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Review

The biodiversity of different traits of pomegranate fruit peels from a broad collection of diverse cultivars

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ABSTRACT

Since ancient times, pomegranate (*Punica granatum*) has been known to have compounds that contribute to human health. Metabolite analysis strongly suggested that unique metabolites belonging to hydrolysable tannins (HTs) and anthocyanins, contributed to these health-promoting activities of pomegranate. The peels of the fruit, which play a significant role in attracting consumers to purchase the fruit, contain high levels of HTs, which usually extracted into the pomegranate juice (PJ). This review focuses on studies performed on the peels of pomegranate fruits by analyzing a broad, bio-diverse pomegranate collection comprised of different cultivars from different countries. The review describes the changes in total phenolics content (TPC), antioxidants activity, color, taste parameters, anti-proliferative and anti-androgenic activities of the different pomegranate cultivars, as well as the relationships between TPC and peel quality during prolonged storage periods. The study shows that both genetic and environmental conditions contribute to the different desired traits.

1. Introduction

The pomegranate tree (*Punica granatum* L.), which is said to have flourished in the Garden of Eden, has been employed extensively in folk medicine remedies of Mediterranean and Asian cultures (Langley, 2000). The traditional importance of pomegranate as a medicinal plant is now backed by data obtained by modern science (Langley, 2000), showing among others, the medicinal potential embedded in the arsenal of secondary metabolites produced in pomegranate. Most studies focused on the fruit and pomegranate juice (PJ), showing that PJ is rich in polyphenols. As found in other polyphenols-rich fruits, pomegranates have been shown to have health benefits relating to their antioxidant and anti-inflammatory properties (Danesi and Ferguson, 2017). Indeed, PJ health bioactive compounds exhibit the ability to treat cancer (Panth et al., 2017), diabetes, and atherosclerosis (Aviram and Rosenblat, 2012; Sahebkar et al., 2017; Vlachojannis et al., 2015). Moreover, studies have highlighted the positive effects of PJ and extract consumption on hyperlipidaemia, respiratory and neurodegenerative diseases (Danesi and Ferguson, 2017), as well as neurodegeneration and skin deterioration (Quideau et al., 2011).

PJ generally includes the arils, which are the edible part of the fruit. However, in some juice industries, the entire fruit is squeezed, involving the extraction of the pomegranate's peels as well. Peels are a rich source of phenolic compounds. The main group is water-soluble hydrolysable tannins (HTs) that include the sub-group of ellagitanins (ETs). ETs in PJ contain unique compounds such as the two isomers of punicalagins, pedunculagin I, punicacortein, punigluconin, punicalin and galloylpunicalin (Fischer et al., 2011). HTs are found in the peel (husk, rind, or pericarp), carpellary membranes and piths of the fruit (Kulkarni et al., 2004). Some HT compounds such as the isomers of punicalagins are most abundant in pomegranate peels and are responsible for more than 50% of the juice's potent antioxidant activity (Adams et al., 2006; Gil et al., 2000). In addition, gallic acid, ellagic acid, gallagic acid and other simple phenolics were also suggested to play a significant role in this activity (Orgil et al., 2014; Orgil et al., 2016). It was proposed that the synergistic or additive action of HTs and other phenols in PJ and fruit extracts (e.g., flavonoids) accounts for their superior antioxidant and anti-carcinogenic properties (Seeram et al., 2005). Generally, the researchers suggest that the composition and levels of these compounds in pomegranate peels are responsible for

Abbreviations: PJ, pomegranate juice; HTs, hydrolysable tannins; ETs, ellagitanins; TPC, total phenolics content; TSS, total soluble solids; TA, titratable acidity

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the health benefits of PJ (Gil et al., 2000; Ismail et al., 2012; Wu and Tian, 2017).

