CHAPTER

37

Apples: an apple a day, still keeping the doctor away?'

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37.1 Background

Apples are fruits of the apple tree, *Malus domestica*. The apple tree belongs to the family of *Rosacea*, to which plum, pear, apricot, and cherry trees, among others, also belong. The modern apple tree originates from from the wild apple *Malus sieversii*, which has its home in the mountains of central Asia, and has been cultivated for several thousand years, with a lesser influence from other wild-type apple species such as *M. sylvestris* (Cornille et al., 2012), as determined via genetic analyses. Many cultivars exist; over 7500 are grown world-wide (USDA, 2015a). In most developed countries however, the market is dominated by merely a dozen or so of the >7500 existing varieties (Table 37.1), including several older cultivars which have been grown for over six decades or so, such as Cox Orange, Boskoop, Golden Delicious, Granny Smith, and rather modern ones, which have been around for only a few decades, such as Gala, Topaz, and Jonagold (Morgan and Richards, 2002). As many varieties are also produced locally, favoring temperate to subtropical climate zones (Fig. 37.1), local apple consumption may have a more favorable CO_2 imprint compared to fruits transported over long distances.

Apples rank, in most cultures, especially in the western world, number one or two (together with bananas) in terms of fruit consumption (USDA, 2012), being often as high as 20−30 kg/capita per year, thus contributing significantly to the "5-a day" recommendation, advertised by many nutrition and health agencies such as the WHO. Many epidemiological studies have highlighted the association between the consumption of fruits and vegetables (especially in raw or limited processed form), encompassing apples, and reduced incidence of several chronic diseases, including cardiovascular diseases (CVD), type-2 diabetes (T2D), and several types of cancer. Though it is not entirely comprehended which constituents of the apple fruit contribute mostly to the associated health benefits, it is thought that the combination of dietary fiber (e.g., pectins), vitamins (such as vitamin C), minerals (e.g., potassium), and trace elements, together with secondary plant compounds or "phytochemicals," including especially polyphenols, phytosterols and triterpenes, are responsible for the observed health benefits.

In addition, apples contain digestible carbohydrates (fructose, glucose, sucrose), contributing to energy intake, approximately 55 kcal/100 g fresh fruit (Souci et al., 2000). Given their important contribution to fruit intake, and the attributed health aspects, "an apple a day keeps the doctor away" became a proverb in the later 19th century. This chapter aims to highlight the important contribution of apples to our daily intake of fibers, micronutrients, and phytochemicals, evaluating whether, based on current scientific criteria, apples can indeed help to keep disease at bay.

37.2 Overview on nutritional and nonnutritional composition

The typical composition of apple fruits, in short termed apple in the following, is summarized in Table 37.1. Apples are generally low in proteins and lipids, and comparatively low in dietary fiber, of which most is

Nutritional Composition and Antioxidant Properties of Fruits and Vegetables.
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TABLE 37.1 Composition of apple fruits with respect to macro- and micronutrients, as well as major phytochemical classes.

Constituent	Amount	Reference(s)
Water (g/100 g)	85	Souci et al. (2000), USDA (2015c)
Lipids (g/100 g)	0.2–0.6	Souci et al. (2000), USDA (2015c)
Proteins (g/100 g)	0.25–0.45	Souci et al. (2000), USDA (2015c)
Carbohydrates (g/100 g)	10.4–11.5	Souci et al. (2000), USDA (2015c)
• Fructose	2.0	Souci et al. (2000)
• Glucose	5.7	Souci et al. (2000)
• Sucrose	2.5	Souci et al. (2000)
Dietary fiber (g/100 g)	2.0–2.4	Souci et al. (2000), USDA (2015c)
• Water soluble	0.5	
• Water insoluble	1.5	
Total minerals (mg/100 g)	300	Souci et al. (2000)
• Magnesium	3–9	
• Calcium	4–11	
• Potassium	100–175	
• Sodium	1	
Phytosterols (mg/100 g)	12/30	Souci et al. (2000), Rudell et al. (2011)
• Beta-sitosterol	11	
• Campesterol	1	
Total polyphenols (mg/100 g)	85–430[a]	Bouayed et al. (2011a)
Total polyphenols (mg/100 g)	50[b]	Rothwell et al. (2013)
Total triterpenes (mg/100 g)	40–350	Jager et al. (2009), Andre et al. (2012)
Vitamin C (mg/100 g)	12	Souci et al. (2000)
Vitamin E (mg/100 g)	0.2–0.5	Souci et al. (2000), USDA (2015c)
Total carotenoids (μg/100 g)	37–46	Souci et al. (2000)

[a] *Determined via Folin–Ciocalteu (bearing the risk of overestimation).*
[b] *Sum of individual polyphenols, determined by HPLC-UPLC.*

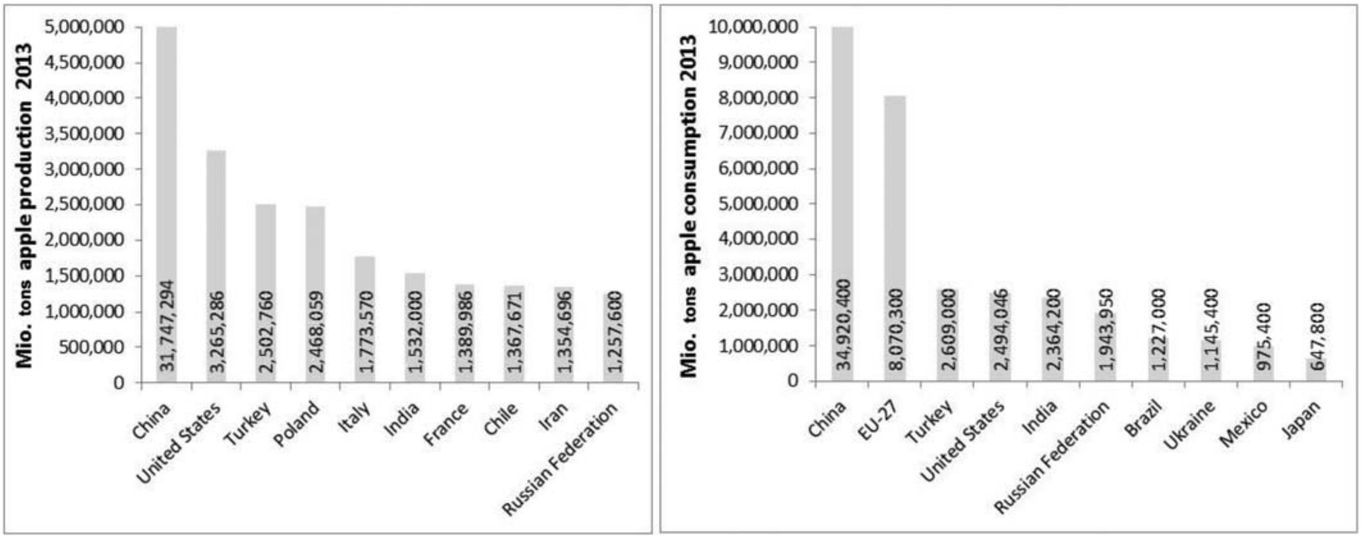

FIGURE 37.1 Graph on apple production (left) and apple consumption (right) worldwide. Source: *Data based on the World Apple and Pear association (http://www.wapa-association.org/asp/page_1.asp?doc_id=446) and index mundi (http://www.indexmundi.com/agriculture/?commodity=apples&graph=fresh-domestic-consumption).*

cellulose (40%), hemicelluloses (20%), lignins (15%), and pectins (10%) (Chen et al., 1988). Apples are relatively rich in sugars, especially glucose, sucrose, and fructose, which are the main energy providing constituents in apples. The mineral content, as with many other fruits, is relatively low, except for potassium. For an appropriate taste, balancing the sugar content, various acids are of importance, notably citric acid and malic acid, with contents of approximately 500 mg/100 g in total (Table 37.2; Souci et al., 2000). However, it has been questioned whether varieties sold nowadays are containing too much sugar, and too little dietary fiber and other healthy constituents such as antioxidants. Thus going for the most frequently sold and optically attractive apple may not be the best strategy with respect to healthy composition.

