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Review

Apples: Content of phenolic compounds vs. variety, part of apple and cultivation model, extraction of phenolic compounds, biological properties

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ABSTRACT

Apples are among the most popular fruits in the world. They are rich in phenolic compounds, pectin, sugar, macro- and microelements. Applying different extraction techniques it is possible to isolate a particular group of compounds or individual chemicals and then test their biological properties. Many reports point to the antioxidant, antimicrobial, anticancer and many other beneficial effects of apple components that may have potential applications in food, pharmaceutical and cosmetic industries. This paper summarizes and compiles information about apple phenolic compounds, their biological properties with particular emphasis on health-related aspects. The data are reviewed with regard to different apple varieties, part of apple, cultivation model and methods of extraction.

1. Introduction

Free radicals may cause oxidative damage to various molecules in human organism like lipids, proteins and nucleic acids, and therefore give rise to many different degenerative diseases such as cancer, cardiovascular disease, asthma, diabetes. Therefore it is very important to eat foods rich in antioxidants (like polyphenols) because of their preventative effect. These compounds possess ability to reduce oxidative stress by several mechanisms, i.e. direct scavenging of reactive oxygen species (Panzella et al., 2013), complexation of metal ions (Michalak, 2006; Flora, 2009) and modulation of cellular response (Birt et al., 2001). According to Boyer and Liu apples have the second (after cranberries) highest level of antioxidants compared to other commonly consumed fruit in USA such as red grape, strawberry, peach, lemon etc. (Boyer & Liu, 2003–2004). There is a strong correlation between phenolic content of apples and antioxidant activity. Chlorogenic acid, the main phenolic acid present in the apple, has a great ability to "scavenge" free radicals (Panzella et al., 2013). Compared to about 18 other antioxidant compounds, including quercetin, gallic acid and α-tocopherol, chlorogenic acid was the second, immediately after the rutin, among antioxidants possessing the highest activity. 100 g portion of apples has an antioxidant activity equal to 1.500 mg of vitamin C (D'Angelo et al., 2007). According to Vinson, polyphenolic antioxidants of apple are mainly responsible for the antioxidant activity of these fruits (Vinson et al., 2001), and the contribution of vitamin C to the total antioxidant potential of apple is less than 0.4% (Drogoudi et al., 2007). Antioxidant properties of apples highly dependent on the fruit variety, agricultural practices, weather, storage conditions and processing. The apples more abundant in phenolic compounds tended to have a higher antioxidant activity (Sun et al., 2002). Phenolic compounds which occur in apple can be divided into several groups (Fig. 1): (a) hydroxybenzoic acids: *p*-hydroxybenzoic acid, protocatechuic acid, gallic acid, syringic acid, gentisic acid, (b) hydroxycinnamic acids and their derivatives: *p*-coumaric acid, caffeic acid, ferulic acid, chlorogenic acid, (c) flavonols: quercetin presents in glycosylated forms, (d) dihydrochalcones: phloridzin and its derivatives, (e) anthocyanids: cyanidines and its glicosides, (f) monomeric flavanols: epicatechin, catechin, (g) oligomeric flavanols: procyanidins.

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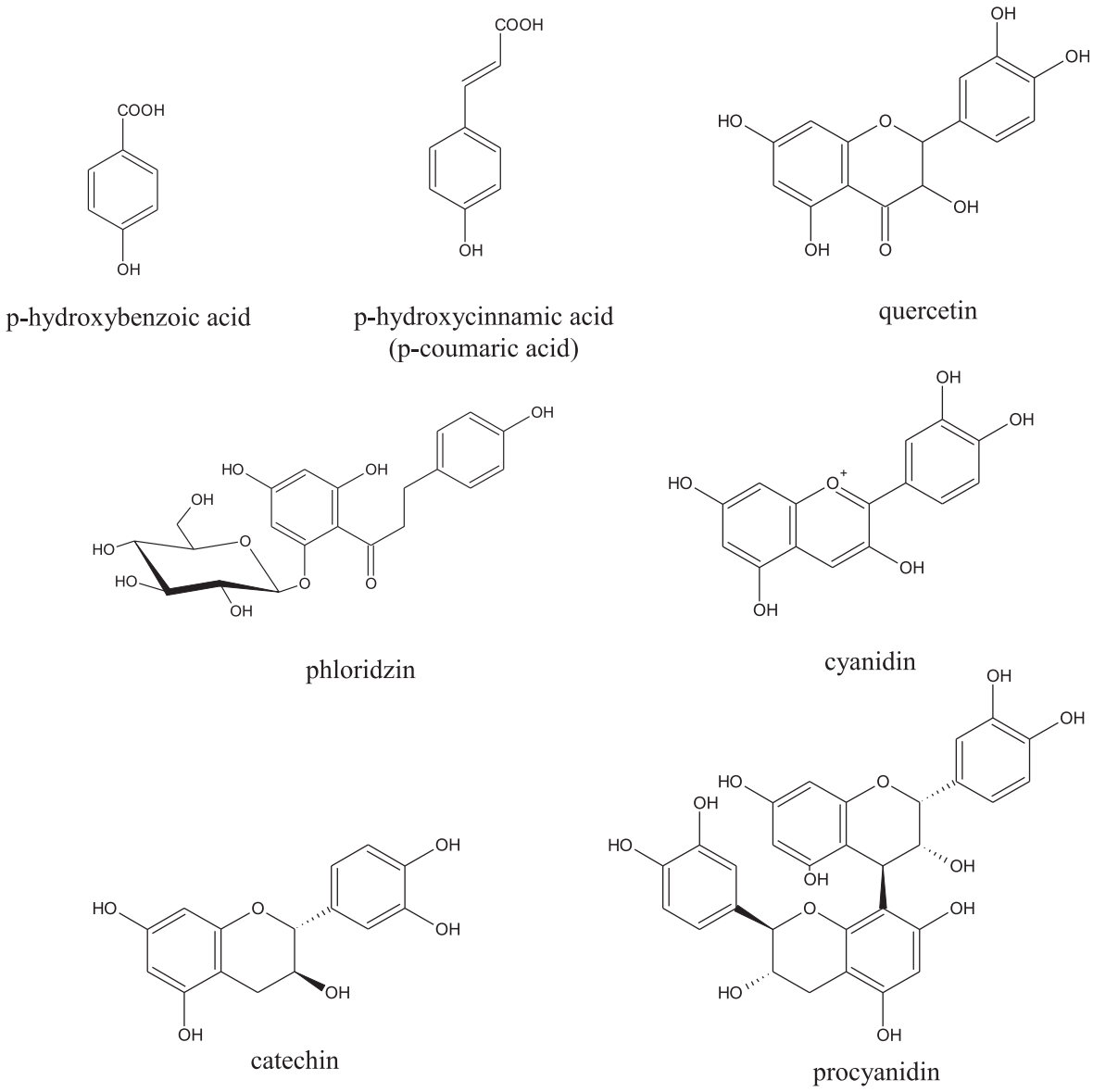

Fig. 1. Selected phenolic compounds present in apples.

The mechanism of action of apple polyphenolics is not only limited to their antioxidant properties. Broad and not fully understood mechanism of biological activity of apple extracts and apple constituents is responsible for the multi-dimensional spectrum of health-promoting effects (Fig. 2). There are several human intervention studies that revealed benefits of apple consumption. Chai et al. studied the effect of dried apple intake on the reduction of the risk factor of cardiovascular disease in the group of menopausal women during 1-year clinical trial (Chai et al., 2012). The consumption of apples caused a decrease in total cholesterol and low-density lipoprotein cholesterol levels by 9% and 16%, respectively after 3 months of the study, and by 13% and 24%, respectively after 6 months and remained constant after that period. In a 6.9-year study of Sesso et al. the connection between flavonoids and apples intake and cardiovascular disease in the group of 40 000 women was studied (Sesso et al., 2003). Women who were on a diet rich in apples were subjected to smaller risk (13–22% decrease comparing to control) of cardiovascular disease. The survey of Feskanish et al. engaged 77000 women and 47000 men in the study on fruit and vegetable consumption and lung cancer risk (Feskanish et al., 2000). The intake of fruits and vegetables caused 21% reduction of risk in lung cancer in the group of women, but this dependency was not seen in the group of men. Moreover, apples were among the fruits, consumption of which strongly correlated with a decrease in lung cancer. In the study of Le Marchand et al. a 40–50% decrease in the risk of lung cancer in the group of the highest consumption of apples, onions and grapefruits was observed (both men and women) (Le Marchand et al., 2000). The high intake of apple reduced the risk of development of colorectal adenomas (Michels et al., 2006). In the clinical study of Jedrychowski et al. a reduction of the risk of colorectal cancer at significant level was observed at the intake of at least one apple a day, and the consumption of more than one apple a day reduced the risk by about 50% (Jedrychowski et al., 2010). Apple and apple polyphenols

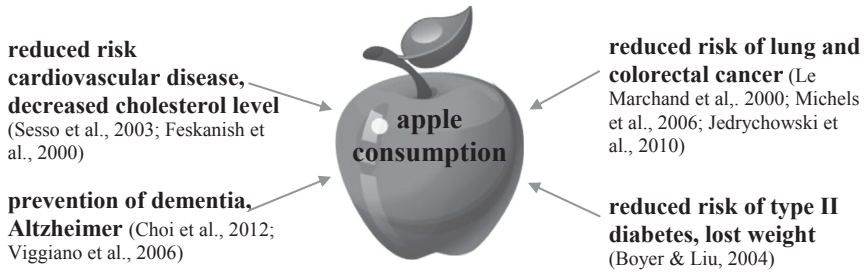

Fig. 2. Health benefits of apple consumption.

consumption reduces not only the risk of cardiovascular disease, lung and colorectal cancer but also of type II diabetes and helps to lose weight (Boyer and Liu, 2004). The mentioned epidemiological studies showed high relevance of apples, apple extracts from particular parts of fruit or individual apple polyphenols as supporting element in an optimal medicinal therapy. In order to fully understand the mechanism of action of phenolic compounds and their pathway of metabolism and bioavailability it is necessary to undertake detailed studies. Because of the natural origin and non-toxicity of apple polyphenols they are in the center of study of many research laboratories which intend to apply apple phenolics as diet supplements, drugs, antioxidants and antimicrobial agents (Fujiwara et al., 2013). For example, the composition of apple peel extract was patented as a product for treating cardiovascular disease; the preparation was found efficient in decreasing cholesterol level and inhibiting low density lipoprotein oxidation (Rapasinghe et al., 2011). New methods of producing fruit extracts and fruit juices that provide a large amount of polyphenols in the final product are in high demand. Among them there is a new way of fruit juice extraction and packaging in oxygen-free environment, which provides higher amounts of biological active substances compared with the juice obtained in a classical way (Knowlton, 2012).

This review discusses the newest reports on apple phenolic compounds, their biological and health-related properties including different apple varieties, part of apple and methods of extraction.

2. The content of phenolic compounds in apple

2.1. The content of phenolic compounds in apples—dependence on the variety and the part of apple

The concentration of individual phenolic compounds in apple is not constant. It depends on the cultivar, maturity of the fruit, conditions of cultivation, rising, harvest, storage and suffered infections. Moreover, there are differences between chemical composition of peel and flesh of apple. Phenolic compounds occur in plants in free form very rarely. They most commonly exist in the form of glycosides or esterified with carboxylic acids. Phenolic compounds can be bonded to fatty acids, sterols and cell walls. They can also occur in depside form. It is inferred that among other edible fruits, apples have the highest amount of free phenolics the most available for eventual absorption into the bloodstream (Boyer & Liu, 2003–2004; Sun et al., 2002).

There is a great abundance of literature data concerning the content of simple phenols (phenolic acids) and polyphenols (possess multiples of phenol structural units) fraction in apple peel. It should be noted that distribution of phenolic compounds in other parts of an apple fruit is less studied, especially in core and seeds. Furthermore the data are difficult to compare due to different measurement techniques applied (HPLC, UV/VIS, GC–MS), the results are expressed in relation to the dry or fresh weight, and in the method with the use of Folin–Ciocalteu reagent a gallic, caffeic or chlorogenic acid equivalents were applied. In Table 1 the composition of individual and total phenolic compounds in selected cultivars of apples are gathered. Generally, apple peel is richer in total phenolic compounds, total procyanidins and total flavonoids than flesh, but it is easy to notice that the content of certain individual phenolic compounds is higher in flesh than peel depending on the apple variety (Table 1). More chlorogenic acid (caffeoylquinic acid) was found in the peel than in the flesh of apples varieties: e.g. 'Elstar', 'Fuji', 'McIntosh', 'Pinova', 'Red Delicious', but 'Idared', 'Golden Decious', 'Granny Smith', 'Reineta' possess higher content of chlorogenic acid in flesh than peel. The peel of 'Granny Smith', 'Golden Deliciuos', 'McIntosh' is more abundant in p-coumaroylquinic acid than the flesh, on the other hand 'Gala' contains higher amount of p-coumaroylquinic acid in flesh than peel. Higher content of quercetin, catechin, epicatechin, phloridzin, procyanidins B2 and C1 was found in the peel than in the flesh of apples independently of the varieties. Whereas more procyanidin B1 is present in the flesh than peel of 'Gloster', 'Elstar' and 'Gala' apples.

