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SECONDARY METABOLITES AND HEALTH IMPORTANCE OF *PUNICA GRANATUM*. AN OVERVIEW

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Abstract

Originally from Central Asia, pomegranate (Punica granatum L.) is one of the oldest fruit crops cultivated, with a high geographical distribution. It is one of the most important crops in the Mediterranean area, some areas of Asia, former soviet countries or countries such as Argentina, Chile or the United States of America. In Romania, the species in cultivated in southern and south western part of the country, mostly as an ornamental plant, but it has potential for crop production. Despite the fact that the genetic diversity of Punica granatum totals more than 500 varieties, only 50 cultivated for their commercial value, reducing the cultivated germplasm. Punica granatum is grown in temperate and subtropical regions and it is highly appreciated in the food industry as a fresh fruit or as preservative, due to its high content in citric acid. Numerous studies mention the antiviral, anticancer, antibacterial, anti-diabetic, anthelminthic and immunomodulatory effects. Latest research identifies Punica granatum as a technical plant, of avail in nanoparticles synthesis due to its high content in antioxidants.

Key words: *Punica granatum, micropropagation, disinfection, culture medium, oxidative reaction.*

INTRODUCTION

Pomegranate is one of the most exotic and culinary fruits consumed all over the world and belongs in the *Lythraceae* family, which only has one genus - *Punica*, and two species - *Punica granatum* and *Punica protopunica* (syn. *Socotria protopunica*, *Punica spinosa, Punica florida*)- which is endemic and can only be found in the island of Socotra, located in the Arabian Peninsula. *Punica protopunica* is considered to be either an ancestor of the species (The Plant List - *Lythraceae*), either as an independent genetic line (Kosenko, 1985). *Punica granatum* is a diploid species, with a haploid number of chromosomes = 8, 2n = 16 for ‘Dholka’, ‘Ganesh’, ‘Kandhari’, ‘Muskat White’ varieties and 2n = 18 for the double flowered varieties ‘Vellodu’ and ‘Kashmiri’ (Mars, 2000). A tetraploid clone was identified in the spontaneous flora of India, a clone whose flowers exceed the standards and whose pollen sterility reaches 85.4%, compared to 7.4 % in the diploid varieties (Chandra et al., 2010). Chandra (2010), places the species as being one of the first to be domesticated by humans, cultivated in 4000-3000 B.C. and one of the oldest edible fruits, mentioned in the Bible and Coran.

According to Levin (2006), the wild species has three main origin basins and five macro-centers (Middle Eastern, Mediterranean, Eastern Asian, American and South African). Studies show that in the endemic micro zone of the species, Kandahar (Afghanistan), grows a variety with the biggest seedless fruit, and in the area of Dashnabad (Uzbekistan), the most resistant to cold variety was found.

Initially cultivated between 41° N and 42° S, commercial plantations are now found in the Mediterranean basin and Asia (Bar-Ya’akov et al., 2008), as well as in countries from the southern hemisphere, Australia, South America and South Africa (Holland et al., 2009). This shows the high level of adaptability this species has to climatic variations. In the area of Romania, the species is found cultivated for ornamental and pomological purposes in the areas of the southern part of the country or in depression areas with warmer weather, as well as in the campus of the Faculty of Horticulture from USAMV Bucharest, in a collection of 14 genotypes from Turkey ('Hicaz', 'Ähmar'), Siria ('Malissi', 'Kandahar', 'Shahvar'), Crimeea ('Nikitski Ranni'), Spain ('Mollar'), Italy ('Dolce', 'Nana' and 'Dolce di Sicilia') and Bucharest (local selection), collection established in 2012.

According to historiography, various preparations from parts of the plant were used in the days of Dioscorides, who indicated in "*de Materia medica*" that flower decoct was helpful to prevent dental loss, the juice of kernels mixed with honey was used for ulcers and the root decoct utilised to eliminate tape worms. Dioscorides points out the difference between *Punica granatum* and *Punica protopunica*, the wild variety being used for its astringent properties (de Materia Medica, 2000).