While apples contain also a variety of other vitamins such as B6, pantothenic acid, nicotinamide (each below 300 μg/100 g), and vitamin E, that is, tocopherols (0.5 mg/100 g), they are possibly most renowned for their contribution to vitamin C intake, though typical contents are around 10 mg/100 g (Souci et al., 2000; Rad et al., 2014),

TABLE 37.2 Composition of various apple varieties with respect to selected macro- and micronutrients, as well as major phytochemical classes (results from Bouayed and Bohn, unpublished), harvested in Luxembourg in 2010/2011.

Variety (year of market introduction)	Dry mass %	Titratable acidity mgCA/100 g	Sugars g/100 g	Total phenolics mgGA/100 g	Flavonoids mgCAT/100 g	FRAP μmol Fe II/100 g	ABTS/VEAC mgVitC/100 g	Anthocyanins mgC3G/100 g	∑macro-minerals mg/100 g	∑trace elements mg/100 g
Jonagold (1968)	12.6	364	11.9	137	92.7	1027	261	1.04	111	0.254
Pinova (1986)	14.9	344	13.5	109	79.0	877	331	0.20	169	0.416
Cox orange (1829)	15.5	428	13.0	166	118.3	1339	396	0.48	153	0.330
Pilot (1830)	15.3	486	13.4	109	77.9	949	322	0.28	157	0.233
Rubinette (1964)	17.8	393	15.3	134	89.5	1065	293	0.13	170	0.289
Winter-Rambour (1904)	16.0	352	13.9	229	153.6	1537	448	0.49	178	0.285
Jonagored (1985)	13.2	239	12.9	163	116.9	1181	398	0.54	107	0.242
Golden Delicious (1914)	15.9	253	13.6	98	66.7	777	253	0.06	140	0.246
Jonaprinz (1994)	15.1	358	13.9	164	135.4	1328	664	1.14	134	0.288
Mutsu (1930)	15.8	328	14.3	176	113.4	1306	370	0.03	123	0.307
Fuji (1930)	14.9	179	14.2	86	59.1	702	232	0.19	121	0.203
Elstar (1950)	15.4	500	14.0	113	64.5	937	261	0.34	143	0.298
Braeburn (1952)	15.0	363	13.6	107	67.2	800	225	0.54	94	0.334
Boskoop (1856)	16.5	699	14.2	234	143.9	1465	632	0.24	135	0.392
Grauapfel (1500)	20.8	789	16.6	434	338.6	3143	1142	0.03	241	0.591
Roter Trierer Weinapfel (1862)	16.5	334	12.7	198	154.7	1685	601	0.89	138	0.302
Graham apfel (1890)	13.1	450	10.2	142	113.6	1104	449	0.04	156	0.229
Florina (1980)	17.0	442	15.3	130	91.9	1097	342	2.27	187	0.417
Eifeler rambour (1904)	16.9	376	11.5	243	189.2	1884	739	0.08	145	0.265
Topaz (1990)	14.9	692	12.7	87	57.2	695	270	0.53	143	0.360
Goldparmane (1800)	18.6	564	15.3	253	161.6	1808	675	0.19	170	0.247
Hilde (?)	14.8	534	11.7	nd	nd	nd	nd	nd	157	0.292
Granny smith (1868)	15.3	742	12.3	nd	nd	nd	nd	nd	183	0.560

Abbreviations: ABTS, 2,2′-azino-bis (3-ethylbenzothiazoline-6-sulfonic acid); GA, gallic acid equivalents; CAT, catechin equivalents; C3G, cyanidin 3-glucoside equivalents; CA, citric acid equivalents; nd, not determined; FRAP, ferric reducing antioxidant power assay; VEAC, vitamin C equivalent antioxidant capacity; ∑ macrominerals, Mg, Ca, K, Na; ∑ trace elements, Fe, Zn, Se, Mn; ?, unknown.

and are therefore not specifically high, considering the recommended dietary allowance (RDA) of 75 mg/d. However, when expressed as total antioxidant capacity, encompassing also tocopherols, polyphenols, and other antioxidants as vitamin C equivalent units, apples contain up to 1140 mg/100 g, contributing significantly to antioxidant intake (Bouayed et al., 2011a).

Most notably, apples are reasonably rich in polyphenols and triterpenes, both up to ca. 100 mg/100 g (Table 37.1), and also contain around 12 mg/100 g phytosterols, all of which will be discussed in more detail in this chapter. As these phytochemicals are not essential, that is, their absence in the diet is not related to the development of a specific deficiency disease, they are not strictly classified as nutrients, though the misnomer "phytonutrients" is occasionally employed. Accordingly, no RDA or similar recommendation exists for phytochemical intake. However, as discussed in the following, their consumption has been related to the reduced risk of several chronic diseases. Historically, in animal trials, several of these phytochemicals have been earlier termed "antinutrients," due to their ability to reduce the bioavailability of several essential nutrients, notably divalent minerals, and in part of proteins and carbohydrates, limiting animal growth rates. These "antinutrients" include several polyphenols, especially tannins (Maniyan et al., 2015), due to their ability to complex digestion enzymes, limiting, for example, glucose uptake, and dietary fiber, chelating (together with polyphenols) several divalent minerals, making them unavailable for absorption (Bohn, 2014). In addition, apples, specifically apple skin, contain low amounts of phytic acid (ca. 90 mg/100 g dry mass (Maniyan et al., 2015)), which also has the tendency to complex divalent minerals, rendering them unavailable (Bohn et al., 2004). Nevertheless, compared to certain cereals or legumes rich in tannins (up to 10% of their dry mass (Berard et al., 2011)) and rich in phytic acid (up to 6% for some bran types such as wheat bran, (Reddy and Sathe, 2002)) apples' antinutritive content and their effects can be judged as low.

Not considering juices, while some apples end up in cakes or as puree, the majority are consumed in raw form. There is a certain controversy whether apples (and also other fruits) should be consumed peeled versus nonpeeled, that is, with or without skin, as emphasized by publications entitled "to peel or not to peel, that is the question" (Hassan and Williams, 2002; Kuhn, 2002). In fact, apple peel or skin, due to its waxy and therefore lipophilic consistency, and being in direct contact with the environment, has a tendency to accumulate certain pesticides at higher concentrations compared to apple flesh (Kovacova et al., 2014). On the other hand, due to their liphophilicity, phytosterols as well as triterpenes are almost entirely found in the peel (Rudell et al., 2011; Andre et al., 2012). In addition, polyphenol content is four (Henriquez et al., 2010) to 10 (Giomaro et al., 2014) times higher in the peel than in the flesh; peeling may remove as much as 25% of total apple phenolics (Kevers et al., 2011). This is in part due to the higher concentration of red-colored anthocyanins, which add (in addition to carotenoids) to apple pigmentation, and are situated almost entirely in the skin. Peel can also contain 15%−40% of total ascorbic acid (Lata and Tomala, 2007). Peeling would thus also entirely result in loss of provitamin A carotenoids, though concentrations are also relatively low in the peel, approximately 40 μg/100 g (Souci et al., 2000), compared to, for example, 10 mg/100 g or so in some leafy vegetables (Biehler et al., 2012). Dietary fiber content is also higher in the peel when expressed as per weight basis (Leontowicz et al., 2007), and peeling may remove as much as 50% fiber (USDA, 2015c). The best solution in this respect may be to opt for organically grown apples (see also Section 37.5.2) and to consume apples with the peel, in order to assure a higher intake of health beneficial constituents.

The most frequently consumed apple product is apple juice, with a consumption of approximately 8.3 L/year per capita in the United States (USDA, 2015b). Compared to whole apples, apple juice is lower in dietary fiber (<1 g) and polyphenol content, which is partly associated with the dietary fiber; and juices also contain less (unless added to counterbalance losses) ascorbic acid (Souci et al., 2000; Rothwell et al., 2013). Consequently, it may be assumed that nutritional and health benefits from juices may therefore be more limited, especially in sight of the negative effects that have been associated with the consumption of fructose-containing beverages (Stanhope, 2016). However, this also depends on the type of juice, with, for example, clear juice being lower in dietary fiber and polyphenols than nonfiltered cloudy apple juice.