On the basis of the results gathered in Table 1 it is easy to conclude that some apple varieties contain higher amount of phenolic compounds than the others. For example, the peel of 'Red Rome', 'Idared', 'Fiesta', 'Fuji', 'Gloster', 'McIntosh' and 'Pilot' contains higher amount of chlorogenic acid compared with other varieties, whereas 'Elan', 'Elstar' and 'Jonamac' have the lowest content of chlorogenic acid. 'Red Rome', 'Prima', 'Pilot' and 'Elstar' possess high amount of catechin and epicatechin in peel. 'Starking Delicious', 'Gloster', 'Golden Delicious', 'Granny Smith', 'Idared' and 'Monroe' possess high content of phloridzin. The peel of 'McIntosh' and 'Reineta' are abundant in procyanidin B1, 'Elstar' and 'Idared' in procyanidin B2, whereas 'Gloster', 'Idared', 'Lobo' and 'Elstar' in procyanidin C1. The composition of peel varies significantly depending on apple variety. However, peel contains most of phloridzin, procyanidines B2 and C1, catechin and epicatechins present in apple fruit (Carbone et al., 2011). The difference in the content of individual phenolic compounds in the apples of different varieties can be explained in terms of biosynthesis pathway of phenolic compounds (Fig. 3) (Treutter, 2001; Wang et al., 2013). The key enzyme in the flavonoids biosynthesis in apples is dihydroflavonol reductase (DFR). DFR catalyzes reduction of dihydroflavonols to leucoanthocyanidins which then are converted to anthocyanidins and anthocyanin. Anthocyanin are responsible for the red skin coloration of apple, therefore the red apple varieties synthetize flavan-3,4-diols and cyaniding glycosides in higher amount compared to yellow and green varieties (Wang et al., 2013). As a result of low activity of DRF dihydroflavonols [in the presence of flavonol synthase (FLS) and glucosyltransferase (GT)] are converted to quercetin glycosides which are accumulated in higher amount in red apples. Moreover red apple varieties possess ability

Table 1
Distribution of selected phenolic compounds in the apple flesh, peel and whole fruit in different apple varieties.

Phenolic compound	Apple variety	Whole apple	Peel	Flesh
Chlorogenic acid	Idared	1.77[a] mg/g DW (Łata et al., 2009)	1.36[a] mg/g DW (Łata et al., 2009) 7.15[a] mg/100 g FW (Duda-Chodak et al., 2011)	11.69[a] mg/100 g FW (Duda-Chodak et al., 2011) 39.78 ± 0.70[a] mg/kg (Dragovic-Uzelac et al., 2005) 20.8 ± 4.5[a] mg/100 g (Kuczynski, 2003)
	Elan	0.52[a] mg/g DW (Łata et al., 2009)	0.38[a] mg/g DW (Łata et al., 2009)	ND
	Elstar	0.41[a] mg/g DW (Łata et al., 2009)	0.26[a] mg/g DW (Łata et al., 2009) 0.05–0.06[f] mg/g DW (Awad & de Jager, 2000) 0.03–0.04[f] mg/g DW (Awad et al., 2000) 16.5 ± 1.3 mg/100 g FW (Veberic et al., 2005)	6.5 ± 2.9[a] mg/100 g (Kuczynski, 2003) 2.9 ± 0.21[a] mg/100 g FW (Veberic et al., 2005)
	Fiesta	1.11[a] mg/g DW (Łata et al., 2009)	1.06[a] mg/g DW (Łata et al., 2009)	ND
	Fuji	1.35[a] mg/g DW (Łata et al., 2009) 16.15 ± 7.74[a] mg/l (Wu et al., 2007)	1.21[a] mg/g DW (Łata et al., 2009) 17.4 ± 3.9[a] mg/100 g FW (Veberic et al., 2005)	10.7 ± 0.92[a] mg/100 g FW (Veberic et al., 2005)
	Gala	1.04[a] mg/g DW (Łata et al., 2009)	0.70[a] mg/g DW (Łata et al., 2009)	14.8 ± 1.9 mg/100 g (Kuczynski, 2003)
	Gloster	1.47[a] mg/g DW (Łata et al., 2009)	0.94[a] mg/g DW (Łata et al., 2009)	20.8 ± 4.5[a] mg/100 g (Kuczynski, 2003)
	Golden Delicious	1.23[a] mg/g DW (Łata et al., 2009) 23.20 ± 7.79[a] mg/l (Wu et al., 2007)	1.19[a] mg/g DW (Łata et al., 2009) 17–37[g] mg/kg FW (Escarpa and Gonzalez, 1998)	20.8 ± 4.5[a] mg/100 g (Kuczynski, 2003) 29–57[g] mg/kg FW (Escarpa and Gonzalez, 1998)
	Granny Smith	0.67[a] mg/g DW (Łata et al., 2009) 6.88 ± 0.85[a] mg/l (Wu et al., 2007)	0.28[a] mg/g DW (Łata et al., 2009) 6-60[g] mg/kg FW (Escarpa and Gonzalez, 1998)	28–71[g] mg/kg FW (Escarpa and Gonzalez, 1998)
	Jonagold	12.1 ± 7.92[a] mg/l (Wu et al., 2007)	0.16–0.33[f] mg/g DW (Awad & de Jager, 2000) 20–24 mg/g DW (Awad et al., 2000)	14.8 ± 1.9 mg/100 g (Kuczynski, 2003)
	Jonamac	0.25[a] mg/g DW (Łata et al., 2009)	0.74[a] mg/g DW (Łata et al., 2009)	ND
	McIntosh	1.52[a] mg/g DW (Łata et al., 2009)	0.85[a] mg/g DW (Łata et al., 2009) 234.5[a] μg/g FW (Khanizadeh et al., 2008)	151.2[a] μg/g FW (Khanizadeh et al., 2008)
	Monroe	1.23[a] mg/g DW (Łata et al., 2009)	1.18[a] mg/g DW (Łata et al., 2009)	ND
	Pilot	1.71[a] mg/g DW (Łata et al., 2009)	1.41[a] mg/g DW (Łata et al., 2009)	ND
	Pinova	1.19[a] mg/g DW (Łata et al., 2009)	1.52[a] mg/g DW (Łata et al., 2009) 24.8 ± 1.9[a] mg/100 g (Veberic et al., 2005)	6.7 ± 0.15[a] mg/100 g FW (Veberic et al., 2005)
	Prima	1.79[a] mg/g DW (Łata et al., 2009)	1.28[a] mg/g DW (Łata et al., 2009)	ND
	Priscilla	0.65[a] mg/g DW (Łata et al., 2009)	0.53[a] mg/g DW (Łata et al., 2009)	ND
	Red Delicious	ND	113–157[g] mg/kg FW (Escarpa and Gonzalez, 1998)	63–106[g] mg/kg FW (Escarpa and Gonzalez, 1998)
	Red Rome	2.31[a] mg/g DW (Łata et al., 2009)	2.33[a] mg/g DW (Łata et al., 2009)	ND
	Reineta	ND	100–440[a] mg/kg FW (Escarpa and Gonzalez, 1998)	266–357[g] mg/kg FW (Escarpa and Gonzalez, 1998)
	Rubin	0.53[a] mg/g DW (Łata et al., 2009)	0.37[a] mg/g DW (Łata et al., 2009)	ND
	Starking Delicious	0.71[a] mg/g DW (Łata et al., 2009)	0.51[a] mg/g DW (Łata et al., 2009)	ND
	Szampion	2.74–9.28[a] mg/100 g FW (Duda-Chodak et al., 2011)	ND	6.5 ± 2.9 mg/100 g (Kuczynski, 2003)
p-Coumaroylquinic acid	Idared	0.56–1.98[a] mg/100 g FW (Duda-Chodak et al., 2011)	ND	ND
	Gala	ND	19.4[a] μg/g FW (Khanizadeh et al., 2008) 0.05–0.19 mg/g DW (Renard et al., 2007)	23.9[a] μg/g FW (Khanizadeh et al., 2008) 0.3–05 mg/g DW (Renard et al., 2007)
	Golden Delicious	ND	9[f] mg/kg FW (Guyot et al., 2002)	0.014[f] mg/g FW (Guyot et al., 2002)
	Granny Smith	ND	3[f] mg/kg FW (Guyot et al., 2002)	0.003[f] mg/g FW (Guyot et al., 2002)
	McIntosh	ND	66.9[a] μg/g FW (Khanizadeh et al., 2008)	47.5[a] μg/g FW (Khanizadeh et al., 2008)
	Szampion	0.74–2.60[a] mg/100 g FW (Duda-Chodak et al., 2011)	ND	ND
(+) Catechin	Idared	0.27–2.32[a] mg/100 g FW (Duda-Chodak et al., 2011) 0.99[a] mg/g DW (Łata et al., 2009)	ND	21.70 ± 1.12 mg/kg (Dragovic-Uzelac et al., 2005)
	Elan	0.38[a] mg/g DW (Łata et al., 2009)	1.38[a] mg/g DW (Łata et al., 2009)	ND
	Telstar	1.16[a] mg/g DW (Łata et al., 2009)	1.97[a] mg/g DW (Łata et al., 2009) 1.83–1.88[f] mg/g DW (Awad et al., 2000)	3.5 ± 3.1[a] mg/100 g FW (Veberic et al., 2005)
	Fiesta	0.60[a] mg/g DW (Łata et al., 2009)	1.74[a] mg/g DW (Łata et al., 2009)	ND
	Fuji	0.88[a] mg/g DW (Łata et al., 2009) 3.15 ± 0.12[a] mg/l (Wu et al., 2007)	2.27[a] mg/g DW (Łata et al., 2009)	ND
	Gala	0.50[a] mg/g DW (Łata et al., 2009)	1.48[a] mg/g DW (Łata et al., 2009) 50.5[a] μg/g FW (Khanizadeh et al., 2008)	ND
	Gloster	0.73[a] mg/g DW (Łata et al., 2009)	1.85[a] mg/g DW (Łata et al., 2009)	ND
	Golden Delicious	0.99[a] mg/g DW (Łata et al., 2009) 3.86 ± 0.12[a] mg/l (Wu et al., 2007)	2.28[a] mg/g DW (Łata et al., 2009) 66–164[g] mg/kg FW (Escarpa and Gonzalez, 1998) 8[f] mg/kg FW (Guyot et al., 2002)	28–49[g] mg/kg FW (Escarpa and Gonzalez, 1998)
	Granny Smith	1.47[a] mg/g DW (Łata et al., 2009) 2.02 ± 0.13[a] mg/l (Wu et al., 2007)	2.43[a] mg/g DW (Łata et al., 2009) 374–486[g] mg/kg FW (Escarpa and Gonzalez, 1998) 40[f] mg/kg FW (Guyot et al., 2002)	136–182[g] mg/kg FW (Escarpa and Gonzalez, 1998)

Table 1 (*continued*)