Another important class of phenolic compounds in pomegranate peel and aril juice is anthocyanins, belonging to the flavonoides group of phenols. Anthocyanins are water-soluble pigments primarily responsible for the magenta-deep red color of the pomegranate arils and the peel's skin (Ben-Simhon et al., 2011; Seeram et al., 2006). These compounds are glycosides represented by only six aglycones, i.e., flavylium cations substituted in various positions by different sugars. Only 3-glucosides and 3,5-diglucosides of cyanidin, delphinidin and pelargonidin are present in pomegranate, but the anthocyanins concentration in pomegranate is relatively very high compared to other fruits (Can et al., 2012; Gomez-Caravaca et al., 2013). These molecules, in particular cyanidin-3-glucoside, the most abundant anthocyanin in pomegranate, are considered to be responsible for the protective effect towards cancer and tumor migration and invasion (Domitrovic, 2011).

Although the pomegranate tree originated in Central Asia, it spread to other regions, and today, the trees are cultivated in many tropical and sub-tropical areas (Holland et al., 2009; Verma et al., 2010). The adaptation to different growth conditions in Africa, Europe, Asia and North America led to different morphological phenotypes and thus to a wide range of cultivars (Fadavi et al., 2005). By analyzing pomegranate germplasm in different collections, it was estimated that overall several hundred pomegranate cultivars exist (Harel-Beja et al., 2015; Ophir et al., 2014).

This review focuses on studies performed on the peels of pomegranate fruits coming from the analysis of broad, bio-diverse pomegranate collections comprised of different cultivars. The importance of the peels is not just attributed to the fact that customer decision to consume the fruit is based on the first impression of the phenotype of the peels, mainly the size, color and shape, but also to the recent accumulated knowledge on their health-benefit properties.

2. Total phenols and antioxidant capacity of the peels

To better understand the range of several important traits of the peels, such as antioxidant capacity, total phenolics content (TPC), color and taste, we selected 29 pomegranate cultivars from a collection of about 150 cultivars in the Newe Ya'ar Research Center, ARO (IBG, website: http://igb.agri.gov.il) (Dafny-Yalin et al., 2010; Tzulker et al., 2007). By analyzing these cultivars, we found that the antioxidant activity of peel homogenates was about 40-fold higher than that measured in aril juice (Tzulker et al., 2007). Significantly higher levels (20- and 23-fold) of this activity in the peels versus arils were also reported by analyzing Peruvian and six Tunisian cultivars (Fischer et al., 2011). Studies also showed that this antioxidant activity is strongly correlated to the levels of TPC that was much higher in the peels than in the arils. Examination of 5 and 28 Chinese cultivars showed that TPC of pomegranate peel extract was 10-fold higher than that of the aril juices (Li et al., 2006, 2016). Pomegranate peel displayed the highest amount of fruit TPC, 67% of the total amount, while the juice contained 29.7% upon examining five Turkish cultivars (Gozlekci et al., 2011). While these studies show a high positive correlation between antioxidant activity and TPC, this correlation was not detected for nine Iranian cultivars (Ardekani et al., 2011).

The ranges between cultivars that have the lowest and highest content of antioxidant activity and TPC within the 29 cultivars were about five and three-fold, respectively (Tzulker et al., 2007). The values are higher than those reported for seven commercially grown cultivars in South Africa, showing a range of 2.1- and 1.6-fold for antioxidant activity and TPC, respectively (Fawole et al., 2012), and for 12 Tunisian cultivars, showing a range of 1.3-fold (Hasnaoui et al., 2014). Statistical analyses of the 29 cultivars also show a high and significant correlation ($r = 0.63$ to $r = 0.85$) between antioxidant activity and the contents of four ET compounds (punicalagin, punicalin, gallagic and ellagic acids). In addition to the higher levels, these results suggest that they are major contributors to this activity in the peel's homogenates (Tzulker et al., 2007). The levels of punicalagin isomers were about 5×10^3-fold higher in the peels compared to the arils. However, unlike in aril juice, no correlation was found between the levels of total anthocyanins to the antioxidant activities of the peel's homogenates (Tzulker et al., 2007).