37.3 Health benefits

37.3.1 *General aspects*

Due to their frequent consumption in many countries, apples and their constituents have been investigated in an array of studies with respect to their potential health benefits. In general, studies can be divided into epidemiological, that is, observational studies, intervention trials (with whole apples or apple constituents or extracts), studies on animals, and those rather focusing on mechanistic aspects, that is, laboratory (in vitro) investigations, often employing cell-culture models such as Caco-2 or other epithelial cells. The difficulty to prove health benefits of apples or apple constituents rests in the complex nature of our diet and food items, including apples, and associated confounding factors. For example, subjects regularly consuming apples may also consume other fruits and vegetables more often, or follow a generally healthier lifestyle. Pinpointing the relevant health beneficial constituents proves even more challenging, as apples are rich in many potentially health beneficial compounds, which often are present simultaneously, for instance, fiber and polyphenols. On the other hand, serving only individual, isolated compounds, may significantly alter important effects that the matrix or synergistically active compounds may have, plus potentially compromising optimal dosing and bioavailability of constituents (see Section 37.6).

37.3.2 Epidemiological evidence

Following large observational studies, many of which have been prospective, it is almost certain that the consumption of fruits and vegetables is positively associated with a reduced risk of developing various chronic diseases, and can reduce overall mortality, though typically three to five or even more portions per day (one portion being defined as 80−100 g) appear to be required to show significant health effects (Joshipura et al., 2001; Crowe et al., 2011).

Does apple consumption keep the doctor away? This colloquial proverb was tested in a cross-sectional study in >8700 non-institutionalized US adults by Davis et al. (2015). More precisely, daily apple eaters consuming at least 150 g apple (one)/d were compared to nonapple eaters, based on 24-h dietary recalls. Within the observation period (1−2 years), 39.0% of apple eaters avoided physician visits versus 33.9% of nonapple eaters ($P = .03$). When however adjusting for sociodemographic aspects and health-related confounders, this effect was no longer statistically significantly different. A marginal significant effect related to fewer prescriptions was however noticed in the apple consumers.

In a cross-sectional study targeting blood pressure (Oude Griep et al., 2013), consuming apples was positively associated with a small but significantly reduced diastolic blood pressure (0.4 mm Hg), though only in Asian subjects ($n =$ ca. 2000), for which in part dietary fiber, potassium, and magnesium were suggested to play a role, with potassium perhaps contributing to lower sodium intake or uptake. Similarly, in a prospective study by Larsson et al. (2013), including almost 75,000 participants from Sweden, the combined consumption of pears and apples was associated with a significantly reduced risk (11%) of stroke, and certain antioxidants (vitamin C, carotenoids, polyphenols) were mentioned that could have been implicated in health beneficial mechanisms.

Wedick et al. (2012) investigated the relation between apple consumption and the incidence of T2D diabetes in 70,359 women of the Nurses' Health Study. It was found that the intake of apples and pears was significantly correlated with lower risk of T2D (pooled HR: 0.77 from a comparison of ≥5 servings/week with <1 serving/month; 95% CI: 0.65, 0.83; P-trend < .001), possibly related to the influence of polyphenols on glucose uptake, on Glut4 expression, and influences on the nuclear receptor NF-κB, involved in proinflammatory cytokine formation. These results have also been corroborated by others (Muraki et al., 2013).

In another study summarizing case-control studies, colorectal cancer rates were lower in subjects consuming more apples (odds ratio (OR): 37%, (Jedrychowski and Maugeri, 2009)). In an additional multicenter case-control study with almost 600 patients, the consumption of apples was significantly associated with reduced risk of several types of cancer, including esophagus, larynx, oral cavity, colorectum, ovary, and prostate, with an OR as low as 0.58 (Gallus et al., 2005), and flavonoids and phenolic acids were mainly discussed as potential responsible agents.

It has to be noted that negative reports, especially related to apple juice consumption, have also been reported. In a cross-sectional study based on the US NHANES data by DeChristopher et al. (2016), intake of apple juice in 2−9-year-old children was associated with increased risk of developing asthma when contrasting >5 times a week versus <1/month consumption, even when adjusting for other beverages (OR 2.43). These negative effects were attributed to higher fructose consumption. In addition, excessive fruit juice consumption has been associated with negative effects on growth in children, possibly due to a reduced intake of other essential nutrients such as proteins (Smith and Lifshitz, 1994).

In summary, despite potential negative effects of excessive apple juice consumption, there is good evidence that whole (raw) apple consumption has health beneficial effects with respect to cardiovascular health, including T2D, and cancer prevention, though these studies cannot, due to their observational nature and the many confounding factors, prove causality, nor can they shed much light on which constituents may be responsible for the observed effects.

37.3.3 *Intervention trials with whole apples or apple juice*

Intervention trials can, if conducted in a well-controlled (e.g., randomized) fashion, establish a cause-and-effect relationship. However, they are more costly and time intensive per subject than epidemiological studies, and due to shorter observation time, hard endpoints (disease, mortality) are more difficult to include. Consequently, often softer, surrogate markers, have to be considered. Furthermore, as raw whole apple constituents are more difficult to measure analytically, and juice more convenient to consume, the majority of trials have been conducted with apple juices.

In a crossover study with 20 healthy subjects by Soriano-Maldonado et al. (2014), vitamin C-rich apple juice (60 mg/L vitamin C and 510 mg catechin equivalents/L) was contrasted with apple juice rich in polyphenols (22 mg/L vitamin C and 993 mg catechin equivalents/L). The vitamin C-rich juice was superior in reducing total-cholesterol as well as the HOMO-IR index, a marker of glucose handling, following 4 weeks of consumption (250 mL/d). ICAM-1 (intercellular adhesion molecule-1) and VCAM-1 (vascular cell adhesion molecule), markers of endothelial function, were also lowered more pronouncedly compared to the polyphenol rich juice group. Pointing perhaps in a similar direction, in a placebo controlled intervention trial, apple consumption (40 g dried apples/d) rich versus low in polyphenols (1.4 vs. 0.2 g/d) did not reduce plasma lipid levels or improve endothelial function during a 4-week period (Auclair et al., 2010), highlighting that polyphenols alone may not be the primary important compounds influencing health markers in apples.

In a 5 × 4 week crossover intervention trial with 34 healthy subjects, various apple sources (whole apple, apple pomace, cloudy apple juice, clear apple juice) were given (Ravn-Haren et al., 2013). While no effects were observed on HDL-C, TG, BP, hs-CRP (high sensitivity C-reactive protein), and markers of glucose metabolism (insulin, IGF-1, IGF-BP3), cloudy apple juice and whole apples reduced LDL-C, suggesting that the effect may stem from dietary fiber. Consumption of cloudy apply juice (750 mL) for 4 weeks (Barth et al., 2012) also significantly reduced the percentage of body fat during this randomized placebo controlled trial in obese (but nondiabetic) subjects.

In a study on postmenopausal women ($n = 100$), consumption of dried apple versus dried plums (75/d during 12 months) was compared. Though no differences were found between the groups with respect to blood lipids, both interventions significantly improved total-C and LDL-C, as well as serum CRP and lipid hydroperoxide levels compared to respective baseline values (Chai et al., 2012), and dietary fiber was speculated to play the major role in explaining these observations.

In conclusion, intervention trials with whole apples or apple juices have shown several health benefits as measured by markers of CVD such as oxidative stress, inflammation, and blood lipids. Based on these results, it may by hypothesized that in addition to polyphenols and vitamin C, also other constituents such as dietary fiber contribute synergistically to the observed health effects. It also appears that fructose, when consumed in apples or apple juices, does not appear to have negative consequences.

37.3.4 *Intervention trials employing animals*

Being somewhat less influenced by ethical restrictions, a number of more invasive, complex and well-controlled studies have been conducted on animals, many of which have focused on neuroprotective aspects and on emphasizing positive effects on colonic microflora.