Phenolic compound	Apple variety	Whole apple	Peel	Flesh
	Jonamac	0.51[a] mg/g DW (Łata et al., 2009)	0.99[a] mg/g DW (Łata et al., 2009)	ND
	McIntosh	0.66[a] mg/g DW (Łata et al., 2009)	1.15[a] mg/g DW (Łata et al., 2009) 37.9[a] μg/g FW (Khanizadeh et al., 2008)	10.3[a] μg/g FW (Khanizadeh et al., 2008)
	Monroe	0.73[a] mg/g DW (Łata et al., 2009)	1.57[a] mg/g DW (Łata et al., 2009)	ND
	Pilot	1.28[a] mg/g DW (Łata et al., 2009)	2.7[a] mg/g DW (Łata et al., 2009)	ND
	Pinova	0.99[a] mg/g DW (Łata et al., 2009)	2.71[a] mg/g DW (Łata et al., 2009)	0.1 ± 0.009[a] mg/100 g FW (Veberic et al., 2005)
	Prima	1.45[a] mg/g DW (Łata et al., 2009)	2.85[a] mg/g DW (Łata et al., 2009)	ND
	Priscilla	0.76[a] mg/g DW (Łata et al., 2009)	2.10[a] mg/g DW (Łata et al., 2009)	ND
	Red Delicious	ND	297–445[g] mg/kg FW (Escarpa and Gonzalez, 1998)	44–70[g] mg/kg FW (Escarpa and Gonzalez, 1998)
	Red Rome	1.18[a] mg/g DW (Łata et al., 2009)	4.42[a] mg/g DW (Łata et al., 2009)	ND
	Reineta	ND	229–460[g] mg/kg FW (Escarpa and Gonzalez, 1998)	113–136[g] mg/kg FW (Escarpa and Gonzalez, 1998)
	Rubin	0.46[a] mg/g DW (Łata et al., 2009)	1.19[a] mg/g DW (Łata et al., 2009)	ND
	Starking Delicious	1.05[a] mg/g DW (Łata et al., 2009)	3.86[a] mg/g DW (Łata et al., 2009)	ND
	Szampion	0.17–1.22[a] mg/100 g FW (Duda-Chodak et al., 2011)	ND	ND
(−) Epicatechin	Idared	2.92–16.22[a] mg/100 g FW (Duda-Chodak et al., 2011) 0.68[a] mg/g DW (Łata et al., 2009)	3.12[a] mg/g DW (Łata et al., 2009)	50.39 ± 3.11 mg/kg (Dragovic-Uzelac et al., 2005) 20.3 ± 8.3[a] mg/100 g (Kuczynski, 2003)
	Elan	0.46[a] mg/g DW (Łata et al., 2009)	1.66[a] mg/g DW (Łata et al., 2009)	ND
	Elstar	0.95[a] mg/g DW[23]	2.26[a] mg/g DW (Łata et al., 2009) 4.2 ± 0.07[a] mg/100 g FW (Veberic et al., 2005)	27.3 ± 4.7[a] mg/100 g (Kuczynski, 2003) 0.7 ± 0.04[a] mg/100 g FW (Veberic et al., 2005)
	Fiesta	0.48[a] mg/g DW (Łata et al., 2009)	2.17[a] mg/g DW (Łata et al., 2009)	ND
	Fuji	0.75[a] mg/g DW (Łata et al., 2009) 29.86 ± 2.02[a] mg/l (Wu et al., 2007)	2.57[a] mg/g DW (Łata et al., 2009) 2.5 ± 0.14[a] mg/100 g FW (Veberic et al., 2005)	0.37 ± 0.015[a] mg/100 g FW (Veberic et al., 2005)
	Gala	0.58[a] mg/g DW (Łata et al., 2009)	1.99[a] mg/g DW (Łata et al., 2009) 438.4[a] μg/g FW[27]	13.9 ± 2.9[a] mg/100 g (Kuczynski, 2003)
	Gloster	0.57[a] mg/g DW (Łata et al., 2009)	2.39[a] mg/g DW (Łata et al., 2009)	66.8[a] μg/g FW (Khanizadeh et al., 2008) 20.3 ± 8.3[a] mg/100 g (Kuczynski, 2003)
	Golden Delicious	0.65[a] mg/g DW (Łata et al., 2009) 21.19 ± 2.03[a] mg/l (Wu et al., 2007)	1.96[a] mg/g DW (Łata et al., 2009) 82-186[g] mg/kg FW (Escarpa and Gonzalez, 1998) 124[f] mg/kg FW (Guyot et al., 2002)	59[f] mg/kg FW (Guyot et al., 2002) 20.3 ± 8.3[a] mg/100 g (Kuczynski, 2003) 19–34[g] mg/kg FW (Escarpa and Gonzalez, 1998)
	Granny Smith	0.97[a] mg/g DW (Łata et al., 2009) 40.40 ± 2.07[a] mg/l (Wu et al., 2007)	2.17[a] mg/g DW (Łata et al., 2009) 246–312[g] mg/kg FW (Escarpa and Gonzalez, 1998) 170[f] mg/kg FW (Guyot et al., 2002)	96[f] mg/kg FW (Guyot et al., 2002) 71–97[g] mg/kg FW (Escarpa and Gonzalez, 1998)
	Jonamac	0.38[a] mg/g DW (Łata et al., 2009)	1.30[a] mg/g DW (Łata et al., 2009)	ND
	McIntosh	0.53[a] mg/g DW (Łata et al., 2009)	1.24[a] mg/g DW (Łata et al., 2009) 258.9[a] μg/g FW (Khanizadeh et al., 2008)	36.9[a] μg/g FW (Khanizadeh et al., 2008)
	Monroe	0.71[a] mg/g DW (Łata et al., 2009)	2.23[a] mg/g DW (Łata et al., 2009)	ND
	Pilot	1.08[a] mg/g DW (Łata et al., 2009)	2.70[a] mg/g DW (Łata et al., 2009)	ND
	Pinova	0.86[a] mg/g DW (Łata et al., 2009)	3.04[a] mg/g DW (Łata et al., 2009) 3.1 ± 0.19 mg/100g[a] FW (Choi et al., 2012)	0.37 ± 0.027[a] mg/100 g FW (Veberic et al., 2005)
	Prima	1.28[a] mg/g DW (Łata et al., 2009)	3.49[a] mg/g DW (Łata et al., 2009)	ND
	Priscilla	0.63[a] mg/g DW (Łata et al., 2009)	2.72[a] mg/g DW (Łata et al., 2009)	ND
	Red Delicious	ND	36–59[g] mg/kg (Escarpa and Gonzalez, 1998)	ND
	Red Rome	1.11[a] mg/g DW (Łata et al., 2009)	5.75[a] mg/g DW (Łata et al., 2009)	ND
	Reineta	ND	238–439[g] mg/kg FW (Escarpa and Gonzalez, 1998)	91–111[g] mg/kg FW (Escarpa and Gonzalez, 1998)
	Rubin	0.42[a] mg/g DW (Łata et al., 2009)	1.41[a] mg/g DW (Łata et al., 2009)	ND
	Starking Delicious	1.06[a] mg/g DW (Łata et al., 2009)	5.17[a] mg/g DW[23]	ND
	Szampion	8.6–22.17[a] mg/100 g FW (Duda-Chodak et al., 2011)	ND	27.3 ± 4.7[a] mg/100 g (Kuczynski, 2003)
Procyanidin B2	Idared	3.88–6.85[a] mg/100 g FW (Duda-Chodak et al., 2011)	358[f] mg/kg (Kołodziejczyk and Kosmala, 2006)	56[f] mg/kg (Kołodziejczyk and Kosmala, 2006) 11.8 ± 1[a] mg/100 g (Kuczynski, 2003)
	Cortland	ND	252[f] mg/kg (Kołodziejczyk and Kosmala, 2006)	126[f] mg/kg (Kołodziejczyk and Kosmala, 2006)
	Elstar	ND	369[f] mg/kg (Kołodziejczyk and Kosmala, 2006)	166[f] mg/kg (Kołodziejczyk and Kosmala, 2006) 16.4 ± 2.7[a] mg/100 g (Kuczynski, 2003)
	Gala	ND	277.2[a] μg/g FW (Khanizadeh et al., 2008)	81.5[a] μg/g FW (Khanizadeh et al., 2008) 10.8 ± 1.2[a] mg/100 g (Kuczynski, 2003)
	Gloster	ND	255[f] mg/kg (Kołodziejczyk and Kosmala, 2006)	91[f] mg/kg (Kołodziejczyk and Kosmala, 2006) 11.8 ± 1[a] mg/100 g (Kuczynski, 2003)
	Golden Delicious	ND	150[f] mg/kg FW (Guyot et al., 2002) 69–166[g] mg/kg FW (Escarpa and Gonzalez, 1998)	72[f] mg/kg FW (Guyot et al., 2002) 11.8 ± 1[a] mg/100 g (Kuczynski, 2003)

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Table 1 (*continued*)

Phenolic compound	Apple variety	Whole apple	Peel	Flesh
				23–32[g] mg/kg FW (Escarpa and Gonzalez, 1998)
	Granny Smith	ND	241[f] mg/kg FW (Guyot et al., 2002) 558–574[g] mg/kg FW (Escarpa and Gonzalez, 1998)	134[f] mg/kg FW (Guyot et al., 2002) 97–105[g] mg/kg FW (Escarpa and Gonzalez, 1998)
	Jonagold	ND	204[f] mg/kg (Kołodziejczyk and Kosmala, 2006)	64[f] mg/kg (Kołodziejczyk and Kosmala, 2006) 10.8 ± 1.2[a] mg/100 g (Kuczynski, 2003)
	Lobo	ND	287[f] mg/kg (Kołodziejczyk and Kosmala, 2006)	88[f] mg/kg (Kołodziejczyk and Kosmala, 2006)
	McIntosh	ND	167.5[a] μg/g FW (Khanizadeh et al., 2008)	56.1[a] μg/g FW (Khanizadeh et al., 2008)
	Szampion	5.32–10.58[a] mg/100 g FW (Duda-Chodak et al., 2011)	185[f] mg/kg (Kołodziejczyk and Kosmala, 2006)	97[f] mg/kg (Kołodziejczyk and Kosmala, 2006) 16.4 ± 2.7[a] mg/100 g (Kuczynski, 2003)
Procyanidin B1	Cortland	ND	51[f] mg/kg (Kołodziejczyk and Kosmala, 2006)	42[f] mg/kg (Kołodziejczyk and Kosmala, 2006)
	Elstar	ND	47[f] mg/kg (Kołodziejczyk and Kosmala, 2006)	68[f] mg/kg (Kołodziejczyk and Kosmala, 2006)
	Gala	ND	16.7[a] μg/g FW (Khanizadeh et al., 2008)	154.2[a] μg/g FW (Khanizadeh et al., 2008)
	Gloster	ND	21[f] mg/kg (Kołodziejczyk and Kosmala, 2006)	35[f] mg/kg (Kołodziejczyk and Kosmala, 2006)
	Golden Delicious	ND	32–53[g] mg/kg FW (Escarpa and Gonzalez, 1998)	10–11[g] mg/kg FW (Escarpa and Gonzalez, 1998)
	Granny Smith	ND	173–241[g] mg/kg FW (Escarpa and Gonzalez, 1998)	61–100[g] mg/kg FW (Escarpa and Gonzalez, 1998)
	Idared	0.64–2.11[a] mg/100 g FW (Duda-Chodak et al., 2011)	54[f] mg/kg (Kołodziejczyk and Kosmala, 2006)	21[f] mg/kg (Kołodziejczyk and Kosmala, 2006)
	Jonagold	ND	14[f] mg/kg (Kołodziejczyk and Kosmala, 2006)	13[f] mg/kg (Kołodziejczyk and Kosmala, 2006)
	Lobo	ND	74[f] mg/kg (Kołodziejczyk and Kosmala, 2006)	39[f] mg/kg (Kołodziejczyk and Kosmala, 2006)
	McIntosh	ND	155.1[a] μg/g FW (Khanizadeh et al., 2008)	15.7[a] μg/g FW (Khanizadeh et al., 2008)
	Red Delicious	ND	127–172[g] mg/kg FW (Escarpa and Gonzalez, 1998)	11–21[g] mg/kg FW (Escarpa and Gonzalez, 1998)
	Reineta	ND	103–242[g] mg/kg FW (Escarpa and Gonzalez, 1998)	57–67[g] mg/kg FW (Escarpa and Gonzalez, 1998)
	Szampion	1.21–2.17[a] mg/100 g FW (Duda-Chodak et al., 2011)	52[f] mg/kg (Kołodziejczyk and Kosmala, 2006)	4[f] mg/kg (Kołodziejczyk and Kosmala, 2006)
Procyanidin C1	Cortland	ND	136[f] mg/kg (Kołodziejczyk and Kosmala, 2006)	55[f] mg/kg (Kołodziejczyk and Kosmala, 2006)
	Elstar	ND	213[f] mg/kg (Kołodziejczyk and Kosmala, 2006)	73[f] mg/kg (Kołodziejczyk and Kosmala, 2006)
	Gloster	ND	138[f] mg/kg (Kołodziejczyk and Kosmala, 2006)	38[f] mg/kg (Kołodziejczyk and Kosmala, 2006)
	Idared	1.26–4.41[a] mg/100 g FW (Duda-Chodak et al., 2011)	200[f] mg/kg (Kołodziejczyk and Kosmala, 2006)	26[f] mg/kg (Kołodziejczyk and Kosmala, 2006)
	Jonagold	ND	131[f] mg/kg (Kołodziejczyk and Kosmala, 2006)	32[f] mg/kg (Kołodziejczyk and Kosmala, 2006)
	Lobo	ND	174[f] mg/kg (Kołodziejczyk and Kosmala, 2006)	42[f] mg/kg (Kołodziejczyk and Kosmala, 2006)
	Szampion	2.85–6.5 mg/100 g FW (Duda-Chodak et al., 2011)	97[f] mg/kg (Kołodziejczyk and Kosmala, 2006)	5[f] mg/kg (Kołodziejczyk and Kosmala, 2006)
Phloridzin	Elan	0.13[a] mg/g DW (Łata et al., 2009)	0.72[a] mg/g DW[23]	ND
	Elstar	0.23[a] mg/g DW (Łata et al., 2009)	1.06[a] mg/g DW (Łata et al., 2009) 0.75–0.81[f] mg/g DW (Awad & de Jager, 2000) 0.46–0.52[f] mg/g (Awad et al., 2000) 8.7–11.9[f] mg/g DW (Awad et al., 2001) 16.6 ± 0.8[a] mg/100 g FW (Choi et al., 2012)	0.7 ± 0.06[a] mg/100 g FW (Choi et al., 2012)
	Fiesta	0.19[a] mg/g DW (Łata et al., 2009)	1.17[a] mg/g DW (Łata et al., 2009)	ND
	Fuji	0.34[a] mg/g DW (Łata et al., 2009) 4.12 ± 0.83[a] mg/l (Wu et al., 2007)	1.81[a] mg/g DW (Łata et al., 2009) 11.1 ± 8.7[a] mg/100 g FW (Choi et al., 2012)	0.5 ± 0.15[a] mg/100 g FW (Choi et al., 2012)
	Gala	0.13[a] mg/g DW (Łata et al., 2009)	0.85[a] mg/g DW (Łata et al., 2009) 52[a] μg/g FW (Khanizadeh et al., 2008)	9.5[a] μg/g FW (Khanizadeh et al., 2008)
	Gloster	0.28[a] mg/g DW (Łata et al., 2009)	1.82[a] mg/g DW (Łata et al., 2009)	ND
	Golden Delicious	0.38[a] mg/g DW (Łata et al., 2009) 4.13 ± 0.84[a] mg/l (Wu et al., 2007)	1.73[a] mg/g DW (Łata et al., 2009) 31–71[g] mg/kg FW (Escarpa and Gonzalez, 1998) 40[f] mg/kg FW (Guyot et al., 2002)	11[f] mg/kg FW (Guyot et al., 2002) 4-8[g] mg/kg FW (Escarpa and Gonzalez, 1998)
	Granny Smith	0.22[a] mg/g DW (Łata et al., 2009)	1.87[a] mg/g DW (Łata et al., 2009) 12[g] mg/kg FW (Escarpa and Gonzalez, 1998) 13[f] mg/kg FW (Guyot et al., 2002)	6[f] mg/kg FW (Guyot et al., 2002) 5[g] mg/kg FW (Escarpa and Gonzalez, 1998)
	Idared	2.05–7.45[a] mg/100 g FW (Duda-Chodak et al., 2011) 0.34[a] mg/g DW[23]	2.08[a] mg/g DW (Łata et al., 2009)	ND