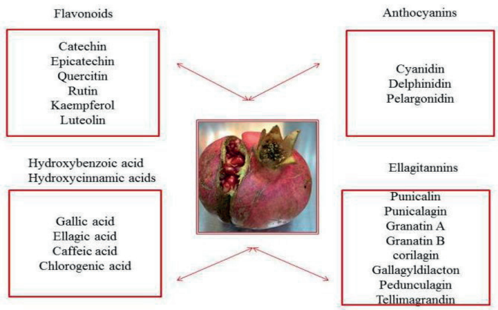

Figure 1. Chemical structure of *Punica granatum* compounds

Pomegranate is recognised now as a superfruit, because of its nutritional values and active principles. The fruit and peel have antioxidant properties and the juice, peel and oil extracted have a mild estrogenic action, which makes the plant useful for the treatment of menopause. Also, it interferes in the proliferation of cancer cells and their multiplication, being associated with other plants with anti-inflammatory role.

The main purpose of this study is to synthetise the main published works and research that indicates the pharmacology importance of this species and the main biocomponents from pomegranate, reviewing only the phenolic compound, tannins, flavonoids, anthocyanins, fatty acids and alkaloids.

I. Chemical composition of pomegranate

The different parts of pomegranate - leaves, fruit, seeds, root or bark have different compounds with remarkable chemical properties (Lanskisi et al., 2007). The main groups of compounds that are found in the plant are synthetized in table 1, grouped depending on their primary localization.

The edible part of the fruit represents about 50% of the whole fruit and it is formed by 40% of the juice generated by the aril and 10% of seeds. While the aril contains about 80 % water and 10% sugars (fructose and glucose) (Mphahlele et al., 2016), organic acids and bio compounds, cafenols, flavonoids, the seeds are a rich source of lipids, fiber and ash, with an average content of 6% pectin and 4.7 % total sugars (El-Nemr et al., 1990). While iron (Fe), copper (Cu), sodium (Na), magnesium (Mg) and zinc (Zn) are found mostly in seeds, the juice has a high potassium (K) content - 49.2% (İncedayi, 2010).

Table 1. Chemical compounds of *Punica granatum*

Source of compounds	Compounds
Juice	anthocyanin (Du et al., 1975), glucose, ascorbic acid (nutrition data); ellagic acid, gallic acid, caffeic acid (Amakura et al., 2000); catechin, EGCG (de Pascual et al., 2000); quercetin, rutin (Gómez-Caravaca et al., 2013); minerals, particularly iron (Lansky et al., 2007); amino acids (Waheed et al., 2004);
Roots and bark	punicalin and punicalagin (Tanaka et al., 1986); piperidine alkaloids (Wu et al., 2017);
Flower	gallic acid, ursolic acid (Li et al., 2008) triterpenoids, including maslinic and asiatic acid (Johanningsmeier et al., 2011);
Leaf	tannins (punicalin and punicafolin) (Yan et al., 2017); flavone glycosides, including luteolin and apigenin (Nawwar, 1994);
Pericarp (peel, rind)	phenolic punicalagins; gallic acid and other fatty acids (Amakura et al., 2000); catechin, EGCG (de Pascual-Teresa et al., 2000); quercetin, rutin, and other flavonols (Gómez-Caravaca, 2013); flavones, flavonones (Nawwar et al., 1994); anthocyanidins (Nodaet al., 2002);
Seed oil	95-percent punicic acid (Schubert et al., 1999); ellagic acid (Rahimi et al., 2020); other fatty acids (Wu & Tian, 2017); sterols (Choi et al., 2006);

II. Phenolic compounds

Phenolic compounds were identified as a result of research on peel, fruit, root system (Akkiraju et al., 2016; Sharma & Akansha Chauhan, 2018), seeds (Derekhshan et al., 2018), rid (Moorthy et al., 2013), mesocarp, exocarp, aril (Jaiswal et al., 2010), juice (Derakhshan et al., 2018), flowers (Yisimayili et al., 2019) and leaves (Yan et al., 2017). Depending on the cultivar or variety, the total content of polyphenols varies (Hmid et al., 2017), being higher in peel than in seeds, leaves and flowers (Elfalleh et al., 2012) and much higher in juice (Akhavan et al., 2015).