In a study by Viggiano et al. (2006), rats fed for 10 weeks with a fresh apple-supplemented diet presented significantly higher antioxidant status (superoxide dismutase (SOD)) and less anxiety compared to a control group. Similar results were obtained following apple juice consumption by mice in a study by Rogers et al. (2004). Animals were prone to develop Alzheimers' disease, and received 0.1% or 0.5% apple juice in drinking water ad libitum for 10 weeks. It was found that apple juice consumption improved TBARs (thiobarbituric acid reactive substances) in brain, and improved performances in Y and T maze tests, suggesting neuroprotective effects. The interrelation between polyphenol consumption and neuroprotection through reduced inflammation and oxidative stress, possibly via altering gene expression, had been emphasized earlier by other researchers (Reglodi et al., 2017). Such effects have even been related to anxiety, which deserves more studies. For instance, rosmarinic acid is a polyphenol in the apple skin, which was shown to reduce anxiety in rats when given at 2–4 mg/kg bw. (Pereira et al., 2005).

As both polyphenols and dietary fiber act via the microbiota, influencing lipid metabolism and bile metabolism, this interrelation has recently been highlighted (Koutsos et al., 2015). Colonic effects regarding gene expression were also shown in a study on rats receiving apple juice for 10 days, showing upregulation of antioxidant ARE-dependent genes in the distal colon, such as GPX2, GSR, CAT, Nrf2, as well as GPX-1 and NQO in the liver

(Soyalan et al., 2011). The superior effect of cloudy apple juice that is richer also in pectins compared to clear apple juice has been shown in a rat study, reducing hyperproliferation and aberrant crypt formation (Barth et al., 2005).

37.4 Biocative phytochemicals—in vitro and cellular trials

37.4.1 Overview

As in apples, the more abundant bioactive compounds include dietary fiber, polyphenols, triterpenes, (Boyer and Liu, 2004; Hyson, 2011), and, to a lesser extent, plant sterols. These plant metabolites will be discussed in the following, though polyphenols have received the most attention. Ascorbic acid contributes to only approx. 0.4% of total antioxidant capacity in apples (Gallus et al., 2005) and will therefore not be further discussed here.

As apples are also rich in sugars, and especially fructose has been shown to potentially have lipidogenic effects, especially when consumed without matrix and in higher concentrations, such as in high-fructose corn syrup (HFCS), it has been speculated whether apples lower in sugar, especially fructose, would be more health beneficial. However, due to their fiber-containing matrix, low glycemic index (GI, around 28−44 (http://www.glycemicindex.com)), even for apple juice (39−44), apples do possibly not pose much burden on either insulin secretion or lipid formation in the liver, especially as the fructose content compared to total sugar content is likewise low, possibly not posing any detrimental health effects (Memon and Kumar, 2013).

37.4.2 Dietary fiber

Apples contain up to ca. 2.5 g/100 g of dietary fiber, the majority being water-insoluble cellulose, lignins, or insoluble hemicelluloses (Fig. 37.2), with the remainder being partly water-soluble hemicelluloses and pectins. While cellulose is of rather crystalline form, very stable during gastrointestinal digestion and poorly fermented (20%−80%) by colonic microbiota, hemicelluloses are partly and pectin fermentable to a large extent, about 60%−80% and almost 100%, respectively, with lignin almost being non-fermentable (FAO, 2015). As in most countries, dietary fiber consumption is below the recommended 25/38 g/d (female/male, RDA), the consumption of apples can significantly contribute to fiber intake, as actual fiber intake is only around 15 g/d for many countries.

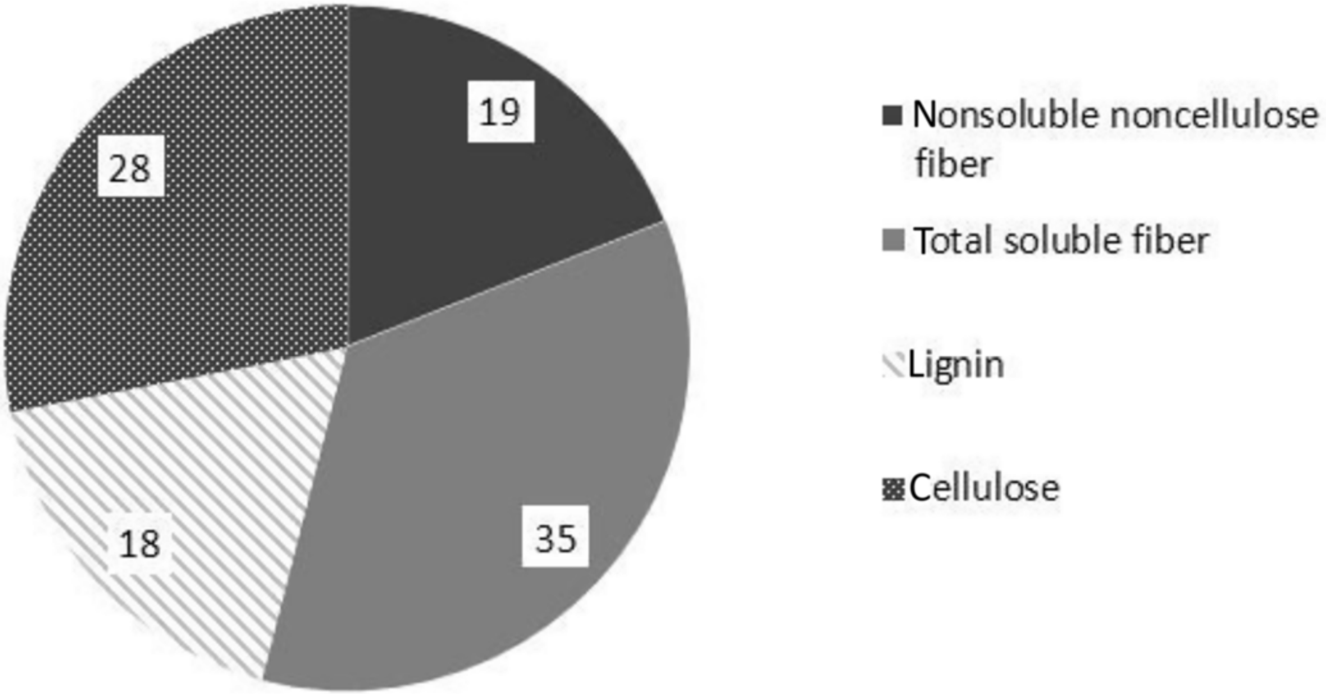

FIGURE 37.2 Dietary fiber composition of apples (according to Anderson and Bridges, 1988).

The soluble and fermentable fibers in particular have raised much interest, due to their potential to produce short-chain fatty acids (SCFA), such as butyrate or propionate, which have been shown to possess antiinflammatory properties. In addition, some types of fibers may act as prebitotics, influencing gut microbiota composition, possibly fostering a more healthy microflora. Though not unanimously accepted, some types of pectins could be counted as prebiotics (Yoo et al., 2012). Furthermore, due to their swelling and gel-forming properties in the gut, pectins may add to satiety (Logan et al., 2015), limiting calorie intake. For example, 12 T2D subjects consuming 20 g apple pectin per day for 4 weeks showed significantly slower gastric emptying and improved glucose tolerance following an oral loading test (Schwartz et al., 1988). This property has resulted in novel ideas toward the production of functional foods. A health claim for pectin and reduced postprandial response has been granted by the EFSA (ID 786).

Finally, dietary fiber decreases gastrointestinal total passage time, increasing the rate of defecation, possibly, in addition to the increased colonic bulk, reducing the likelihood of negative interactions between the gut epithelium and potential toxic compounds, decreasing cancer incidence (Bradbury et al., 2014). Going into further detail here would be beyond the scope of this article, but health benefits of pectins have been reviewed elsewhere (Babbar et al., 2016).