Table 1 (*continued*)

Phenolic compound	Apple variety	Whole apple	Peel	Flesh
	Jonagold	2.19 ± 0.89[a] mg/l (Wu et al., 2007)	0.88–1.1[f] mg/g DW (Awad & de Jager, 2000) 0.71–0.81[f] mg/g DW (Awad et al., 2000) 18[f] mg/g DW (Awad et al., 2001)	ND
	Jonamac	0.14[a] mg/g DW[23]	1.31[a] mg/g DW (Łata et al., 2009)	ND
	McIntosh	0.41[a] mg/g DW[23]	1.71[a] mg/g DW (Łata et al., 2009) 66[a] μg/g FW (Khanizadeh et al., 2008)	6.5[a] μg/g FW (Khanizadeh et al., 2008)
	Monroe	0.41[a] mg/g DW[23]	2.29[a] mg/g DW (Łata et al., 2009)	ND
	Pilot	0.32[a] mg/g DW[23]	1.29[a] mg/g DW (Łata et al., 2009)	ND
	Pinova	0.24[a] mg/g (Łata et al., 2009)	1.47[a] mg/g (Łata et al., 2009) 12.8 ± 1[a] mg/100 g FW (Veberic et al., 2005)	0.1 ± 0.01[a] mg/100 g FW (Veberic et al., 2005)
	Prima	0.28[a] mg/g DW[23]	1.29[a] mg/g DW[23]	ND
	Priscilla	0.32[a] mg/g DW[23]	2.17[a] mg/g DW[23]	ND
	Red Delicious	ND	104–159[g] mg/kg FW (Escarpa and Gonzalez, 1998)	13–14[g] mg/kg FW (Escarpa and Gonzalez, 1998)
	Red Rome	0.24[a] mg/g DW[23]	1.75[a] mg/g DW[23]	ND
	Reineta	ND	83–418[g] mg/kg FW (Escarpa and Gonzalez, 1998)	16–20[g] mg/kg FW (Escarpa and Gonzalez, 1998)
	Rubin	0.11[a] mg/g DW[23]	0.71[a] mg/g DW[23]	ND
	Starking Delicious	0.43[a] mg/g DW[23] 0.23–3.82[a] mg/100 g FW (Duda-Chodak et al., 2011)	2.42[a] mg/g DW[23]	ND
	Szampion	0.23–3.82[a] mg/100 g FW (Duda-Chodak et al., 2011)	ND	ND
Quercetin-3-galactoside	McIntosh	ND	213.4[a] μg/g FW (Khanizadeh et al., 2008)	ND
	Idared	1.51–4.31[a] mg/100 g FW (Duda-Chodak et al., 2011)	ND	ND
	Szampion	1.27–3.34[a] mg/100 g FW (Duda-Chodak et al., 2011)	ND	ND
Quercetin-3-glucoside	McIntosh	ND	161.9[a] μg/g FW (Khanizadeh et al., 2008)	ND
	Elstar	ND	3.80–4[g] mg/g DW (Awad & de Jager, 2000) 0.70[f] mg/g DW (Awad et al., 2000)	ND
	Idared	0.16–0.39[a]mg/100 g FW (Duda-Chodak et al., 2011)	ND	ND
	Jonagold	ND	6.74–8.71[g] mg/g DW (Awad & de Jager, 2000) 0.53[f] mg/g DW (Awad et al., 2000)	ND
	Szampion	0.28–0.56[a] mg/100 g FW (Duda-Chodak et al., 2011)	ND	ND
Quercetin-3-rhamnoside	McIntosh	ND	95.1[a] μg/g FW (Khanizadeh et al., 2008)	ND
	Jonagold	ND	2.66[f] mg/g DW (Chai et al., 2012)	ND
	Elstar	ND	0.58[f] mg/g DW (Awad et al., 2000) 17.4 ± 2[a] mg/100 g FW (Veberic et al., 2005)	ND
	Fuji	ND	18 ± 10.8[a] mg/100 g FW (Veberic et al., 2005)	ND
	Pinova	ND	13.1 ± 1.3[a] mg/100 g FW (Veberic et al., 2005)	ND
Total phenolic compounds	Idared	ND	140.69 mg/100 g FW (Duda-Chodak et al., 2011)	22.09 mg/100 g FW (Duda-Chodak et al., 2011)
	Antanovka	ND	290[b] mg/100 g DW (Huber and Rupasinghe, 2009) 21.4[c] mgGAE/100 g DW (Huber and Rupasinghe, 2009) 1.25[d] gTE/100 g DW (Huber and Rupasinghe, 2009) 10.3[e] gTE/100 g DW (Huber and Rupasinghe, 2009)	ND
	Red Delicious	ND	380[b] mg/100 g DW[32] 25.3[c] mgGAE/100 g DW (Huber and Rupasinghe, 2009) 2.17[d] gTE/100 g DW (Huber and Rupasinghe, 2009) 12.5[e] gTE/100gDW (Huber and Rupasinghe, 2009)	ND
	Royal Gala	ND	484 mg/100 g DW[32] 22.4 mgGAE/100 g DW (Huber and Rupasinghe, 2009) 1.74 gTE/100 g DW[32] 13.5 gTE/100 g DW[32]	ND
	McIntosh	ND	296[b] mg/100 g DW (Huber and Rupasinghe, 2009) 17.2[c] mgGAE/100 g DW (Huber and Rupasinghe, 2009) 1.33[d] gTE/100 g DW (Huber and Rupasinghe, 2009)	341[a] μg/g FW (Khanizadeh et al., 2008)

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Table 1 (*continued*)

Phenolic compound	Apple variety	Whole apple	Peel	Flesh
			5.25[e] gTE/100 g DW (Huber and Rupasinghe, 2009) 2154[a] μg/g FW (Khanizadeh et al., 2008)	
	Golden Delicious	57.85[a] mg/l (Wu et al., 2007)	1764[f] mg/kg FW (Guyot et al., 2002) 304.66 ± 3.74 mgGAE/100 g FW (Vieira et al., 2011)	624[f] mg/kg FW (Guyot et al., 2002) 128.33 ± 4.51 mgGAE/100 g FW (Vieira et al., 2011)
	Granny Smith	62.68[a] mg/l (Wu et al., 2007)	3149[f] mg/kg FW (Guyot et al., 2002)	929[f] mg/kg FW (Guyot et al., 2002)
	Jonagold	35.66[a] mg/l (Wu et al., 2007)	ND	ND
	Gala	132 mg/100 g DW (Cieślik et al., 2006) 964 mg/100 g FW (Cieślik et al., 2006)	ND	ND
	Apple yellow	99.7[c] mg GAE/100 g FW (Marinova et al., 2005)	ND	75.8 mg GAE/100 g FW (Marinova et al., 2005)
	Apple red	125.4[c] mg GAE/100 g FW (Marinova et al., 2005)	ND	104.3 mg GAE/100 g FW (Marinova et al., 2005)
	Apple green	118.1[c] mg GAE/100 g FW (Marinova et al., 2005)	ND	97.5 mg GAE/100 g FW (Marinova et al., 2005)
	Granny Smith	ND	303.8 ± 5.9[c] mgGAE/100 g FW (Drogoudi and Pantelidis, 2011)	31.2 ± 1[c] mgGAE/100 g FW (Drogoudi and Pantelidis, 2011)
Total Procyanidins	Granny Smith	ND	2727[f] mg/kg FW (Guyot et al., 2002)	439[f] mg/kg FW (Guyot et al., 2002)
	Golden Delicious	ND	1282[f] mg/kg FW (Guyot et al., 2002)	753[f] mg/kg FW (Guyot et al., 2002)
	McIntosh	ND	619.5[a] μg/g FW (Khanizadeh et al., 2008)	119[a] μg/g FW (Khanizadeh et al., 2008)
Total Flavonoids	Golden Delicious	ND	58.24 ± 1.44 mgGAE/100 g FW (Vieira et al., 2011)	11.73 ± 0.72 mgGAE/100 g FW (Vieira et al., 2011)
	Elstar	3–10[f] mg/apple (Awad et al., 2001)	6.78–7.01[f] mg/g DW (Awad & de Jager, 2000) 4.42–9.36[f] mg/g DW (Awad et al., 2000)	ND
	Jonagold	8–20[f] mg/apple (Awad et al., 2001)	10.63–12.61[f] mg/g DW (Awad & de Jager, 2000) 4.79–14.66[f] mg/g DW (Awad et al., 2000)	ND

Methods used to determine phenolic compounds: a – HPLC; b – HPLC-MS; c – with Folin-Ciocalteu reagent; d – FRAP; e – ORAC; f – RP-HPLC; g – HPLC with DAD; h – aluminium chloride colorimetric assay.
DW – dry weight; FW – fresh weight.
GAE – gallic acid equivalents; TE – Trolox equivalents.
ND – no data.

to increased synthesis of monomeric and oligomeric flavanols from leucoanthocyanidins in the presence of leucoanthocyanidin reductase (LAR) compared to yellow and green varieties (Treutter, 2001; Wang et al., 2013). The other factor that influence the concentration of particular phenolic compounds in apple peel and flesh is fruit maturation (Treutter, 2001). For example, the amount of dihydrochalcones in very young apple fruits is very high. After the 14 weeks the level of dihydrochalcones, flavonols and chlorogenic acid decreases both in flesh and skin. The quantity of flavanols remains almost constant during this period of time. The activity of particular enzymes also changes during fruit maturation.

Many studies revealed that independently of apple varieties and other circumstances the antioxidant properties of apple parts may be ordered as follows: peel > core > flesh. Generally, peel contains from two to six times more phenolics than the flesh (Kalinowska et al., 2012a,b,c). Therefore the consumption of apples with peel is highly recommended (Kalinowska et al., 2012a,b,c, 2012, Kalinowska et al., 2012a,b,c).

2.2. The dependency of the content of phenolic compounds in apples on the cultivation model (conventional vs. organic farming)

Some studies showed that fruits and vegetables from organic production may contain more phenolic compounds, and other antioxidants such as vitamin C, than products form conventional farming (Caris-Veyrat et al., 2004; Mitchell et al., 2007). Organically grown 'Annurca' apples showed a greater content of polyphenols, both in the pulp and the peel (Fratianni et al., 2007). Depending on the type of agricultural system the concentration of phenolic compounds in apple peel was significantly different. Eleven organically grown apple varieties and eleven apple varieties of integrated production were tested by Veberic et al. for the content of phenolic compounds (Veberic et al., 2005). Organically grown apples exhibited a higher content of phenolic substances in the apple pulp compared with the apple varieties of integrated production. The results are inconclusive, because the authors used in this study different apple varieties grown in two different ways. So, the higher content of phenolic compounds in the pulp of organically grown apple may be caused either by the different genotype source or by the differences in the technology of cultivation. Stacke et al. reported that 'Golden Delicious' apple from organic farming were characterized by 14–19% higher level of phenolic substances than apples from conventional cultivation and this relationship repeated in subsequent years (Stracke et al., 2009). Petkovsek et al. also showed that cultivation type had an important effect on the phenolics and polyphenols level and antioxidant activity of apple fruits and leaves (Petkovsek et al., 2010). Organic and integrated orchards were located close to each other, so that the effects of microclimate and soil type could be reduced. The differences in climatic conditions were partially compensated by a two-year period of the study. Apples from organic production showed a higher content of hydroxycinnamic acids, flavanols, dihydrochalcones, quercetins and total phenolic compounds than apples from integrated cultivation. Wojdyło et al. studied the chemical composition and antioxidant activity of the three varieties of apple: 'Topaz', 'Szampion', and 'Pinova' from conventional and organic farms (Wojdyło et al., 2010). Nevertheless the organic and conventional farms were not in close neighborhood, and the type of soil and the degree of sunlight may have affected the results. The studies showed that organically grown 'Szampion' and 'Topaz' possessed higher content of phenolic compounds and higher antioxidant properties than the same varieties from conventional farming. Conversely, in case of 'Pinova' the higher content of phenolic substances and the higher