According to Li et al. (2006) pomegranate leaves extract induces apoptosis and inhibits migration and invasion of cancers cells. The peel extract is about 10 times richer in polyphenols than the one obtained from pulp, and the extraction in H_20 + EtOH (1:1 v/v) and temperature control of the probes has improved the efficiency (Venkataramanamma et al., 2016).

Generally, the total content of polyphenols from a plant is reported in the content of gallic acid, the highest level being reported in kale (*Brassica olerace*a var. *sabellica* - 16.3-18.8 mg GAE/g) and other vegetables such as tomatoes (*Solanum lycopersicum*), rhubarb (*Rheum rhabarbum*), spinach (*Spinacia oleracea*) and broccoli (*Brassica oleracea* var. *italica*) (Zhou & Yu, 2006). Also, the studies on the antioxidant capacity of the molasses obtained from pomegranate indicated a concentration of 52.6 mg GAE/g dry mass (Yılmaz et al., 2007), compared to the values of other economically important species such as Fuji apple variety *(Malus domestica*), kiwi (*Actinidia* sp.), pear (*Pyrus communis)*, orange (*Citrus sinensis*), where values of phenolic compounds varied between 1.2 and 5.1 mg GAE/g dry mass. Malic acid, glusides derivated such as hydroxybutanedioic acids were reported in the structure of pomegranate, alongside with quinic acid, quinic acid methyl ester and acetyl glucoside derivates. (Al-Rawahi et al., 2014).

The presence of gallic acid, togheter with cafienic acid was reported in chinese cultivars with values of 2.53 and 0.03 mg/100 mg (Song et al., 2016), while studies on peel indicated values up to 8.91 mg/g (Ma et al., 2015) of gallic acid or 30.4 mg/g in metanolic extract for the turkey variety. Poyrazoglu et al., in 2002, determined the main acids present in 13 pomegranate cultivats from the mediterranean area of Turkey. Citric acid was determined as the most present organic acid, found in an average concentration of 4.85±2.83 g/L, followed by mallic acid, in an average concentration of 1.76 ± 1.59 g/L, and oxalic and tartric acid, found in a concentration of 1.16 ± 2.07 g/L and 0.87 ± 0.75 mg/L, respecttively. Analysing the main phenolic compounds, the following compounds and concentrations resulted: gallic acid 4.55 ± 8.55 mg/L, protocatechuic acid 0.84 ± 0.64 mg/L, catechin 3.72 ± 2.29 mg/L, chlorogenic acid 1.24 ± 1.42 mg/L, caffeic acid 0.78 ± 0.79 mg/L, p-coumaric acid 0.06 ± 0.07 mg/L, ferulic acid 0.01 ± 0.02 mg/L, o-coumaric acid 0.17 ± 0.08 mg/L, phloridzin 0.99 ± 1.47 mg/L, quercetin 2.50 ± 1.96 mg/L (Poyrazoglu et al., 2002).

The presence of gallic acid, quercitin, catechin, chlorogenic acid and o-coumaric acid was previously signaled in peel and aril (Poyrazoğlu et al., 2020). Caffeic acid (3.88-75.19 μg/g), p-coumaric acid (0.12-14.87 μg/g), ferulic acid (0.15-8.84 μg/g), sinapic acid (2.13-3.58 μg/g), syringic acid (15.17-88.24 μg/g) and vanillic acid (65.87-108.36 μg/g) were identified as the main phenolic acids from pomegranate peel in a study on some cultivars from Pakistan (Mushtaq et al., 2015).