The antioxidant activity and TPC levels in peels are not dependent solely on genotype; it was found that environmental conditions also significantly affect their levels. By analyzing the peels of 11 cultivars grown in Israel's southern Arava Valley (desert region) and in the Mediterranean region, it was found that the levels of these two parameters, as well as those of punicalagin and punicalin, are much higher in the southern Arava Valley than in the Mediterranean region (Schwartz et al., 2009). The reasons for this are not yet understood, but it could be related to the higher temperatures and radiation found in the southern Arava Valley (Schwartz et al., 2009). The levels of major phenolic compounds in tomatoes significantly increased when fruit temperature was elevated from 27 °C to 32 °C, as well as when light intensity increased, compared to low-light plants (Gautier et al., 2008). The higher TPC might protect the fruit against greater oxidative stress induced by high temperature and radiation.

3. The anti-proliferative and anti-androgenic activity of different pomegranate cultivars

Over the past 20 years, different studies have shown that PJ containing compounds from non-edible sections of the fruit exhibits anti-carcinogenic and anti-proliferative activities (e.g., Adhami et al., 2012; Panth et al., 2017). The compounds considered to be the main contributors to these activities are ETs. ETs are hydrolyzed in mammals to ellagic acid under physiological conditions; ellagic acid is then metabolized by the intestinal microbiota to urolithins (hydroxy-6H-dibenzopyran-6-one derivatives) that play a major role in the anti-carcinogenic activities (Landete et al., 2015). Consumption of ETs and ellagic acid-rich food is proposed to protect against prostate, pancreatic and colon cancer cell growth (Sanchez-Gonzalez et al., 2014). However, PJ contains many other phenolic compounds that can be absorbed and contribute *in vivo* to anti-proliferative activities (Adams et al., 2006; Adhami et al., 2009; Orgil et al., 2016).

To gain more knowledge about the ability of the different cultivars to inhibit the growth of cancer cell lines, we examined the same 29 cultivars that were tested for their antioxidant capacity (Tzulker et al., 2007). Peel water extracts of these cultivars were monitored for their anti-proliferative activity against hormone-dependent and independent breast cancer cell lines, MCF7 and MDA-MB-453, and androgen-dependent and independent prostate cancer cell lines, LNCaP and PC-3, respectively. These four types of cancer cell lines are known to be inhibited by PJ produced from the whole fruit, including peel extracts (Adhami et al., 2009; Kim et al., 2002). The anti-proliferative activities against LNCaP, an androgen-dependent cell line, ranged in these cultivars from 24% to 91% (Orgil et al., 2016). However, the same peel homogenates exhibited only a slight (up to 12%) anti-proliferative activity against PC-3, an androgen-independent cell line, which is an advanced stage of this cancer and has a high metastatic potential (Pulukuri et al., 2005).

Inhibition of proliferation of the MCF-7 cell line ranged from 12% to 93%, and the pattern of inhibition was relatively similar between MCF-7 and MDA-MB-453 (Orgil et al., 2016). Of the 29 cultivars, four showed high anti-proliferative activities when LNCaP, MCF-7 and MDA-MB-453 were examined, while three showed relatively low inhibition. Four cultivars exhibited high inhibition activity against LNCaP but relatively low activity against MCF-7, while one cultivar exhibited high inhibition ability against MCF7 compared to LNCaP (Orgil et al., 2016). These data suggest that the pomegranate cultivars reflect high diversity in metabolites that have specific anti-proliferative activity to each of these cancer cell lines. Significant positive correlations were found between the anti-proliferative activity of MCF-7, LNCaP and MDA-MB-

453 to TPC/antioxidant activity (Orgil et al., 2016), as previously suggested (Lansky and Newman, 2007). However, such a relationship was not found to PC-3 (Orgil et al., 2016).

Peels exhibited significantly higher (about five-fold) anti-proliferative activity against LNCaP cells compared to arils and seeds (Li et al., 2016; Orgil et al., 2014, 2016). Since peels have significantly higher levels of TPC than the other two tissues (Tzulker et al., 2007), we strongly proposed that these compounds contribute greatly to anti-proliferative activities. Higher ability of the peels to inhibit two cancer cell lines (HepG2 and CT-26) was also shown when five Chinese cultivars were tested in comparison to the other fruit and the tree organ's flesh, seeds, aril juice and leaves (Li et al., 2016; Orgil et al., 2014, 2016). The best inhibitory effect was observed at the highest concentration of peel sample (80 μg/mL) in which the HepG2 and CT-26 cell viability decreased to 12.7% and 15.2%, respectively. According to these results, the peel and flesh accounted for more than 83% of total TPC content of an entire pomegranate, thus the researchers speculated that the cytotoxicity of the fruit parts was related to their TPC content (Li et al., 2016; Orgil et al., 2014, 2016).