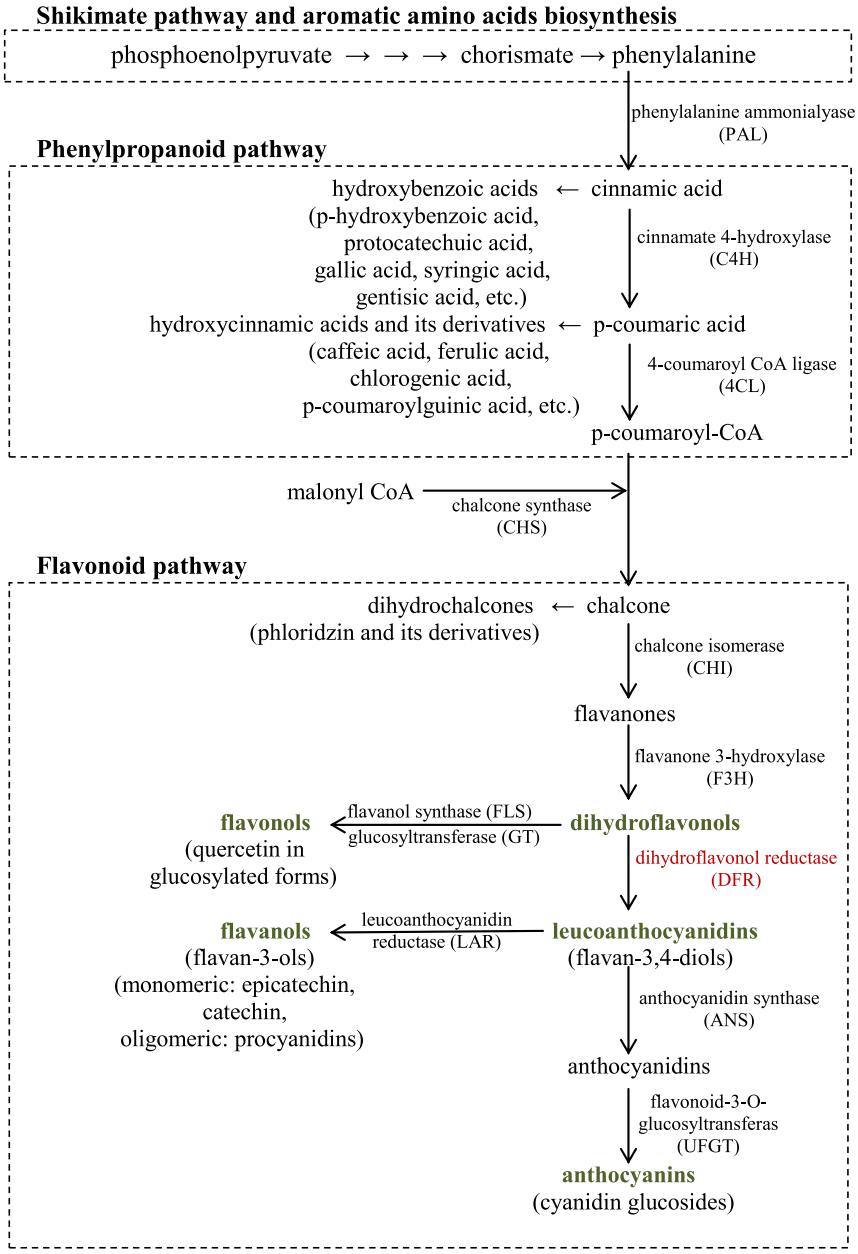

Fig. 3. Biosynthesis pathway of apple phenolic compounds.

antioxidant properties were found for apples from conventional cultivation. According to the authors, some apple varieties can possess higher than other genotypic ability to produce increased amounts of flavones and anthocyanins when exposed to intense sunlight. This could explain the lower antioxidant activity of 'Pinova' from organic cultivation compared to conventional one. Wojdyło et al. recommend apple varieties that can synthesize increased amounts of flavonols and anthocyanins. In terms of organic production they are able to create a natural barrier against the attack of pathogens by increased synthesis of phenolic compounds. Vrhovsek et al. showed that among three studied apple varieties, two of them were more abundant in phenolic compounds when they were grown organically (Vrhovsek et al., 2004). The higher antioxidant activity of apples from conventional farming compared with organic one may be explained by an exposition of the latter to different kinds of stress. In the organic production, synthetic chemicals (fertilizers, pesticides) that are used in integrated fruit production are not allowed. An extensive production of phenolic compounds in organically grown varieties could result from the action of defense mechanisms in plants (Carbone et al., 2011; Wojdyło et al., 2010; Bryant et al., 1983). There are also papers that indicate that cultivation system does not influence the antioxidant properties of apples (Valavanidis et al., 2009; Briviba et al., 2007). Comparative studies of antioxidant activity and phenolics and polyphenols content in fruits are believed to be difficult to evaluate, because of different extraction methodologies, apple cultivars, growing regions, soil type and different time of light exposure. The new research of Belviso et al. demonstrated that content of phenolic compounds changed over a three year period of study (Belviso et al., 2013). They showed that chlorogenic acid and phloridzin were significantly affected by the harvesting year, whereas catechins and procyanidins were not.

Table 2
Methodology of apple extraction and chemical compounds identification.

	Material for research: apple variety, sample preparation	Extraction methodology	Analytical/ Identification method	Extract composition/identified compounds	Biological activity	Ref.
1.	*Malus pumila* Apple peels collected and dried at room temperature for 10 days prior to extraction	Peel extraction with n-hexane, chloroform, methanol, successively. Purification of chloroform extract by silica gel chromatography, isocratical elution with chloroform/methanol (20:1, v/v); 11 fractions were collected.	^{1}H NMR	In the chloroform extract: ursolic acid and a trace amount of oleanolic acid.	n-Hexane, chloroform, methanol extracts showed cytotoxic activities against mouse leukemia P388 cells with IC_{50} > 25, 13 and> 25 μg/ml, respectively. The chloroform extract: IC_{50} 5.5 μg/ml for VCR-resistant P388 leukemia cells and 6.9 μg/ml for normal P388 leukemia cells.	(Yamaguchi et al., 2008)
2.	'Royal Gala', 'Granny Smith' apple peels	Peels extracted at 60 °C with: A, acetone:water:acetic acid; B, ethyl acetate:methanol:water; C, ethanol:water. Extracts concentrated in a rotatory evaporator at 35 °C to avoid hydrolysis, redox and polymerization reactions. Suspension of concentrates in 50 ml methanol; kept at −18 °C, avoiding direct contact with light and oxygen.	total phenolic content (Folin-Ciocalteu, F–C)	Extract A, 'Granny Smith', TP = 6.80 ± 0.15 mgGAE/g $_{\text{apple skin}}$ Extract A, 'Royal Gala', TP = 3.49 ± 0.14 mgGAE/g $_{\text{apple skin}}$	Extract A, 'Granny Smith', diameter of inhibition zone: 6–10 mm; Extract A, 'Royal Gala', diameter of inhibition zone: 3–4 mm; Control (+): Chloramphenicol, diameter of inhibition zone: 11–36 mm depending on bacteria type. Tested microorganisms: *E. coli*, *E. coli* ATCC 25922, *E. coli* ATCC 35218, *S. aureus* ATCC 25923, *S. aureus* ATCC 29213, *P. aeruginosa* ATCC 27853, *E. faecalis* ATCC 29212, *L. monocytogens*.	(Alberto et al., 2006)
3.	'Red Delicious'	Homogenization of apple peels with chilled 80% acetone (1:2, w/v). Filtration. Evaporation of filtrate under vacuum at 45 °C. Suspension of residue in water and extraction with the same volume of ethyl acetate, then extraction with water saturated n-butanol. Purification of the ethyl acetate fraction by silica gel chromatography and gradient elution with CH_2Cl_2/MeOH (the ratios of CH_2Cl_2/MeOH were from 100:0 to 0:100). Subjection of CH_2/Cl_2 eluant to silica gel column chromatography and elution with hexane/ethyl acetate. Purification of certain triterpenoid from hexane/ethyl acetate (10:1) fraction. Purification of hexane/ethyl acetate (3:1) fraction on semipreparative HPLC, elution with 80% ethanol in water. - compound no. 10. Obtainment of compound no.1 from CH_2Cl_2/MeOH (100:1) elution of ethyl acetate fraction using silica gel chromatography. CH_2Cl_2/MeOH (20:1) elution of ethyl acetate fraction. Subjection to silica gel column, elution with CH_2Cl_2/MeOH. Purification of CH_2Cl_2/MeOH (50:1) eluent with HPLC using 83% methanol. - isolation of compounds no.2–9.	HPLC, MS, ^{1}H and ^{13}C NMR and DEPT	1) ursolic acid 2) 2α-hydroxyursolic acid 3) 3β -*trans*-*p*-coumaroyloxy-2α- hydroxyurs-12-en-28-oic acid 4) maslinic acid 5) 3β-*cis*-*p*-coumaroyloxy-2α-hydroxyurs-12-en-28-oic acid 6) 2α-hydroxy-3β-{[(2*Z*)-3-phenyl-1-oxo-2-propenyl]oxy} olean-12-en-28-oic acid 7) 3β -*trans*-*p*-coumaroyloxy-2α -hydroxyolean-12-en-28-oic acid 8) 3α -*cis*-*p*-coumaroyloxy-2 α -hydroxyolean-12-en-28-oic acid 9) 2α,3β,13β -trihydroxyurs-11-en-28-oic acid 10) 3β,13β -dihydroxyurs-11-en-28-oic acid	Some of identified triterpenoids displayed antiproliferative activity against HepG2 liver cancer cells, MCF-7 breast cancer cells, and Caco-2 colon cancer (MTS assay).	(He and Liu, 2007)
4.	Apple peel and pulp 11 varieties	The samples of 10 and 5 g of pulp and peel were extracted with methanol containing 1% 2,6-di-*tert*-butyl-4-methylphenol (BHT) using an ultrasonic bath. The samples were extracted with 10 ml of solvent for 1 h, 10 ml for 30 min, and finally 5 ml for 30 min. The fractions were combined to a final volume of 25 ml.	HPLC-UV (identification of individual phenolics)	chlorogenic acid, *p*-coumaric acid, procyanidin B3, protocatechuic acid, (−)-epicatechin, phloridzin, rutin, quercetin-3-rhamnoside	–	(Carbone et al., 2011)
5.		Commercial product				(Du et al., 2011)

	Apple skin polyphenol powder produced by Apple Poly LLC (Morrill, Nebr., U.S.A.) as		total phenolic content (F–C)	Total phenolics = 995.3 mg chlorogenic acid/100 g dried weight	Antioxidant activity 14.4 mg Trolox/g dried weight *L. monocytogenes*: minimum inhibitory concentration = 1.5% (w/w)	
6.	Apple waste from juice extraction	Maceration of apple waste in blender, filtration, concentration by rotary evaporation. Hydrolysis of apple waste by addition of NaOH under nitrogen. Neutralization with HCl. Extraction of aqueous phase with ethyl acetate pH of residual aqueous phase was adjusted to 7 and applied to a solid phase extraction (SPE). Elution of phenolics with 20% methanol and concentrated in a rotatory evaporator; the concentrate was extracted with ethyl acetate. Next, SPE columns were eluted with ethyl acetate as mobile phase. The above ethyl acetate phase were combined and concentrated in a rotary evaporator.	total phenolic content (F–C), flavonoid content, anthocyanin content, HPLC-UV (identification of individual phenolics)	- flavan-3-ols (catechin, procyanidin B, epicatechin), - phloretin glycosides (dihydrochalocones, - dihydroflavanones, phloretin xyloglycoside, phloridzin), - quercetin glycosides (rutin, isoquercitrin, - quercetin glycoside, avicularin, quercetin), - cyanidin glycoside (ideain), - hydroxycinnamic acids (chlorogenic acid, *p*-coumaric acid)	A crude extract of apple phenolics beneficially influences key stages of carcinogenesis in colon cells HT29, HT115, CaCo-2.	(McCann et al., 2007)
7.	Apple pomace for following apple varieties: 'Pinova', 'Reinders', 'Jonagold', 'Iduna', 'Braeburn'	Extraction at room temperature using ultrasonic bath with different amounts of 80% methanol: 160 ml in 60 min, 80 ml in 60 min, 80 ml in 30 min. Evaporation under reduced pressure to dryness.	total phenolic content (F–C), flavonoid content, anthocyanin content, HPLC	Rutin Quercetin-glycosides Chlorogenic acid Caffeic acid (+)-Catechin (−)-Epicatechin Phloridzin	The highest SPPH (EC_{50}^{DPPH} = 6.33 mg/ml) and hydroxyl (EC_{50}^{OH} = 26,11 mg/ml) radical scavenging activities were obtained in case of 'Reinders' pomace.	(Ćetković et al., 2008)
8.	Apple pomace 'Granny Smith'	Extraction at room temperature using ultrasonic bath with different amounts of 80% methanol.	total phenolic content (F–C), total flavonoid content (Markham's method), total flavan-3-ols (vanillin assay), HPLC-UV (identification of individual phenolics)	Total phenolics:7.02 mg chlorogenic acid equivalents/g dry weight Total flavonoids: 0.51 mg as mg rutin/g dry weight Total flavan-3-ols: 8.8- mg mg catechin equivalents/g dry weight Phenolic acids: caffeic and chlorogenic acid, flavan-3-ols: (+)-catechin and (−)-epicatechin, flavonols: rutin and dihydrochalcones: phloridzin	IC_{50}^{DPPH} = 9.51 mg/ml IC_{50}^{OH} = 29.17 mg/ml IC_{50}^{HeLa}=26.40 mg/ml IC_{50}^{HT-29} = 22.47 mg/ml IC_{50}^{MCF7} = 21.26 mg/ml	(Savatović et al., 2008)
9.	Apple pomace (different cultivars)	Spectra of apple pomace, without extraction.	Infrared spectroscopy and partial least squares regression (PLSR)	Determination of total phenolic compounds by IR spectroscopy	–	(Queji et al., 2010)
10.	Appple pomace	Separation of phenolics and pectin from apple pomace using styrene–divinylbenzene copolymerisate resin.	HPLC	11,8% of polyphenolics in lyophilisate recovered from apple pomace. Main phenolics in lyophilisate [mg/g]: phloridzin 40.4, chlorogenic acid 14.3, quercetin 3-galactoside 11.4, epicatechin 9.3, procyanidin B2 9.3, phloretin xyloglucoside: 8.0, quercetin: 6.5.	–	(Schieber et al., 2003)
11.	Apple 'Gala', Zonouz (Iran)	Apple were peeled, dried at 25 °C, and grinded. Two step extraction in ultrasonic bath: (1) n-hexane (removal of lipids and waxy compounds), (2) MeOH:H2O (1:1). Then extract filtered and centrifuged.	HPLC, UV/VIS detector	the content of particular phenolics change during the fruit development	–	(Mehrabani and Hassanpouraghdam, 2012)