37.4.3 Polyphenols

Polyphenols, produced in plants via the shikimate or the acetate pathway, with several thousand compounds existing (Bohn, 2014), comprise quite a diverse group of different compounds. Polyphenols possess at least one phenolic group, though exact definitions vary. A major differentiation can be made between flavonoids and nonflavonoids. Table 37.3 lists major polyphenols occurring in apples, with the main classes being flavonoids and

TABLE 37.3 Major polyphenols in raw (unpeeled) apples.

Polyphenol	Polyphenol class	Concentration (mg/100 g)	Reference
	Phenolic acids		
Gentisic acid	Hydrobenzoic acids	0.22	Rothwell et al. (2013)
Syringic acid		0.90	Rothwell et al. (2013)
Chlorogenic acid	Hydroxycinnamic acids	12–16	Bouayed et al. (2012)
	Cryptochlorogenic acid	<0.1	Bouayed et al. (2012)
	Caffeic acid	<0.1–0.3	Bouayed et al. (2012), Rothwell et al. (2013)
	p-Coumaric acid	0.3–1.14	Rothwell et al. (2013), Bouayed et al. (2012)
	Flavonoids		
Cyanindin-3-*O*-galactoside	Anthocyanins	0.81	Rothwell et al. (2013)
Quercetin-3-*O*-galactoside	Flavonoles	2.6–6.6	Rothwell et al. (2013), Bouayed et al. (2012)
Rutin		1.2	Bouayed et al. (2012)
Quercetin-3-*O*-glucoside		0.3–0.9	Bouayed et al. (2012)
Quercetin-3-*O*-rhamnoside		1.3–3.7	Rothwell et al. (2013), Bouayed et al. (2012)
Quercetin 3-*O*-arabinoside		1.4	Bouayed et al. (2012)
Quercetin 3-*O*-xyloside		0.8	Rothwell et al. (2013)
Catechin	Flavan-3-ols	1.22	Rothwell et al. (2013)
	Epicatechin	4.8–8.4	Bouayed et al. (2012), Rothwell et al. (2013)
	Procyanidin B2	5–15	Bouayed et al. (2012), Rothwell et al. (2013)
Phloridzin	Dihydrochalcones	2.2–2.8	Bouayed et al. (2012)
	Phloretin 2′-*O*-xylosyl-glucoside	2.58	Rothwell et al. (2013)

phenolic acids. As many polyphenols can act as antioxidants (Scalbert et al., 2005; Bouayed and Bohn, 2010), many health effects have been attributed to these secondary plant compounds.

As can be seen in Fig. 37.3, total phenolics in apples correlate well with antioxidant measurements such as FRAP and ABTS (Bouayed et al., 2011a), highlighting that polyphenols can act as radical scavengers, at least in vitro. However, this scenario cannot be simply transferred to the situation in vivo. Polyphenols are heavily metabolized during digestion, most pronouncedly in the colon (Bohn, 2014; Bohn et al., 2015), but also in the epithelium and in tissues, due to phase II enzyme activities. Furthermore, they are to a large extent either re-excreted rapidly into the gut via efflux-transporters (P-gp, BCRP, etc.) or further metabolized, or rapidly excreted into urine following their absorption, resulting overall in a rather low bioavailability for many polyphenols (Bohn, 2014). It also has to be considered that in the human body, many other compounds such as other exogenous antioxidants (vitamins E and C), endogenous compounds (uric acid, albumin), as well as antioxidant enzymes (SOD, GPx) play a main role in antioxidant defense mechanisms, and polyphenols consequently do contribute very little to direct antioxidant effects. Also a role as potential prebiotics has been discussed (Kaulmann and Bohn, 2016). However, it appears that their major role could rest in altering gene expression, for example, boosting the body's own antioxidant defense mechanisms (Joven et al., 2014). For example, many cellular models have suggested that polyphenols are able to reduce the expression of NF-κB (Bouayed and Bohn, 2010), responsible for the expression of further downstream proinflammatory cytokines such as IL-1ß, TNF-α, and IL-6. In addition, it has been demonstrated that polyphenols can enhance the translocation of Nrf-2 to the nucleus, boosting the bodies' production of antioxidant defense enzymes, such as SOD and heme-oxygenase-1 (OH-1) (Scapagnini et al., 2011; Stepanic et al., 2015).

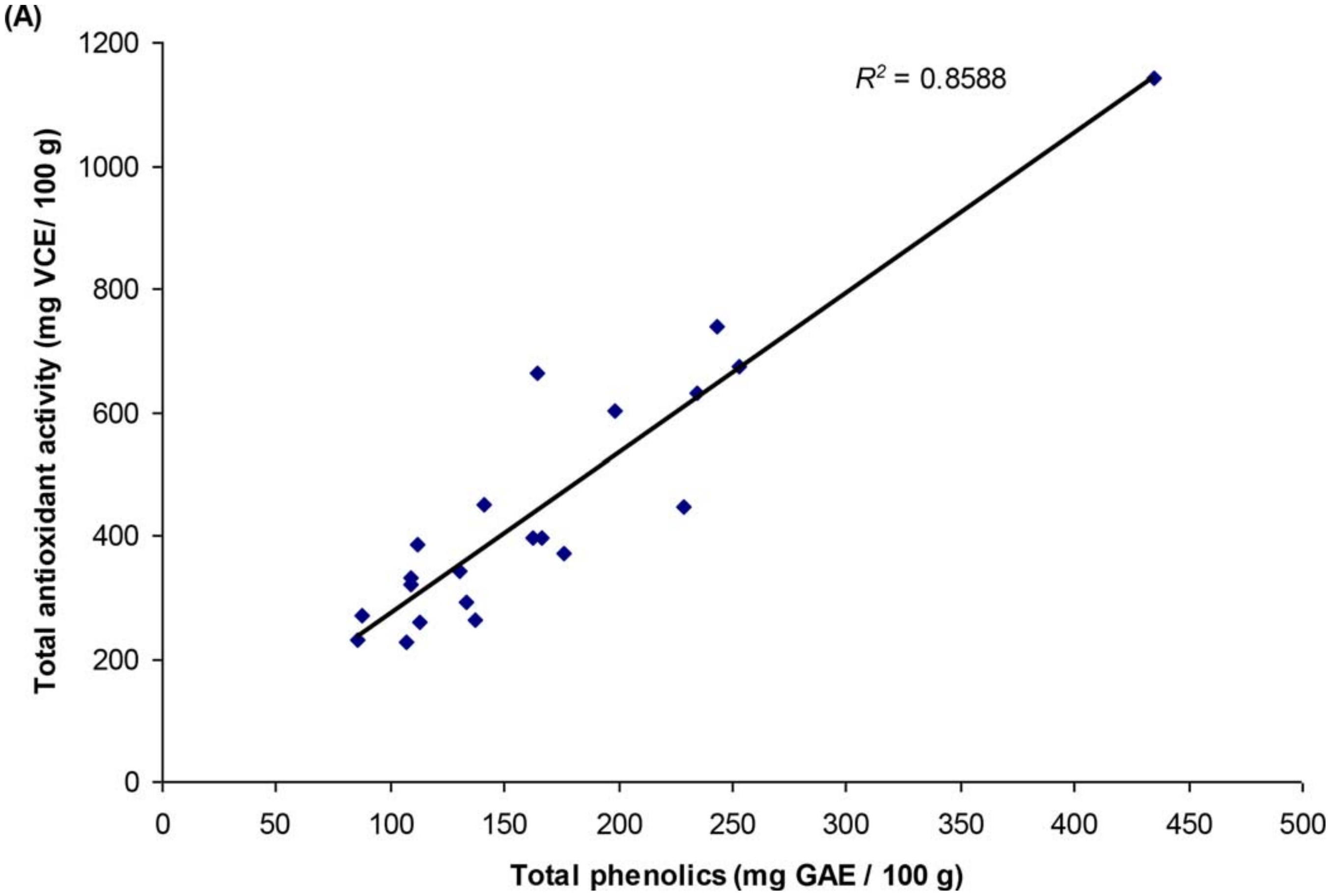

FIGURE 37.3 Correlation between total polyphenols and antioxidant capacity in 22 apple varieties (Jonagold, Pinova, Cox Orange, Pilot, Rubinette, Winter-Rambour, Jonagored, Golden Delicious–Weinberg, Jonaprinz, Mutsu, Fuji, Golden Delicious, Elstar, Braeburn, Boskoop, Grauapfel, Roter Trierer Weinapfel, Graham Apfel, Florina, Eifeler Rambour, Topaz, Goldparmäne) from Luxembourg obtained in 2010. VCE, vitamin C antioxidant equivalents; GAE, gallic acid antioxidant equivalents (Bouayed and Bohn, unpublished results).