By studying the effect of eight cultivars on the androgen receptor in LNCaP cells, we proposed that several compounds could interfere with androgen receptor function and thus assist in the inhibition of the proliferation of androgen-dependent cancer cells such as LNCaP (Li et al., 2016; Orgil et al., 2014, 2016). In general, this study demonstrated the importance of exploiting natural pomegranate variation to identify cultivars exhibiting potential selective activity for the treatment of specific types of cancer.

4. Peel color

The skin color of the peel is the first trait affecting consumer choices. By analyzing color parameters in the 29 cultivars, we found that the fruit's skin color is similar to their aril color in 25 cultivars (Dafny-Yalin et al., 2010). However, the color of the peels cannot predict the appropriate day of harvest, aril quality, or levels of total soluble solids (TSS), titratable acidity (TA), organic acids and sugars of the aril juices that determines the PJ taste (Dafny-Yalin et al., 2010).

Color varies significantly between cultivars, from white-yellow through orange-pink, to intense red and purple (Fig. 1) (Dafny-Yalin et al., 2010). The color examined by a colorimeter is divided into five parameters: L* defines lightness, a* green-red transition, b* blue-yellowness, C saturation, and H° hue angle; the latter was shown to be effective in predicting visual color appearance, where 0° or 360° = red purple, 90° = yellow, 180° = green, and 270° = blue. It was previously suggested that the a* values could serve as a valid estimate for anthocyanin concentration in PJ (Borochov-Neori et al., 2009). Different measurements suggest that most of the compounds contributing to color are anthocyanins (Borochov-Neori et al., 2009), whose total levels significantly varied in the peel homogenates of 29 Israeli cultivars, from 0.4 to 4.3 × 10^2 mg cy-3-glu/L (10.75-fold) (Dafny-Yalin et al., 2010). Analysis of four Turkish cultivars revealed a significantly lower range of 0.058–0.293 g/mg (five-fold) (Orak et al., 2012), and in six Tunisian cultivars a range of 63.76–84.31 mg of CyE/g dry weight (1.3-fold) was measured (Kalaycıoglu and Erim, 2017).

Fig. 1. Seven pomegranate cultivars representing the biodiversity found in the Israeli collection.

The levels of the different color parameters are dependent on both genotype and environmental conditions. Analysis of fruits from 11 cultivars grown in the two different climates in Israel showed that the color parameters in peel significantly differ between fruits from the two locations (Schwartz et al., 2009). Fruits originating from the Mediterranean region were more colorful than those from the southern Arava valley. The b*, L* and C values were found to be higher in most cultivars grown in the southern Arava valley, indicating that these fruits have more of the yellow color component. The a* and H° values, however, were higher in the Mediterranean region, indicating that these fruits have more of the red color. The value of a* that indicates the green-red transition ranged from 19 to 47 in the Mediterranean and 7 to 43 in the southern Arava valley (Schwartz et al., 2009). It was also reported that Turkish cultivars have a significantly higher value of a* than pomegranate cultivars grown in hotter climates (India, Egypt and Oman) (Caliskan and Bayazit, 2012; Opara et al., 2009).

As previously suggested by Borochov-Neori et al. (2009), the results obtained from anthocyanin measurements correlated with those obtained from color measurements. Total anthocyanin content was higher in the Mediterranean region (up to 45-fold) than in the southern Arava valley (Schwartz et al., 2009). These results indicate that higher temperatures in the southern Arava valley reduced the levels of total anthocyanins in the peels. This could probably be attributed to anthocyanin degradation at high temperatures (Oren-Shamir and Nissim-Levi, 1999). Indeed, the intensity of the red color was found to be inversely related to the sum of heat units accumulated during fruit development and ripening (Borochov-Neori et al., 2009). Light intensity may also have an effect on the levels of anthocyanins in the pomegranate peels. Fruits oriented directly toward the sunlight accumulated more anthocyanins in their peels compared to those located on the inner branches (Gil et al., 1995).