(*continued on next page*)

Table 2 (*continued*)

	Material for research: apple variety, sample preparation	Extraction methodology	Analytical/ Identification method	Extract composition/identified compounds	Biological activity	Ref.
12.	Apple (10 typical native cultivars from Central Europe)	Apples were homogenized in an extraction mixture hydrochloric acid: methanol: water in the ratio 2:80:18.	Total phenolic content (F–C)	The highest total phenolic content (grams of gallic acid/kg fresh mass) was determined in: Matcino (3.12), Panenske ceske (3.03), Strymka (3.29).	–	(Rop et al., 2011)
13.	Apples *Malus domestica*, 'Annurca' (organic and conventional farming)	Frozen samples were incubated for 1 h at 4 °C in solution acetone: ethanol: methanol (70:15:15); solvent was evaporated, residue was resuspended in methyl alcohol and filtersterilized.	total phenolic content (F–C) HPLC	Total phenolics [μmol Quercetin/g of FW]: Organic farming: pulp 66.88; peel 941.17 Conventional farming: pulp 12.29; peel 267.09.	Organic farming: *B. cereus* DSM 4313, extract concentration 19 μmol, inhibition zone: 6 mm *E. coli* EC101, extract concentration 38 μm, inhibition zone: 13 mm; Conventional farming: *B. cereus* GN105, DSM 4313, DSM 4384, extract concentration 38 μmol, inhibition zone: ~10 mm; Inhibition zone for chloramphenicol: 28 mm	(Fratianni et al., 2007)
14.	4 traditional Portuguese apple cultivars and five exotic varieties	Apples (flesh and peel) were extracted with 80% acetone (1:2, w/v) in blender. Homogenates were filtered, solvent was evaporated. The remaining extracts were diluted in distilled water to make a concentration of 2 g of fresh apple/mL. Extracts were filtered.	HPLC	catechin, epicatechin, chlorogenic acid, phloridzin, quercetin-3-glucoside, kaempferol-3-glucoside and quercetin-3-rhamnoside, procyanidin B1 and B2	The cutivars with the highest antioxidant properties: 'Malapio Fino' ORAC: 2236 μmol of trolox equivalents/ 100 g HORAC: 1183 μmol of caffeic acid equivalents/100 g LDL: 58.1 Intracellular antioxidant activity, Caco2 cells [% of inhibition capacity]: t-BHP: 40,2, H2O2: 19,4. 'Bravo de Esmolfe' ORAC: 1503 HORAC 796 LDL = 37.2 Intracellular antioxidant activity, Caco2 cells [% of inhibition capacity]: t-BHP: 47.9, H_2O_2: 19,3. 'Reineta Parda' antiproliferative activity $ED_{50}^{HT29} = 21,1$, $ED_{50}^{MKN45} = 9,0$	(Serra et al., 2010)
15.	'Red Delicious' apples	Apples were cut into slices, frozen. The freeze-dried samples were ground to powder and stored at −20 °C. Phenolics extraction: 80% aqueous methanol in ultrasound bath with a continual stream of nitrogen gas purging to prevent oxidative degradation of phenolics. Mixture was filtered.	Total phenolic content (F–C), total flavonoids (Markham's method)	Total phenolics = 155.6 [mg gallic acid equivalent/100 g] Total flavonoids = 99.0 [mg catechin equivalent/100 g]	Apple extract protected the rat pheochromocytoma neuronal (PC-12) cells from H_2O_2-induced oxidative toxicity *in vitro* in a dose-dependent manner.	(Heo et al., 2004)
16.	Apple juice (*Malus domestica* Borkh.)	Apples without cores were squeezed, ascorbic acid and sodium fluoride were added in order to inactivate polyphenoloxidases and prevent phenolic degradation, centrifuged.	Reversed-phase HPLC, UV/VIS detector	procyanidin B1, procyanidin B2, (+)-catechin, 5′-caffeoylquinic acid, (−)-epicatechin, *p*-coumaric acid, phloretin-2′-*O*-xyloglucoside, quercetin-3-*O*-glucoside, phloretin-2′-*O*-β-glucoside,	–	(Abad-Garcia et al., 2007)

				quercetin-3-*O*-arabinoside, quercetin-3-*O*-rhamnoside		
17.	Apple juice (different cultivars)	Clarification by microfiltration and ultrafiltration.	RP-HPLC analysis of phenolics without prior treatment of the sample.	procyanidin B1 and B2, (−)-epicatechin, p-coumaric acid, chlorogenic acid, phloretin 2-xyloglucoside, phloridzin	–	(Suarez et al., 1998)
18.	19 English cider apples (*Malus* × *domestica*) and one dessert apple ('Golden Delicious')	Apple were peeled, cut into quarters (core was removed), frozen in liquid nitrogen, lyophilized, ground and then stored at −30 °C. Aliquots of freeze-dried apple powder were extracted in 1.2 ml of methanol containing 10 ml/l acetic acid. Samples were centrifuged at 4 °C.	HPLC/MS	The cutivars with the highest antioxidant properties: 'Medaille d'Or' Flesh: 4920 mg/kg fresh weight (FW) Peel: 5528 mg/kg (FW) 'Yarlington Mill' Flesh: 3877 mg/kg (FW) Peel: 6306 mg/kg (FW)	–	(Marks et al., 2007)
19.	'Fuji' 'New Red Star' apple seeds	Soxhlet extraction	GC−MS analysis of fatty acids	Main compounds: linoleic acid (50.7−51.4 g/100 g) and (oleic acid 37.49 −38.55 g/100 g)	'Fuji': Antioxidant activity $IC_{50}^{DPPH} = 8.34$ mg/ml 'New Red Star': $IC_{50}^{DPPH} = 7.91$ mg/ml Antimicrobial activity against 10 species microorganisms MIC: 0.3−0.6 mg/ml	(Tian et al., 2010)
20.	Essential oil of leaves of *M. domestica*	Fresh leaves of *M. domestica* were by using Cleavenger-type apparatus for three hours	GC	Major compounds: eucalyptol (43.7%), phytol (11.5%), α-farnesene (9.6%), pentacosane (7.6%).	C-6 (glioma cells) I = 98.2% C = 2000 μg/ml, A549 (human lung carcinoma) I = 76.7% C = 2000 μg/ml, CHOK1 (Chinese hamster ovary cells) I = 70.8% C = 1500 μg/ml, THP-1 (human acute monocytic leukemia cell) I = 65.7% C = 1000 μg/ml. I - growth inhibition percentage, C = concentration of essential oil	(Walia et al., 2012)

2.3. Extraction of phenolic compounds from apples

Different techniques are applied to separate phenolic compounds from apple and apple juice. There are some phenolic compounds in apple which cannot be determinated by extraction like phenolic components of cell wall (lignins, proantocyanides as well as ferulic acid and *p*-coumaric acid in esterified form with pectins, arabinoxylans or polisaccharides). In order to separate bonded phenolic compounds some chemical (acid, alkaline or enzymatic hydrolysis) or physical (ultrasonic bath extraction) methods can be applied (Table 2). Different precautions are used in order to avoid phenolic compounds oxidation during the extraction, inter alia oxygen-free environment, low temperature of storage, protection from light and chemical additives: 2,6-di-*tert*-butyl-4-methylphenol (BHT) or sodium fluoride. Depending on the used methodology the obtained apple extracts possessed different composition and therefore diverse biological activity. Extraction with the use of several solvents (one after the another or mixture of solvents) allowed a better separation of phenolic compounds compared with the simple extraction (with one or two solvents). Application of an acetone:water:acetic acid mixture to an apple peel extraction gave an extract with higher amounts of phenolic compounds and higher antimicrobial activity than the one obtained after extraction with commonly applied ethanol:water (or methanol:water) eluents. The use of solid phase extraction (SPE) or silica gel chromatography and different eluents allowed to successfully separate the individual components of apple extracts. The method with the use of Folin- Ciocalteu (F–C) reagent to determine the total content of phenolic compounds is commonly applied but it is hard to compare the results obtained by various authors. This is due to different methodology (variant amount of chemicals, time and temperature of sample incubation) and expressed value of phenolic compounds either in the form of gallic, caffeic or chlorogenic acid equivalents. Moreover according to many authors, including Everette et al., the F–C reagent is active toward many different compounds present in plants extracts beside phenolics, i.e. proteins, thiols, vitamin derivatives, inorganic anions Fe^{2+}, Mn^{2+}, I^-, SO_3^{2-} (Everette et al., 2010). Therefore the F–C assays more likely measure the total antioxidant capacity of a given sample than the total phenolic content. Besides HPLC, the FT-IR spectroscopy is also used to evaluate the total phenolic content. GC–MS can also be used in the analysis of fatty acids extracted from apple seed or phenolic compounds from apple extract but then the hydrolysis is needed to obtain low mass phenolic compounds.

3. Selected biological properties of apples

3.1. Antimicrobial properties

There are many literature data on the antimicrobial properties of extracts from apples. For example, extracts from the peel of the 'Royal Gala' and 'Granny Smith' varieties inhibited to the highest degree the growth of *Escherichia coli* ATCC 25922, *Pseudomonas aeruginosa* ATCC 27853 and *Staphyloccocus aureus* ATCC 29 213 (Table 2) (Yamaguchi et al., 2008). The extracts derived from 'Granny Smith' were characterized by significantly higher antimicrobial activity than those derived from the variety 'Royal Gala'. According to Fattouch et al. peels of 'Red Delicious' apples showed antimicrobial activity against *Staphylococcus aureus*, *P. aeruginosa* and *Bacillus cereus* (Fattouch et al., 2008). The minimum inhibitory and bactericide concentrations were from 102 to 104 μg of phenolic compounds/ml. In the study of Moore et al. the effectiveness of apple extract to inactivate *Salmonella Newport* on four types of organic leafy greens was shown (Moore et al., 2011). Fratianni et al. studied antimicrobial properties of 'Annurca' apples that were originated from organic and conventional farming (Fratianni et al., 2007). The study revealed different antimicrobial activity and different phenolic content in the extracts from the two types of apples. The conventionally produced apples showed a good inhibitory effect against *Bacillus cereus*. On the other hand the peel from organic apples possessed a good inhibitory effect against *E. coli* 0157:07 (Table 2). According to the next study of Fratianni et al. the mechanism of antimicrobial activity of the extract from 'Annurca' apples may rely on cell growth regulation or inhibition of quorum sensing (a cell–cell signalling) mechanism (Fratianni et al., 2011; Fratianni et al., 2012). Muthuswamy and Rupasinghe studied the antimicrobial activity of tree major phenolic compounds present in apples, i.e. catechin, chlorogenic acid and phlorizin. All the phenolics inhibited growth of *E. coli* O157:H7, *Listeria innocua* and *Penicillium chrysogenum* at concentration 25 mM (Muthuswamy and Rupasinghe, 2007). Growth of *Saccharomyces cerevisiae* was inhibited only by chlorogenic acid and phloridzin. Growth of probiotic bacterium *Lactobacillus rhamnosus* was not affected by the three phenolic compounds at any tested concentration (except by 25 mM phloridzin). In the study of Yanagida et al. apple phenolic compounds did not affect the growth of the cariogenic bacteria, whereas apple condensed tannins were effective against *S. sobrinus* and *S. mutant* and the 50% inhibitory doses were 1.5 μg/ml and 5 μg/ml, respectively (Yanagida et al., 2000). Unlike other phenolic compounds, apple extract and apple condensed tannins only to a small extend inhibited salivary alpha-amylase activity, and they may have a potential application in oral hygiene. The extract obtained from the leaves of apple trees has antimicrobial activity against *S. aureus* (Kitahara et al., 2003).