In line with the hypothesis of reinforcing the bodies' own defense mechanisms, in a human trial by Godycki-Cwirko et al. (2010) with 12 healthy subjects consuming 1 L of clear apple juice, it was found that the increase in plasma antioxidant capacity did not occur due to increased polyphenol levels, but due to fructose-induced uric acid concentration, thus pointing out the limited effects of polyphenols on the body's direct antioxidant capacity. Earlier trials on animals have suggested similar effects.

Decreased blood lipid levels were also found in an intervention trial with apple polyphenol extracts, which were given for 12 weeks (600 mg/d) to 71 subjects (Nagasako-Akazome et al., 2007), decreasing total-C and LDL-C, and also improving visceral fat and adiponectin levels. It appeared plausible that polyphenols did bind to cholesterol and/or bile acids, increasing fecal losses; hampering digestion enzymes was also discussed as a possible mechanism. Similar hypotriglyceridemic effects of apple polyphenols (extracts) were also found in a mice study, upregulating lipoprotein lipase (Yao et al., 2014). In a rat study by Serra et al. (2012), consuming three different apple cultivars significantly reduced oxLDL (and decreased serum LDL-C, total-C and triglycerides (TG)), especially in varieties rich in the polyphenols catechin, epicatechin, procyanidin B1, but also beta-carotene.

Another effect of polyphenols seems to be their potential to complex digestion enzymes, as well as transporters responsible for sugar, that is, glucose uptake. Schulze et al. (2014) demonstrated that apple polyphenols reduced SGLT-1 (sodium-glucose linked transporter 1) glucose absorption from the gut in rats and in humans. Similarly, an unripe apple recipe rich in the polyphenol phlorizin (also containing pectins) improved glucose handling during an oral glucose loading test in six healthy volunteers (Makarova et al., 2015), possibly further enhancing the already glucose-lowering effect of dietary fiber.

In conclusion, it is likely that apple polyphenols may hamper digestion enzymes, limiting glucose and lipid uptake, which consequently could contribute to improved T2D and blood lipid markers. In addition, polyphenols may act on gene expression, fostering anti-inflammatory processes and strengthening the body's own antioxidant system.

37.4.4 *Triterpenes*

Triterpenes or triterpenoids (if further functional groups are present), as the name implies, can be thought of consisting of three terpene or six isoprene units. Apples, especially apple peel, contains comparatively high amounts of triterpenoids, specifically in so-called russeted varieties with a slightly rough, greenish-brownish surface, while apples with a waxy surface are considered to rank lower in triterpenoids. The predominant triterpenoids constitute derivatives of ursolic acid, oleanolic acid, and betulinic acid (Table 37.4).

Apple triterpenoids have shown anticancer properties in in vitro cell culture trials, exhibiting antiproliferative effects on various cells (He and Liu, 2007). In addition, they have been found to act as anti-inflammatory compounds, reducing the expression levels of proinflammatory genes (TNF-α, IL-8, IP-10) in cellular trials (Mueller et al., 2013).

Though no human trials have been reported with these interesting compounds so far, a limited number of animal trials have meanwhile been performed. In a mouse model, apple triterpenoids at 50 mg/kg/d inhibited the

TABLE 37.4 Main apple triterpenoids, concentrations and triterpenoid-rich cultivars.

Compounds	Concentrations (mg/100 g fw[a])	Varieties	References
Oleanolic acid	c. 5–85	Merton Russet-Niagara	Jager et al. (2009), Andre et al. (2012)
Ursolic acid	c. 5–350	Merton Russet-Niagara	Jager et al. (2009), Andre et al. (2012)
Betulinic acid	c. 1.5–21	Rae Ime-L-Grauapfel	Jager et al. (2009), Andre et al. (2012)
2α-hydroxyursolic acid, 2α-hydroxy-3ß-olean-12-en-28-oic acid, 3ß-trans-p-coumaroyloxy-2α-hydroxyolean-12-en-28-oic acid, 2α-hydroxyursolic acid, 3ß-trans-p-coumaroyloxy-2α-hydroxyolean-12-en-28-oic acid	not quantified	Red Delicious	He and Liu (2007)

[a] *Fw, fresh-weight base in skin.*

growth of a mammary tumor in a nude mouse xenograft model (Qiao et al., 2015), enhancing apoptosis, with upregulation on mitochondrial Bax/Bcl-2, regulated by SIRT1 and p53. In a mouse rheumatic model of arthritis, ursolic acid at 50 mg/kg reduced inflammation, lowering IL-1ß and TNF-α (Padua et al., 2014).

Though no human trials to date have been published, the use of triterpenoids for treating cancer and CVD has been advertised (Han and Bakovic, 2015). A present limitation for application may rest in their limited oral bioavailability, as, due to their apolarity, micellarization is required prior to their epithelial uptake, similar as for carotenoids and lipid-soluble vitamins. Consequently, bioavailability of these lipid-soluble constituents from pure apple matrix can be assumed to be rather low.

37.4.5 *Phytosterols*

Phytosterols are a group of molecules including plant sterols and plant stanols, with structural similarity to cholesterol, belonging to the steroids, characterized by the 5-ring system and various side-chains. Apples contain beta-sitosterol and campesterol in particular (Table 37.2). Phytosterols have been advertised for their health potential, due to their possible cholesterol-lowering effects. They also have received an EFSA health claim with respect to helping to reduce serum cholesterol levels, given that at least 0.8 g of the compound(s) are consumed per day. For consuming apples, this would imply consuming more than 1 kg (Table 37.2), as apples contain much less phytosterols, compared to, for example, olive oil or wheat bran, containing up to 150 mg/100 g (Souci et al., 2000). Thus it is unlikely that phytosterols on their own contribute significantly to any observed health benefits, but may rather act in conjunction with dietary fiber and polyphenols. The potential mechanisms for lowering cholesterol are still under debate, but may include (1) competition with cholesterol for absorption, as both compounds, due to their lipophilicity, require micellarization prior to epithelial uptake, that is, emulsification (Bohn et al., 2007); or (2) competition for cylcoenzyme A cholesterol acyltransferase-2 (ACAT-2), required for intracellular cholesterol reesterification. In addition, phytosterols also appear to lower TG, via a yet to be confirmed mechanism (Plat et al., 2015), in addition to other potential benefits such as improving immune cell functioning.

37.5 Factors influencing bioactive content

It has to be considered that the individual macronutrient, micronutrient, and also phytochemical content of apples can depend on many factors, including the genetic background, that is, variety, soil, and climate, notably temperature and precipitation, and also storage of the apple fruit. These factors will be briefly discussed in the following. As sugars and polyphenols constitute the most predominant macro- and microconstituents, respectively, most studies have focussed on these two classes.

37.5.1 *Genotype variation*

The variability in polyphenol composition in 93 apples genotypes (80 *M. domestica* and 13 *M. sieversii*) grown at one site in New Zealand was investigated by Volz and McGhie (2011). While the genotype could explain 46%−97% of the variation of total polyphenols and individual groups in the flesh and skin of apples, the influence of year and genotype × year were rather small, except for some peel flavonols in *M. domestica*, highlighting the predominant importance of genotype (Table 37.5). This is to some extent in line with earlier reports, stating that seasonal influences are more important for polyphenol constituents of the peel, while the genotype rather determines flesh and overall polyphenol profile (Lata and Tomala, 2007). This was also corroborated in another study of antioxidant capacity and total flavonoids, with a very limited influence of year in three out of four varieties (van der Sluis et al., 2001).