5. The levels of total soluble solids, titratable acidity sugars and organic acids in the peels of different cultivars

Pomegranate peels are inedible due to their bitter taste and firm dry texture. But since some PJ industries squeeze the fruits, resulting in some compounds from the peels being extracted to the juice (Gil et al., 2000), it is also important to study the contents of sugars and organic acids in the peels. By analyzing the peel homogenates of the 29 cultivars, we showed that the homogenates have lower levels of total soluble solids (TSS) compared to the aril juice (by about 2–3 fold) (Dafny-Yalin et al., 2010). TSS varied in the cultivars examined, from 5.2 to 11.3 g/100 g, similar to the values reported for four Turkish cultivars (3.82–6.41 g/100 g) (Orak et al., 2012), but much lower than those reported for 12 cultivars from Tunisia (16.88–19.66 g/100 g) (Hasnaoui et al., 2014). As in aril juice, the peel homogenates contained glucose and fructose, but also maltose (whose concentration varies among the cultivars by about 50-fold), and sucrose that was found in only six cultivars (Dafny-Yalin et al., 2010). This composition of sugars differs from that reported in ten Tunisian cultivars, where arabinose and xylose were the most prevalent sugars, representing more than 60% of the total content, followed by galactose (14%), glucose (~10%), mannose (~5%), rhamnose (~4%) and fucose (~1.5%) (Hasnaoui et al., 2014).

The range in the levels of titratable acidity (TA) among the 29 cultivars between cultivars having the lowest and highest levels was 0.27–1.23% (4.5-fold) (Dafny-Yalin et al., 2010), which is lower than those reported for the five Turkish cultivars (0.97–1.39%) (1.4-fold) (Gozlekci et al., 2011). However, this range is within the values

