in *Chaenomeles japonica* leaves is ursolic acid, which is known with its cardioprotective and immunomodulatory activities as well as its ability to suppress nuclear factor-kB, responsible for regulation of expression of genes, involved in cancerogenesis [62]. Chojnacka et al. compared the phytochemical composition of crude phenolic extract and purified phenolic-rich extracts of Japanese quince leaves and found out that both extracts contained diversified phenolic compounds, with the predominance of chlorogenic acid and naringenin hexoside [65]. The authors investigated the cytotoxic activity of the extracts towards colon cancer cells SW-480 and HT-29 and reported that the purified phenolic-rich extract exhibited greater cytotoxic and antioxidant properties. In another study, the Japanese quince phenol-rich leaf extract showed chemoprotective effects on colon cancer cells by downregulation of both the activity and protein expression of MMP-2 and MMP-9. The authors suggest modulation of extracellular signal-regulated kinases/AKT signaling pathway [66].

In a study of *in vitro* lipopolysaccharide-induced inflammation *Chaenomeles japonica* leaf phenol extract inhibited COX-2 and iNOS expression both at the mRNA and protein level and significantly decreased the expression of TNF-α, IL-6 and IL-1β [67].
With ever growing bacterial resistance to current antimicrobials, the search for new plant sources of antibiotics is increasing. Kikowska et al. reported antiamebic and antimicrobial activity of several extracts obtained from the fruits and leaves of Chaenomeles japonica [68]. A remarkable amebicidal effect against the trophozoites and antibacterial activity against Staphylococcus aureus was reported for the extract of leaves.

**Flowers**

Flowers are most oftenly pink, orange or red, with an average size of 3-4 cm in diameter and a characteristic brightening at the base or at the top of the petals, contributing to the esthetic properties of the plant [69].

The biologic activities of Chaenomeles flowers are still not studied. However, Komar-Tyomnaya et al. established that the flowers contain a higher amount of essential macro- and microelements compared to the fruits and seeds of the plant [70]. Therefore, the authors suggest that they could be a valuable raw material with various beneficial effects. Flavonoid profile of petals was determined by Shen et al. [71].

**Conclusion**

In recent years, interest in Chaenomeles sp. has increased significantly, with growing evidence suggesting promising organoleptic properties, prophylactic, therapeutic, and cosmetic applications of the plant. Future research should focus on the impact of Japanese quince fruit juice and fruit extract consumption on metabolic and neoplastic diseases, as this represents an important direction for investigation.

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