Differences in additional bioactive constituents, including total ascorbate, glutathione, and phenolics were investigated in 56 apple cultivars harvested over 2 years (Lata et al., 2005), likewise emphasizing the greater importance of genotype over year, though this depended also on the cultivar studied, that is, some cultivars were described as more stable than others. In earlier trials, up to 5.4 times variations in total phenolics and 3.6 times in ascorbate were reported (reviewed by Lata et al., 2005).

Several reports have mentioned that a number of newly developed cultivars tended to be poorer in certain polyphenols (less astringency taste, see Table 37.1) and in triterpenes (more smooth surface) than some of the old

TABLE 37.5 Influence of genetic and environmental factors on apple constituents.

Factor	Constituent studied	Variation	Reference
Genotype	Polyphenols—total in flesh (mg/100 g) FW[b]	57.4–127.4 (>100%) of 13 *M. domestica*	Volz and McGhie (2011)
	Polyphenols—total in peel (μg/cm^2) FW[b]	224–871 (>100%) of 13 *M. domestica*	Volz and McGhie (2011)
	Phenolics—total (mg/100 g)[a] FW	86–434 (>100%) in 22 cultivars	Bouayed and Bohn (unpublished)
	Phenolics—total (mg/fruit)[a] FW	36–149 (>100%) in 19 cultivars	Lata and Tomala (2007)
	Phenolics—total (mg/100 g) FW in flesh[b]	3–788 (>100%) in 109 cultivars	Andre et al. (2012)
	Total sugars (g/100 g)	10.2–16.6 (>50%) in 22 cultivars	Bouayed and Bohn, (unpublished)
	Ascorbic acid (mg/fruit)	8.75–50.2 in 19 cultivars	Lata and Tomala (2007)
	Ascorbic acid (mg/100 g) FW in skin and flesh, respectively	1.6–11.3 and 0.4–3.1 in 109 cultivars	Andre et al. (2012)
	Triterpenoids (mg/100 g FW)	4.5–352 for ursolic acid in skin	Andre et al. (2012)
Year	Polyphenols—total in flesh (mg/100 g) FW[b]	Below 20% between 3 years	Volz and McGhie (2011)
	Phenolics—total (mg/fruit)[a]	Up to 300% in 19 cultivars between 2 years	Lata and Tomala (2007)
	Ascorbic acid (mg/fruit)	Up to100% in 19 cultivars between 2 years	Lata and Tomala (2007)
Production	Phenolics—total (mg/100 g)[b] FW	On average c. 10% lower from conventional production (GD) between 3 years, large variations	Stracke et al. (2009)
Climate change	Acidity,	−0.16 g/L,	Sugiura et al. (2013)
	Soluble content	−0.21° Brix	
	Firmness	−0.18 kg for firmness	
	Watercore	−0.28 for watercore rating/decade due to climate change, globally	

[a] *As mg gallic acid equivalents.*
[b] *Sum of individual polyphenols; GD, golden delicious.*
FW, fresh weight.

varieties (Andre et al., 2012; Francini and Sebastiani, 2013), in order to increase visual and sensory attractiveness. However, care should be taken, as not all studies have confirmed this finding (Wojdylo et al., 2008), possibly due to large differences with respect to variety and provenience.

37.5.2 Environmental variation and agronomic conditions

Climate, notably temperature and precipitation, have been reported to have a strong impact on general plant growth conditions, however, our understanding of how these factors influence bioactive constituent concentrations is quite limited.

As climate change may result in significant increases of local temperature in some areas, the effect of higher temperature on fruit growth has been studied. Temperatures above 29°C have been shown to result in reduced cell production and cell expansion of apple fruitlets (Flaishman et al., 2015). It has been reported that already the past decades of global warming have resulted in certain trends in apple fruits, decreasing acidity levels and firmness in addition to watercore development (a disorder characterized by filling of intercellular spaces with water), while soluble solids (sugars) appeared to have increased (Sugiura et al., 2013). The average estimated changes per decade were −0.16 g/L for acid concentration, −0.21° Brix for soluble-solids concentration, −0.18 kg for firmness, and −0.28 for watercore rating. Higher temperature (5−10°C) has also been reported to reduce anthocyanin content to half in apple fruit, reducing in part polyphenol content (Lin-Wang et al., 2011). However, in studies on other plants, generally both low temperature (cold stress) as well as warmer temperatures together with a more dry climate (heat/drought stress) may increase polyphenol content (Rivero et al., 2001). It also can be expected that climate change will alter pest levels that infest apple trees.

Some information is available on production techniques. In a study by Stracke et al. (2009), the influence of organically grown versus conventionally grown apples was compared to the effect of season regarding polyphenol content and antioxidant capacity. Year to year variations of polyphenol content varied by up to 20%, which was more significant than differences according to production, which was up to 15% higher in some cases, but for some years was similar.

Since organically grown products are typically advertised as being richer also in polyphenols, a short-term randomized crossover study with six healthy subjects (consuming 1 kg of apples) and a long-term (4-week) intervention trial with 43 subjects (consuming 0.5 kg apple/d) was performed to compare organically grown versus conventionally grown apples (Stracke et al., 2010) with comparable polyphenol content. No differences in major urine or plasma polyphenols were found in the first study, while no increases in polyphenols compared to baseline were found in the second trial, suggesting that also from this perspective, organically grown apples do not provide additional benefits.

Soil temperature is known to influence nitrogen uptake by the tree and amino acid concentration (Dong et al., 2001), and may therefore have pronounced influences on additional pathways, however, the effect on polpyhenols, triterpenoids, or other bioactives is generally unknown.

37.5.3 Storage

Also time of storage can have influences—typically resulting in lower vitamin C content with time, with losses as high as 75% after 1 week of domestic storage (Kevers et al., 2011), though having apparently a more limited effect on certain polyphenols such as flavonoids, not negatively effecting total antioxidant capacity (van der Sluis et al., 2001). Nevertheless, postharvest storage effects on phenolic constituents seem to depend on the variety and storage time, with effects being hard to predict. For example, in one study a drastically decreased polyphenol content in the skin (50%) and the flesh (20%) in one of four studied apple varieties (Hilwell), was found, but not in the others (Golden clone B, Fuji clone Kiku8, and Braeburn), following 1°C storage for 1 month (Carbone et al., 2011). Slight reductions were also encountered in other studies, while short-time storage, even at higher temperature (20°C) did not appear to cause any decline in other trials, even slight increases were encountered (Francini and Sebastiani, 2013). In contrast, in a study by Rossle et al. (2010) on 10 cultivars, total phenolic content following storage at 2−4°C, even for 5 days, significantly reduced their levels in all cultivars (up to 15% for some polyphenol groups). It also appears that changes in the flesh are somewhat less pronounced during storage than in the peel (Veberic et al., 2010).

Sugar content appears to be reasonably stable over storage time, as shown over 21 days at room temperature (Veberic et al., 2010), though sucrose was transformed to some extent to fructose and glucose. Regarding fiber, storage had likewise no effect on total or soluble fiber, while lignins appeared to increase somewhat with storage time (12 months commercial storage time, (Marlett and Marlett, 2000)).

Taken together, it can be summarized that the influence of conditions on apple bioactive constituents, mostly measured as polyphenols, seems to follow the order genetic makeup > climate > production technique. Due to further expected climate changes, apples likely will contain more sugar, and be less acidic in the future. With respect to storage, only vitamin C loss truly appears to play a major role.

37.6 Bioavailability of apple bioactive constitutents

Given the importance of apple secondary plant compounds, especially of the more abundant polyphenols and triterpenoids, it should also be discussed whether they are easily released from the matrix upon ingestion, and can be used by the human body; in other words, to scrutinize their bioavailability, that is, the fraction of a compound that can be taken up and used for physiological functions and/or storage (Fig. 37.4).