Natural plant extracts or individual substances of natural origin are potential new antimicrobial agents that can be applied alone or in the mixture with other commonly used preservatives or in the form of phenolic substances-pectine edible films that can serve as an additional barrier against pathogenic and spoilage microorganisms that contaminate food surfaces. Du and colleagues studied the effectiveness of antimicrobial edible films obtained from apple peel phenolic compounds that could be used in food technology (Tian et al., 2010). Film formed at a concentration of 1.5% phenolic compounds inhibited the growth *of Listeria monocytogenes*. However, phenolic substances from apple peel did not show antimicrobial properties against *E. coli* O157:H7 and *Salmonella enterica* even at 10% level. The film possessed high total phenolic compound content that equals 995.3 mg chlorogenic acid per 100 g dried weight. Previous studies conducted by Ravishankar et al. revealed that addition of carvacrol or cinnamaldehyde (in concentration 0.5%, 1.5% or 3%) to apple edible film improved its antimicrobial activity toward *S. enterica* and *E. coli* O157:H7 (Ravishankar et al., 2009). The protection of the edible film from apple extract was greater than that by carrot or hibiscus films and the tested films were more effective when applied on ham than on bologna (Ravishankar et al., 2012). The apple edible films containing carvacrol and cinnamaldehyde were successfully tested for antibacterial properties against antibiotic resistant and susceptible *Campylobacter jejuni* strains on chicken (Mild et al., 2011). The films with addition of cinnamaldehyde were more effective than carvacrol films. The temperature was also an important factor because the inhibition of growth of *C. jejuni* at 23 °C was greater than those at 4 °C. Juneja et al. tested ability of apple extract to overcome sodium chloride-induced heat resistance of *L. monocytogenes* in 75% lean beef (Juneja et al., 2013). They created an accurate model which allowed determining the appropriate concentration of NaCl, apple phenolic compounds and temperature to protect food from growth of harmful

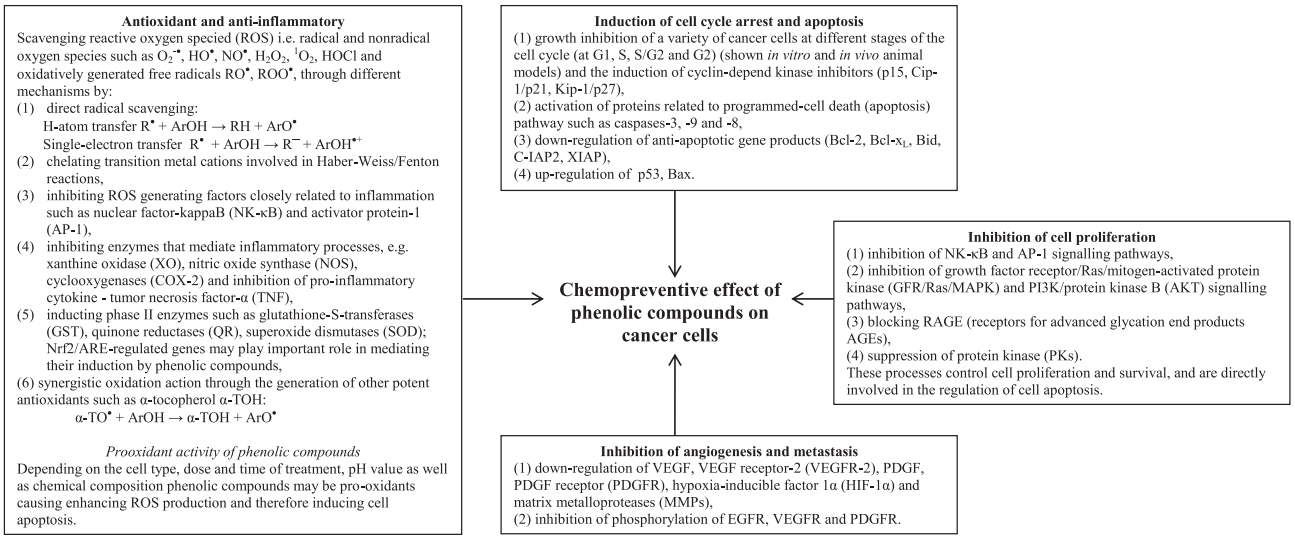

Fig. 4. Summarized selected mechanisms of cancer preventive properties of phenolic compounds (Rudak et al., 2011).

microorganisms. In the study of Rounds et al. the mixture of apple skin extract (bought in Apple Poly LLC, Morrill, NE), olive extract and onion powder caused inactivation of *E. coli* O157:H7 and decrease the level of heterocyclic amines in grilled beef (Rounds et al., 2013). Addition of 5% apple skin extract to grilled ground beef reduced population of *E. coli* O157:H7 to below the detection limit and at the same time decreased the amount of heterocyclic amines by 76–82% compared to the sample without addition of apple extract (Rounds et al., 2012). The same apple extract (obtained from Apple Poly LLC, Morrill, NE) did not possess antimicrobial properties against three strains of *Mycobacterium avium* subsp. *Paratuberculosis* (Wong et al., 2008). The high in bioactive compounds plant extracts that are candidates for use as antimicrobials in food technology were studied by Friedman et al. (Friedman et al., 2013). They used the parameter BA_{50} to describe the concentration of tested extract or compound that kills 50% of the initial amount of bacteria under specified test conditions. The antimicrobial activity of apple peel extract toward selected microorganisms could be expressed as BA_{50} that amounted to 0.007 (*L. monocytogenes* 2199), 0.002 (*S. aureus* 1200), 1.39 (*S. enterica* 1309) and >2.7 (*E. coli* 1484). The apple extract was effective against gram-possitive (*L. monocytogenes* and *S. aureus*), and rather ineffective toward gram-negative bacteria (*E. coli* and *S. enterica*). The apple polyphenol phloridzin did not seem to be responsible for the antimicrobial activity of the extract, because it was active only against *S. enterica*.

There is little information in the literature on the relation between the apple variety, cultivation model and the antimicrobial activity of apple extract. It is supposed that apple varieties with the higher total content of phenolic compounds should possess higher antimicrobial activity. The same concerns the part of apple, i.e. peels are mainly tested for their antimicrobial activity due to the higher content of phenolic compounds compared with other parts of apple. The most studies describe the antimicrobial activity of individual phenolic compounds present in apples e.g. catechin, chlorogenic acid, phloridzin, procyanidines, but the results are often contrary and depends on applied methodology. Studying the antimicrobial properties of apples extract in terms of biological activity of individual phenolic compounds the synergistic effect of phenolic compounds, which rely on mutual reinforcement of the action of several substances when they present together in the extract, should be taken into account.

3.2. Cancer preventive properties

There are many *in vitro*, *in vivo* and epidemiological studies on cancer preventive properties of apple and apple products. Mechanism of anticancer activity of apples among others relies on: antimutagenic properties, inhibition of cancer cell proliferation, modulation of phase 1 and 2 of carcinogen metabolism, antioxidant properties, induction of tumour suppressor gene expression, inhibition of cell growth, induction of apoptosis, modulation of signal transduction pathways, enhancement of immune system (Fig. 4) (Gerhauser, 2008; Koch et al., 2009). Many research studies have shown that apples have *antiproliferative activity* against cancer cells. According to Savatović et al. the IC_{50}^{HeLa} (human cervical cancer cell), IC_{50}^{HT29} (human colon cell lines) and IC_{50}^{MCF7} (breast cancer cell line) values obtained for 'Granny Smith' apple pomace were 26.40 mg/ml, 22.47 mg/ml and 21.26 mg/ml, respectively (Savatović et al., 2008). Eberhardt and colleagues found high activity of acetone extract of apple in relation to colon cancer cells. The extract obtained from the fruit with the skin possessed higher activity than that without the skin. Apple extract at a concentration of 50 mg/ml decreased tumor cell proliferation by 43% (extract from the fruit with the skin) and 29% (without skin extract) (Eberhardt et al., June, 2000). Wolf and colleagues also found that extract from apple peel inhibited the proliferation of Hep G2 cells to a greater extent than that of the whole apple (Wolfe and Liu, 2003). The EC_{50} values (concentration causing 50% inhibition of proliferation of cancer cells) for 'Idared' apple peel was 13.6 mg/ml, while for the whole apple EC_{50} = 125.1 mg/ml. McCann's studies have shown high efficacy of the extract of apples in inhibiting colon cancer cell growth (McCann et al., 2007). Different varieties of apples have different effects on liver cancer cell proliferation (Liu et al., 2001). Extract from 'Fuji' apples at a concentration of 50 mg/ml inhibited the proliferation of Hep G2 cells by 39%, and the extract of 'Red Delicious' apples inhibited cell proliferation by 57% (Boyer & Liu, 2003–2004). While the extract of 'Northern Spy' apples had no effect on tumor cell proliferation. According to Lee and colleagues some flavonoids such as quercitin, epicatechin and procyanidins B2 determined the anticancer activity of apple extract (Lee et al., 2005). According to He and Liu, the triterpenoids isolated from the skins of apples were responsible for the anticancer properties of the extract (He and Liu, 2007). The research of Yamaguchi and colleagues suggested that ursolic acid isolated from the chloroform

extract of dried apple peel was a potential anticancer agent (Yamaguchi et al., 2008). Serra et al. showed that among studied nine apple cultivars 'Reineta Parda' is the best in promoting antiproliferative effect against human colon (HT29) and gastric (MKN45) cancer cells (Serra et al., 2010). Using statistical analysis they reported that procyanidins (B1 and B2), phloridzin and epicatechin played an important role against human cancer cell proliferation. The essential oil from apple leaves is also a valuable source of anticancer compounds. Recently, Walia et al. reported chemical composition and *in vitro* cytotoxic activity of essential oil of leaves of apples growing in Western Himalaya (India) (Walia et al., 2012). Eucalyptol (43.7%), phytol (11.5%), α-farnesene (9.6%), and pentacosane (7.6%) were the major compounds of apple essential oil. High cytotoxic activity of essential oil toward C-6 cell lines (glioma cells) (98.2%) at concentration of 2000 μg/ml compared to control was shown.

According to Schaefer et al. polyphenolic apple juice extracts and their major constituents can *reduce oxidative damage* in human colon cell lines Caco-2 and HT29 (Schaefer et al., 2006). The individual extracts at the concentration from 50 to 250 μg/ml affected DNA damage in Comet assay and redox status (in dichlorofluorescein assay) in a concentration-dependent manner. Apple phenolic compounds: rutin, epicatechin and caffeic acid significantly reduced oxidative DNA damage of Caco-2 line, chlorogenic acid decreased cellular reactive oxygen species level (HT29, Caco-2). The aglyca quercetin and phloretin exhibited the highest preventive/antioxidant capacity in all assays. In other study, Heo et al. demonstrated that apple phenolic compounds protected PC-12 cells (rat pheochromocytoma neuronal cells) from oxidative H_2O_2 toxicity *in vitro* (Heo et al., 2004). In this study PC-12 cells were pretreated with apple extracts (100 μg extract = 500 mg fresh apple) for 10 min, and then the cells were treated with 400 μM H_2O_2 (in 2,7-dichlorofluorescein diacetate assay). Additionally, to confirm the cytoprotection of apple on the H_2O_2-induced membrane damage, the trypan blue exclusion assay was also done. According to the authors quercetin was one of the major flavonoid in apples that was mainly responsible for this protective effect. Apple polyphenols affect the expression of numerous genes that are involved in the antioxidant defense system. In the study of Solayan et al. polyphenol-rich apple juice increased the expression of antioxidant response element (ARE)-dependent genes and this properties differed with juice type, i.e. cloudy apple juice > clear apple juice ~ smoothie (Soyalan et al., 2011). In the distal colon, the presence of apple juice considerably induced most genes e.g. GPX2 (gastrointestinal glutathione peroxidase), GSR, CAT (chloramphenicol acetyltransferase), Nrf2 (nuclear factor erythroid-2-related factor 2), whereas in the liver only GPX1 (glutathione peroxidase 1) and NQO1 (NAD(P)H quinone oxidoreductase 1) mRNA genes were upregulated; other hepatic target genes i.e. SOD1 (superoxide dismutase 1), SOD2 (superoxide dismutase 1) and GSR (glutathione reductase) were not affected or down-regulated. Denis and co-authors studied the antioxidant and anti-inflammatory properties of apple peel extract and purified polyphenol fraction derived from dried apple peel powder using human epithelial colorectal adenocarcinoma Caco-2/15 cell line (Denis et al., 2013). According to the authors apple peel extract and apple peel phenolic compounds possessed significant capacity in scavenging reactive oxygen species and neutralizing inflammation process in intestinal absorptive cells. It is concluded that the increase in the antioxidant/anti-inflammatory defense can be achieved by: (a) preventing lipopolysaccharide-induced inflammation via reduction of the pro-inflammatory expression and activity of cyclooxygenage-2 (COX-2); (b) excluding lipopolysaccharide-mediated cytokine production through down-regulation of the transcription factor nuclear factor-kappa B (NF-κB), and (c) upregulating the expression of transcription factors such as nuclear factor erythroid-2-related factor 2 (Nrf2) and peroxisome proliferator-activated receptor gamma coactivator-1 alpha (PGC-1α). Different phenolic compounds from apple pomace had different inhibitory effect on COX-2 expression (Yue et al., 2012). Yue et al. revealed that procyanidin B2, hyperin and quercetin played an important role in COX-2 suppression. Carrasco-Pozo et al. also tested antioxidant/anti-inflammatory activity of apple peel extract (Carrasco-Pozo et al., 2010). The study showed protective properties of apple peel extract toward heterogeneous human epithelial colorectal adenocarcinoma cells (Caco-2 cells) against the harmful effects of indometacin on cellular oxidative status, mitochondrial function and cell viability possibly through its ability to scavenge reactive oxygen species. Graziani et al. studied the protective effect of apple extract in gastric cancer cell line (MKN-28) incubated with xanthine–xanthine oxidase or indomethacin (Graziani et al., 2005). Apple extract from apple flesh of the 'Annurca' cultivar decreased induced injury to gastric epithelial cells by 50%, moreover apple extract caused a fourfold increase in intracellular antioxidant activity and it decreased indomethacin injury to the rat gastric mucosa by 40%. According to Andre et al. the mechanism of anti-inflammatory action may vary depending on apple cultivars (Andre et al., 2012). The 5 from the 109 studied apple cultivars considerably differ with respect to their chemical composition. Cultivars exhibiting high contents of procyanidins inhibited NF-κB activity while apples rich in triterpene reduced the promoter activity of the tumor necrosis factor-alpha (TNFα) gene.