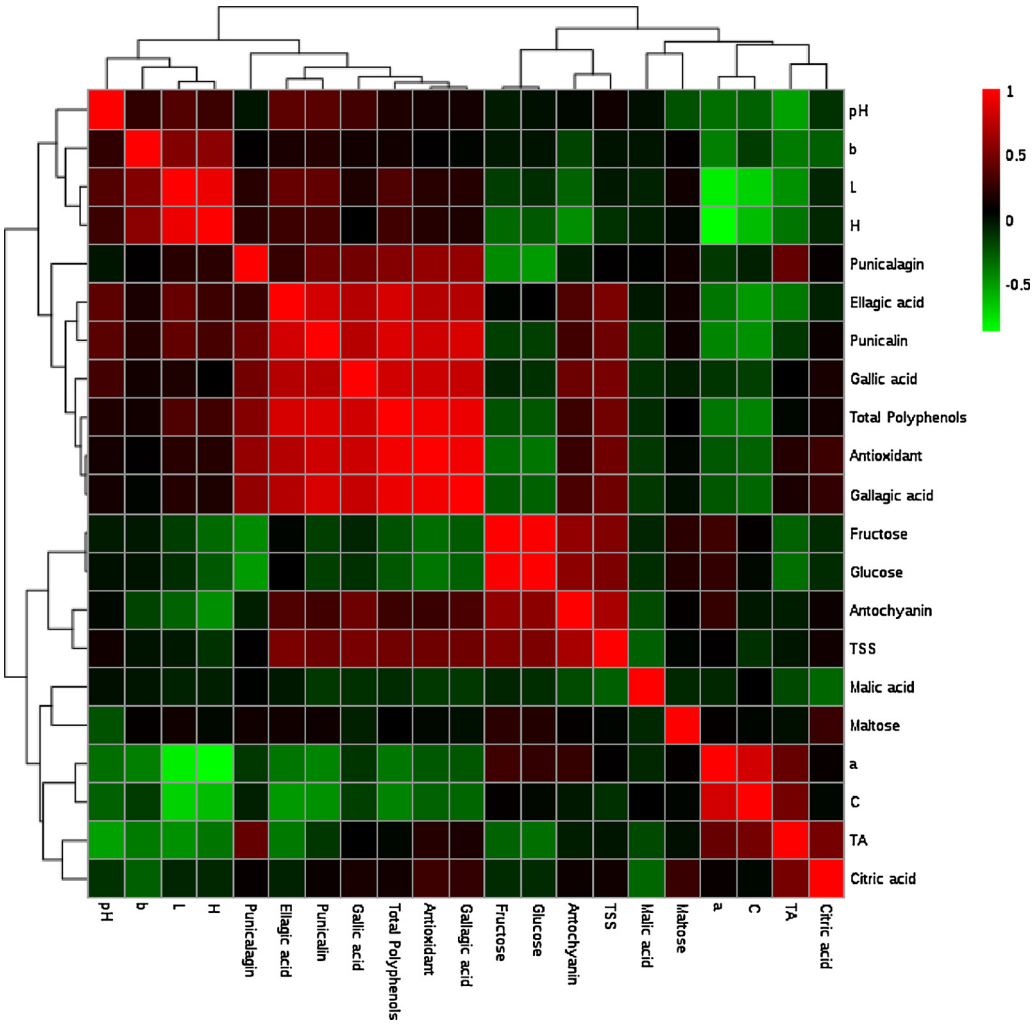

Fig. 2. Heat map of different traits of peels examined in 29 cultivars grown in Israel. The data represent five replicates for each type of plant. Spearman analysis was used.

measured in aril juice. The citric acid level in the peels, however, was lower by about three- to five-fold compared to the arils, varying among the 29 different cultivars from 0.03 to 0.39% (13-fold) (Dafny-Yalin et al., 2010). The values are lower than those reported for six Georgia cultivars (0.51–1.68%; 3.3-fold) (Pande and Akoh, 2009), and four Turkish cultivars, 1.48–3.66% (Orak et al., 2012). In addition to citric acid, all of the 29 Israeli cultivars have malic and succinic acids, while oxalic acid was detected only in nine cultivars (Dafny-Yalin et al., 2010). Oxalic and other organic acids reported for the Israeli cultivars were also found in all six Georgia cultivars (Pande and Akoh, 2009).

6. Heat map analysis of the 29 cultivars

To seek a relationship between the different parameters examined in the peels, a heat map analysis was performed (Fig. 2). This analysis employs the raw data from the different analyses of the peels of the 29 cultivars. In agreement with our earlier correlation tests (Tzulker et al., 2007), the heat map showed positive relationships between antioxidant activity, TPC, punicalagin, punicalin, gallic acid, ellagic acid and gallagic acid. Positive relationships were also found, although to a slightly lesser extent, between these parameters to total anthocyanin, TSS, pH, and b*, L*, H color parameters. This group of parameters tends to exhibit a negative relationship to the levels of glucose, fructose, maltose, TA, citric acid, malic acid, a* and C color parameters (Fig. 2). Additional studies conducted with large collections during fruit development and ripening are required to reveal if the color and taste parameters are indeed related in order to gain more knowledge for determining the appropriate day of harvest.

7. Factors that help maintain peel quality during prolonged periods in storage

The pomegranate harvest season is relatively short (lasting about three weeks for each cultivar and usually totaling less than three months for the entire collection). Therefore, it is important to find post-harvest conditions to extend the marketing season of fresh fruit and prolong the time of its availability to the market and to the processing industry. Although several commercial storage protocols have been used to store pomegranates for several months [reviewed by (Ben-Arie et al., 1984; Caleb et al., 2012; Defilippi et al., 2006)], the stored fruits exhibit significant quality loss over time. The main factors limiting prolonged storage of pomegranates are related to the peel phenotypes. These include shrinkage due to weight loss, decay caused by pathogenic fungi, peel scald (superficial browning of fruit peel) and chilling injury symptoms (Pareek et al., 2015) (Fig. 3). These visually defective disorders prevent customers from purchasing the fruit, even when the arils are of good quality. Since these symptoms develop with time, they significantly reduce the period that the fruit can be stored.