Though polyphenols are generally rather water soluble, they have to be first released, that is, become bioaccessible, before they could be absorbed via the intestinal epithelium. Bouayed et al. (2011b) have shown in four

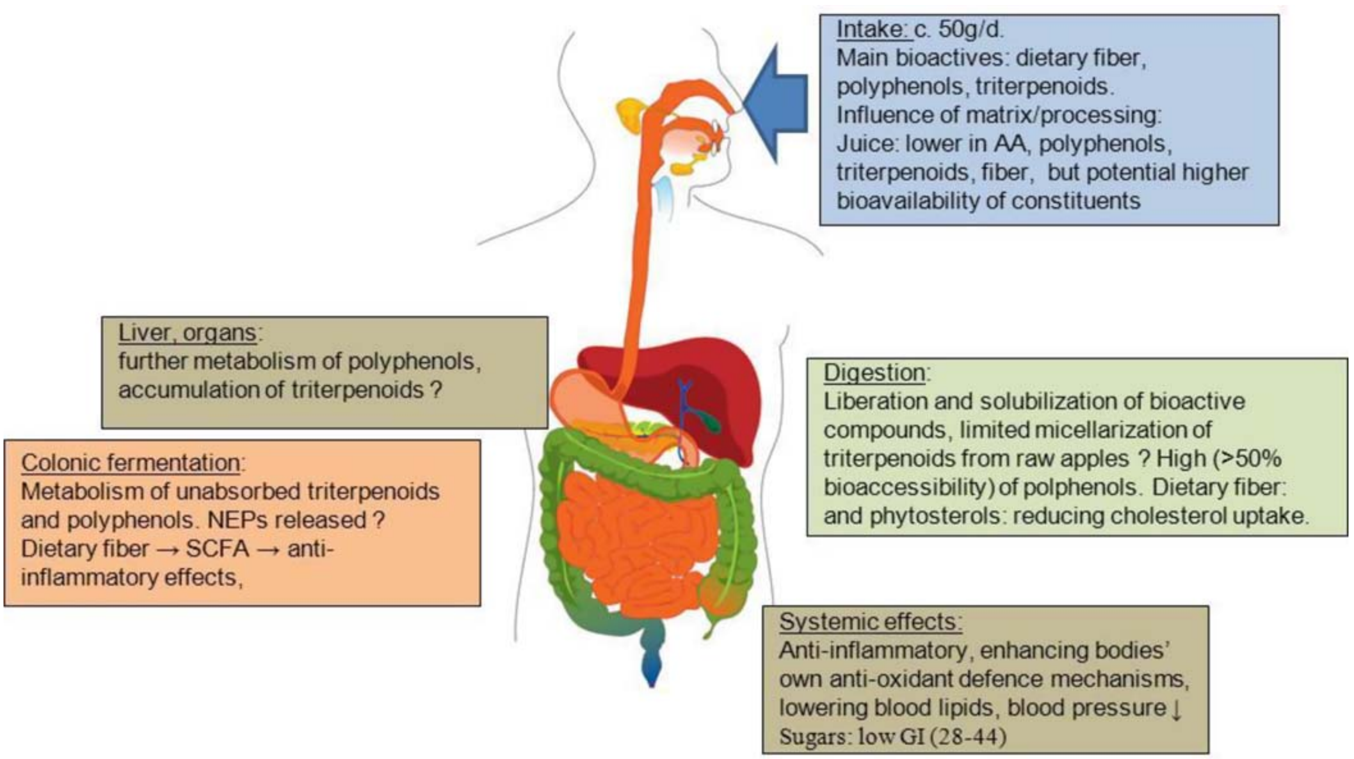

FIGURE 37.4 Summary of potential health beneficial compounds in apple fruits and their method of action. AA, ascorbic acid; GI, glycemic index; NEPs, nonextractable polyphenols; SCFA, short-chain fatty acids.

apple varieties, that the recovery of phenolics/antioxidant capacity (ABTS) is approximately 65/80%, 75/100%, and 55/55% of the native values in the gastric, small intestinal stage of digestion, and in the dialyzable fraction, respectively, emphasizing that in general, apple polyphenols are reasonably well released from the matrix and are potentially available for absorption. It has however been also stated that certain polyphenols, especially phenolic acids, are strongly bound to the matrix (to hemicellulose) and are not easily extracted, that is, the nonextractable polyphenol (NEP) fraction. This constitutes so far a much understudied domain. For example, NEP has been shown to be 2−4 times higher (depending on the methods of extraction chosen) than the extractable fraction (Tow et al., 2011), being in line with earlier findings (Arranz et al., 2009). Whether or not this fraction is partly released during digestion, for example, in the colon, following fermentation, is unknown.

Surely, the apple matrix appears to have some negative influence on certain polyphenol availability. In a study by Hollands et al. (2013), epicatechin absorption (as measured via plasma levels) was lower from apple puree compared to an extract (in beverage form), containing similar amounts of this flavan-3-ol, 59% versus 44%, possibly due to negative interactions with dietary fiber. Epicatechin was shown almost to be entirely degraded in an in vitro trial of four apple cultivars, following gastric and small intestinal digestion, and chlorogenic acid, a major polyphenol constituent, was reduced by 40%−70%, depending on variety (Bouayed et al., 2012). This compound was in part transformed into crypto- and neochlorogenic acid, and likely hydrolyzed to caffeic acid and quinic acids. Thus the main human-related transformations may include cleavage of certain glucosides due to acidic pH in the stomach and beta-glucosidase activity, possibly ester-cleavage, and further phase I/II metabolism in the enterocytes and other tissues such as the liver (methylation, glucuroniation etc. (Bohn, 2014; Bohn et al., 2015)). Furthermore, colonic changes include further metabolism (deglucuronidiation, ring fission, etc.), breakdown into smaller fragments, many of which may also have health beneficial effects. However, the matrix may also have positive effects. The sugar content of the apple may further foster bioavailability of certain phenolics, due to a potential uptake via SGLT-1 (Bohn, 2014).

Phytosterols and triterpenoids, as opposed to most polyphenols, are poorly soluble in water, and therefore require micellarization prior to intestinal uptake in order to be bioavailable. This emulsification is improved in general for lipophilic constitutes if a certain amount of fat (a few g) is codigested with the respective compounds, as shown, for example, for apolar polyphenols such as curcumine, lipid-soluble vitamins, or carotenoids (Bohn, 2008). For example, the bioavailability of α-tocopherol in humans was assessed after the consumption of d6-α-tocopherol spiked apples. When these were consumed together with a breakfast containing no fat, 10% of the 22 mg d6-α-tocopherol was detected in the plasma of the subjects. Increasing the breakfast fat content to 6% and 21%, 20% and 33% of the d6-α-tocopherol was detected, respectively (Bruno et al., 2006). As apples contain only very low amounts of lipids, and apple triterpenoids are situated to a large extent in the waxy skin of apples which cannot be easily broken down during digestion, it can be speculated that triterpenoids from raw apples should be poorly available, compared to, for example, cloudy apple juice or puree, where processing and heat treatment has already macerated cell walls, or to products containing certain amounts of lipids, such as apple cakes, especially when consumed with cream. Nevertheless, in a study with mice it was shown that triterpenes (0.5% mixed in a regular diet), given in pure form, were reasonably well absorbed, with limited metabolism (Yin et al., 2012), and tended to accumulate over time, especially in the liver. In a study with human subjects, oleanolic acid was likewise found to be absorbable, and plasma peaks were not reached within 4 h postadministration (Kanellos et al., 2013), similar as for other liposoluble compounds. As triterpenoids are more polar than carotenoids, their bioaccesibility may be superior. Efforts to enhance triterpene bioavailability via encapsulation techniques are under way (Soica et al., 2014).

37.7 Concluding remarks and future trends

Apples are among the most frequently consumed fruits, available in most countries all over the world. Many apple constituents have been related to health beneficial effects, especially dietary fiber, polyphenols, phytosterols, but also triterpinoids. Plausible mechanisms of action are summarized in Fig. 37.4, and it can be assumed that the additive or synergistic actions of various ingredients, rather than a single component, contribute to the related health benefits. Contradictory to earlier assumptions, indirect effects such as influences on gene expression, rather than, for example, direct antioxidant effects, are likely to play important roles, in addition to potential influences on the gut flora, a still poorly comprehended area. Some concerns for the future may be climate change, which is potentially associated with more sugar-rich apple varieties, and the breeding of cultivars for market appearance, rather than for healthy constituents.

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