Beside an antiproliferative, antioxidant and anti-inflammatory properties, apple phenolic compounds have been shown to increase expression of the phase II gene glutathione S-transferase T2 (GSTT2) in colon epithelial cells and according to Peterman et al. this may contribute to primary chemoprevention effect of apple polyphenols toward colon cancer (Petermann et al., 2009). According to the study of the mentioned authors phenolic apple extract directly enhanced GSTT2 promoter activity. In the HT29 colon epithelial cells that were pretreated with apple extract the genotoxicity of the GSTT2 substrate cumene hydroperoxide was significantly reduced. Overexpression of GSTT2 in HT29 cells significantly reduced cumene hydroperoxide and induced DNA damage. According to Miene and co-authors the effect of apple phenolic compounds on activity regarding GSTT2 induction depends on its specific composition which changes during storage (Miene et al., 2009). In another study of Miene et al. the influence of selected intestinal phenolic compound metabolites on activity of enzymes (glutathione S-transferase T2 and cyclooxygenase-2, COX-2) involved in detoxification and inflammation in human adenoma cells LT97 was tested (Miene et al., 2011). The LT97 cells were treated with 3,4-dihydroxyphenylacetic acid and 3-(3,4-dihydroxyphenyl)-propionic acid, metabolites of apple phenolic compounds, i.e. quercetin, and chlorogenic and caffeic acids, respectively. Phenolic compounds metabolites did not affect cell number but significantly increased GSTT2 expression and decreased COX-2 what possibly can contribute to the chemopreventive potential of phenolic compounds after degradation in the gut. DNA damage induced by cumene hydroperoxide was significantly reduced compared to the control. To better understand the colon cancer preventive effect of phenolic compounds it is necessary to undertake studies with polyphenol metabolites. It should be emphasized that chemopreventive activity of apples cannot be only explained be phenolic compounds activity. Apples are rich in pectin which is substrates for butyrate synthesis by the microflora of the colon. This short-chained fatty acid suppresses colonic inflammation by inhibition of the IFN-γ/STAT1 signaling pathways partially through the inhibition of histone deacetylase (HDAC). Waldecker et al. investigated the activity of the fermented apple pectin, fermented polyphenol-rich apple juice extract and combined pectin + apple juice extract to inhibit cell proliferation

and HDAC activity in HeLa Mad 38, HT29 and Caco-2 cells (Waldecker et al., 2008). Fermentation supernatants from all samples showed HDAC inhibition, but only supernatant from fermentations with pectin possessed high content of butyrate; in the other two samples the content of this compound was significantly lower. It suggested that in the fermented apple juice extracts there were present other substances beside butyrate that can act as HDAC inhibitors. According to Licht et al. administration of 7% apple pectin in the diet of rat resulted in the increase of the population of butyrate- and beta-glucuronidase producing *Clostridiales*, and in the decrease the *Bacteroidetes* in the rat gut (Licht et al., 2010). This effect was not observed in the group fed with whole apples, apple juice, purée or pomace.

Apple constituents also affect *the proliferation and apoptosis* of cancer cells through modification of their *signaling pathways*. Mutations that lead to epidermal growth factor receptor (EGFR, ErbB1) up-regulation have been associated with a several types of cancer. EGFR exists on the cell surface and is activated by binding of its specific ligands, including epidermal growth factor and transforming growth factor α (TGFα). The inhibitors of EGFR are one of the targets of strategies for cancer therapy (Harari, 2004). Polyphenol apple extracts are known to inhibit the activity of the epidermal growth factor receptor EGFR. Procyanidins B1 and B2 as well as glycosides of quercetin had significant contribution to EGFR-inhibitory properties of apple extract (Kern et al., 2005; Fridrich et al., 2007). Teller et al. showed that among apple polyphenols oligomeric procyanidins had the highest contribution to the inhibitory effects towards members of the ErbB-receptor family (the inhibition of the activity of the EGFR and ErbB3 in cell culture with an IC_{50} 100 μg/ml and IC_{50} 10 μg/ml, respectively) (Teller et al., 2013). One of the cancer treatment strategies is induction of apoptosis. According to Miura et al. apple procyanidins, had a greater impact on cell proliferation and induced apoptosis *in vitro* compared to other apple polyphenols such as chlorogenic acid, (−)-epicatechin and phloridzin (Miura et al., 2008). The apple procyanidins increased mitochondrial membrane permeability and cytochrome c released from mitochondria as well as activated caspase-3 and caspase-9 in the cancer cells. D'Angelo et al. showed that 'Annurca' apple polyphenols induced apoptosis in epithelial cells by triggering a death receptor-associated extrinsic pathway p53-independent (D'Angelo et al., 2012).

The presented results suggest that polyphenols (especially: procyanidins, epicatechin, phloridzin, ursolic acid) play a more significant role in cancer preventive properties of apples than simple phenolic acids. The strength and mechanism of anticancer activity of apple phenolic compounds depends on their chemical structure. E.g. quercetin – polyphenol with high antioxidant activity mainly contributed to the chemopreventive effect through reduction of the oxidative damage, whereas procyanidins showed different mechanism of action: antiproliferative activity, it induced apoptosis, inhibited NF-κB activity, activated caspase-3 and caspase-9 cycles, and inhibited members of the ErbB-receptor family. Many studies indicate that apple extracts may have significant importance in colon cancer prevention through the increase of GSTT2 and decrease COX-2 expression, and these properties are determined not only by the presence of phenolic compounds, but mainly pectin which is substrates for butyrate synthesis by the microflora of the colon. Butyrate act as inhibitor of histone deacetylase. Moreover, it occurred that the other constituents of apple extracts might have a significant contribution to the anticancer activity of apple extract. Li et al. demonstrated that apple polysaccharide can prevent colon cancer growth (Li et al., 2013). They obtained apple oligosaccharides by alkaline hydrolysis and enzymolysis of apple polysaccharides, and purification by the use of anion column chromatography. The results showed that apple oligosaccharides enhanced the expression of Bax, decreased the levels of Bcl-2 and Bcl-xl in HT29 cells and inhibited cell cycle in the S phase.

3.3. Cardiovascular disease (CVC) and lower plasma cholesterol

There are many studies that connect apple consumption with the lowering of plasma cholesterol and reduction in the risk of cardiovascular disease. According to the survey done by Jensen et al. a daily intake of approximately three apples caused a decrease in the level of total cholesterol at 5–8% and the effect is more significant in the hypercholesterolemic group (Jensen et al., 2009). What is important - the size of apple particles and the processing affect the outcomes of the studies. The patients who consumed blended apple pulp had greater reduction in the total cholesterol than the group consuming apple slices. According to authors the blended form possessed smaller particle size than sliced or grinded what increased the surface area and therefor the capacity to bind cholesterol in the gut (Canella et al., 1963). The major mechanism of cholesterol-lowering effect of apples relies on an enhanced faecal excretion of bile acids and cholesterol. These wholesome properties of apples arise from their chemical composition with particular reference to pectin, phytosterols and polyphenols. These substances are known to interact with lipid metabolism and influence plasma cholesterol level (Jensen et al., 2009). No significant effect on plasma cholesterol or on triglicerides was observed after consumption of filtered apple juice. This effect was caused by the lack of fiber, lower content of polyphenols and phytosterols and higher content of fructose compared with cloudy juice. Aprican et al. conducted studies in rat fed with fodder supplemented with apple pectin or apple phenolic compounds or both apple pectin and phenolic compounds (Aprikian et al., 2003). The latter resulted in a significantly higher reduction in the total plasma cholesterol compared with the group fed with either pectin or phenolic compounds along. This suggested strong synergistic and additive effect between these two components. Lam et al. studied the effect of apple phenolic compounds on blood cholesterol level and gene expression of cholesterol-regulating enzymes in Golden Syrian hamsters (Lam et al., 2008). The fodder enriched with 0.3 or 0.6% of apple phenolic compounds did not affect plasma total cholesterol, but it increased HDL cholesterol and decreased non-HDL-C in the population. This diet did not influence the sterol regulatory element-binding protein 2 (SREBP-2), LDL receptor (LDLR), 3-hydroxy-3-methylglutaryl coenzyme A reductase (HMGR), and cholesterol-7alpha-hydroxylase (CYP7A), but inhibited plasma cholesteryl ester transport protein (CETP). According to authors, apple phenolic compounds may improve distribution of cholesterol in lipoproteins through inhibition on CETP activity. In the another animal study of Yao et al. apple phenolic compound extract reduced triglyceride level in the mechanism which relies on up-regulation of lipoprotein lipase activity (Yao et al., 2012).

4. Concluding remarks

The consumption of fruits, including apples, is associated with a lower risk of many degenerative diseases such as cancer and cardiovascular disease. The content of individual phenolic compounds as well as pectin, sugars, macro- and microelements significantly depends on apple variety, type of farming, weather conditions, processing. Therefore it is very important to select the apple varieties with the highest contents of phenolic compounds and accurately determine in what way various factors influence the phenolic level. Moreover, there is a strong need for an long-term extensive study on large group of apple varieties grown under different conditions which will involve appropriately selected extraction methods, sophisticated methods of phenolic compound

determination and screening for biological properties of obtained extracts or individual apple phenolic compounds. There are many studies that discuss biological properties and effect of phenolic compounds on human health and little information about metabolites of phenolics formed in the gut by the microbiota. Phenolic compounds are metabolized to different compounds in human body and their concentration and activity differs from primary phenolic compounds tested in the *in vitro* studies. It is assumed that the daily intake of plant phenolic compounds is about 150–1000 mg (Aura, 2008; Stahl et al., 2002). An assumption that less than half of the amount is metabolized in colon gives about several hundreds of miligrams of phenolics that may cause diverse effect in the digestive system and in the whole body (Aura, 2008). If swallowed phenolic compounds undergo different transformations before being absorbed (deglycosylation or deconjugation) (Rechner et al., 2004; Scalbert et al., 2002). In the colon the microbial metabolites of phenolic compounds are absorbed and then can be metabolize in the liver to glucuronidated and sulphated derivatives (Materska, 2008; Borges et al., 2013). The metabolites of phenolic compounds have a long resistance time in the blood reaching 24–48 h after the intake of their precursors (Aura, 2008). The concentration of phenolic compounds and their metabolites accumulated *in vivo* in plasma after a normal dietary intake is lower (about 1 μmol/l) than those observed for antioxidants such as ascorbic acid, α-tocopherol or glutathione (Halliwell et al., 2000; Stoupi et al., 2010; Crozier et al., 2009). The plasma concentration of some metabolites of apple phenolics – chlorogenic acid (i.e. caffeic, ferulic, isoferulic, and *p*-coumaric acids) is about 1.0 μmol/l, whereas the maximum plasma concentration of total chlorogenic acid isomers in humans is ~15 μmol/l (one of the most abundant isomer of chlorogenic acid, i.e. 5-*O*-caffeoylquinic acid, 5-CQA: 1 μmol/l) (Rocha et al., 2012). Therefore, the concentration of phenolic compounds and their metabolites seems to be too low to exert antioxidant properties which rely on lowering of the free radical levels in the body, but it is enough to affect the cell signaling pathways (Aura, 2008; Crozier et al., 2009). It was shown that metabolites of phenolic acids with the concentration 0.01–417 μmol/l inhibited COX-2 enzyme in the study with HT20 colon cancer cells (Karlsson et al., 2005). In order to fully understand the mechanism of action of apple phenolic compounds the study with metabolites of phenolic compounds should be intensively carried out. There are many papers that cover the biological properties of apple extracts and individual phenolic compounds but the research on phenolic compound metabolites are rarely described. The new models and methods in studying the regulation of biological processes are developed (Deusser et al., 2013; van Duynhovena et al., 2011). Designing the studies on bioavailability and biological activity of apple phenolic metabolites there should be taken into account the results of several papers indicating that the concentration of apple phenolic compounds and their metabolites in plasma is stable after regular consumption of apples during several months (Jedrychowski et al., 2010; Boyer and Liu, 2004).

Contribution

PhD Monika Kalinowska – the originator of the idea of this article and she was responsible for the chapter: “Selected biological properties of apples”.

BSc Aleksandra Bielawska and PhD Hanna Lewandowska-Siwkiewicz were responsible for chapter: “The content of phenolic compounds in apple”.

Prof. Włodzimierz Lewandowski and Prof. Waldemar Priebe – initiators of the discussion on the work, responsible for the substantive part of the work.

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