To gain greater knowledge about the processes occurring in the peels during storage, we selected seven cultivars that differ in peel

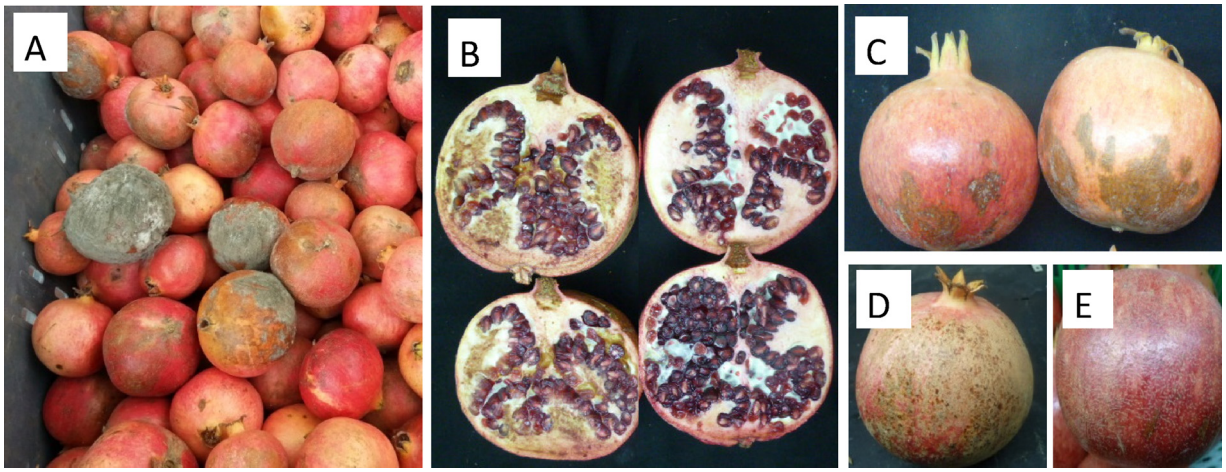

Fig. 3. Defects that can occur in the peels of pomegranates. A, B, C and D are defects that occur during prolonged storage of the fruit, while D and E can occur during the development of the fruit in the plantation. A. Decay caused by mold fungi that leads to rotting. B. Chilling injury that affects mostly the inner part of the peels causing internal browning. The left panel shows fruits that are inflicted by this symptom, while the right panel shows fruits that are not. C. Husk scald. D. Rough peels. E. Cracking peels.

antioxidant capacity and TPC. The post-harvest fruits were stored for five months, and the husk disorders were measured on the day of harvest and thereafter every month (Matityahu et al., 2013, 2016). It was detected that the TPC and antioxidant activity of the peels increased slightly but significantly during the storage of most cultivars (Matityahu et al., 2013, 2016). The level of punicalagin significantly decreased during storage in all cultivars. The fruits having a high antioxidant capacity, TPC and levels of punicalin (up to two-, three- and 6-fold, respectively, compared to the other cultivars), have a better ability to resist fungal decay and weight loss, in addition to being more tolerant to peel scalding (Matityahu et al., 2013, 2016). The results also suggest that cultivars having a green-yellow color are more sensitive to chilling injury, even though they have the highest antioxidant activity. The observations raise the possibility that while scald development is repressed by antioxidant compounds, the development of chilling injury symptoms is probably not affected by these compounds. The results also indicated that the development of most husk disorders are not associated with the contents of TSS, TA, punicalagin, anthocyanin, or peel color (Matityahu et al., 2013, 2016).

The finding that punicalagin is not correlated to the higher ability to resist fungal decay is in some way unexpected, since we had previously identified antifungal compounds in pomegranate peels that inhibit the growth of several pathogenic fungi decaying vegetables and fruits during storage (Glazer et al., 2012). We showed that aqueous extracts of peels from two cultivars inhibit the growth rate of three out of six rot fungi. The growth rate inhibition of these three fungi was correlated to the levels of TPC in the extract and particularly to punicalagin (Glazer et al., 2012).

To study the effects of regular air (RA) and controlled atmosphere (CA: 2 kPa O_2 + 5 kPa CO_2) at 7 °C on the quality of peels, we next selected three pomegranate cultivars that differ in their TPC in their peels (Matityahu et al., 2013, 2016). The fruits were sampled at monthly intervals during five month of storage. The results show again that the cultivar with the highest TPC and antioxidant capacity of the three cultivars had the lowest scald score, whereas the cultivar with the lowest antioxidant activity and TPC had the highest score. The levels of TPC and antioxidant capacity did not differ significantly between fruits stored in RA and CA, whereas the scald score was significantly reduced by the latter storage regime (Matityahu et al., 2013, 2016). Thus, we suggest that other factors related to oxidative metabolism and enzymatic activity are affected by storage conditions (temperature and atmosphere) and probably play a role in scald development (Matityahu et al., 2013, 2016). Taken together, the results indicate that with respect to peel scald and decay development, CA is a better storage regime than RA, albeit RA being more beneficial for maintaining the anthocyanin level. However, differences were found between the three cultivars in the contents of most of the parameters examined during storage, suggesting that in the future, each cultivar may require a specific storage protocol with regard to atmospheric composition (Matityahu et al., 2013, 2016).

8. Summary and future perspectives

The usage of a large pomegranate collection rich in trait variation is a valuable and powerful resource to increase our knowledge about the biodiversity that can be found in pomegranates. Moreover, such analyses can also provide greater knowledge and a broader picture of the various factors that contribute to the fruit's health benefits and marketing. In addition, the overall data collected can assist breeders and growers to respond to consumer and industrial preferences. By examining large collections, some relationships between different compounds in the peels to human health benefits were found. For example, the levels of some HTs were found to be correlated to anti-carcinogenic, antioxidant activity, antifungal ability and some post-harvest parameters. Moreover, the diversity of activities and levels of compounds that were detected suggest that some cultivars are more suitable for specific activity than others. By analyzing the 29 cultivars, we can identify that some have higher antioxidant activity and others have higher anti-proliferative activity against prostate and breast cancer cell lines. This information can lead in the future to the production of more specific PJ, which contains distinct peel components, that will be used as functional food against selected diseases. The studies have also shown that both genetic and environmental conditions contributed to the desired traits. The studies with large collections also added to our knowledge about the factors contributing to taste, post-harvest period, color, and other nutritional and marketing traits.

Despite this accumulating knowledge, the relationship between the different health benefit activities and PJ composition still requires additional studies and research efforts. Many compounds in the PJ still remain to be annotated, and the synergism between the different compounds should be determined. The metabolic profiling is missing from many cultivars, which could provide more knowledge about the diversity of the compounds. Chemical analysis should be carried out together with the genomic analysis in order to reveal the molecular basis underlying the accumulation of the HTs, ETs and additional compounds in the peels. In the past few years, several studies were

performed in order to reveal the genes in the biosynthetic pathway leading to HTs (Ono et al., 2016), and those regulating the levels of anthocyanin content (Ben-Simhon et al., 2011), but efforts are still required to understand better the genes/enzymes in the biochemical pathways in pomegranates.

In recent years, several scientific tools were developed. For example, a detailed genetic map of pomegranate based on 1092 SNPs was published and 25 QTLs for fruit traits were determined. The map includes QTLs for TSS, fruit weight, seed hardness, aril color and plant height (Harel-Beja et al., 2015; Ophir et al., 2014). In addition, the genome of pomegranate was recently published (Qin et al., 2017; Yuan et al., 2017), providing us with much more knowledge about the genes. These accumulating data, as well as metabolite content, will enable us to discover the pathways leading to the bioactive compounds and their regulation. Such knowledge will facilitate the breeding process to obtain nutritious pomegranate cultivars with larger variety and higher content of desired health promoting bioactive compounds that also possess other important traits such as longer storage and better taste.

Conflict of interest

None.

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