III. Tannins

Tannins and flavonoids are found in high quantities in the pericarp and mostly in wild cultivars, compared to the commercial ones (Tzulker et al., 20078). In pomegranate fruits, the concentration of tannins can reach 19.3%, having the one of the highest concentrations, after *Rhus semialata* (47%) and *Acacia catechu* (41.2%) (Cai et al., 2004). The study identified that in *Punica granatum*, tannins are both hydrolysable and condensed, and the condensed ones have a more complex structure and are more widespread in plant compared to the condensed ones. Hydrolysable tannins are found in the whole plant, in juice, in fruit or seeds, leaves or bark (Tanaka et al., 1985), in peel, in the form of ellagitannins or gallotannins (Çam & Hışıl, 2010), with a value of 262.7 mg tanninic acid equivalents (TAE)/g extracted with pressurized water extraction method. If analysed comparatively, the content of tannins from peel obtained from aqueous, methanol and ethanol extracts from four Turkish cultivars shows that the highest concentrations were obtained from the methanol extraction (124.10-183.18 μg TAE/ mg) (Orak et al., 20212) For four cultivars of pomegranate from Tunisia, the reported values were between 470.7-504.8 mg TAE/g (Elfalleh et al., 2012).

In 1985, a new ellagitannin, punicafolin, was isolated from the leaves of *Punica granatum* and punicalin and puninalagin were also identified in the roots and bark (Tanaka et al., 1985). In a cultivar from Peru, ellagitannins were identified in peel, in concentration of 44 g/kg (the most representative being punicalagin - 10.5 g/kg, pedunculagin I - 3.5 g/kg, granatin B - 5.9 g/kg, punigluconin - 3.8 g/kg, lagerstannin C - 3.9 g/kg) and gallatonnin (digalloylhexoside) in concentration of 4.3 mg/kg (Fischer et al., 2011). Punicalagin is the most studied compound from pomegranate, having multiple pharmacological properties and it is identified as the main phenol in Chinese pomegranate peel (Song et al., 2016). Hydrolysable tannins that contain isomers punicalagin are responsible of about half of the oxidative response of the pomegranate juice, followed by punicalin, ellagic acid and gallic acid (Tzulker et al., 2007).

A concentration of 39.6 mg/g and 32 mg/g concentration of punicalagin and ellagic acid from the extract of pomegranate leaves inhibited the cellular proliferation in the case of non-small epithelial pulmonary cancer and flow crytometry technology revealed the fact that the extract interfered with the progress of H1299 cells in G2/M and generated apoptosis (Li et al., 2016).The punicalagin content of the peel extract from three cultivars from Pakistan - 'Badana', 'Desi' and 'Kandhari' on dry weight was 88.70, 110 and 118.60 mg/g (Khalil et al., 2017). Punicalagin-β was isolated from the extract of three cultivars from Maroc - 'Beni Mellal', 'Berkane' and 'Settat', sin concentrations higher than 200 mg/g (Sabraoui et al., 2020). The present variations of punicalagin depend on the cultivar/variety and culture conditions. A comparative study from peel, flower, seed and leaf on 'Gabsi' variety from Tunisia showed that there are remarkable differences between the total content of hydrosoluble tannins, which explains the interest of traditional medicine of (using) pomegranate as a medicinal plant, especially for its anti-ischemic activity: peel (139.63 ± 4.25), seeds (29.57 ± 4.54), leaves (128.02 ± 4.49) and flowers (148.24 ± 10.29) – results expressed in mg TAE/g DW (Elfalleh, 2012).

Using the methanol extraction technique, ellagic acid was isolated from the peel of six Spanish cultivars in concentrations between 9.8-16.5 mg/g and the antimicrobian and antifungal activity was tested for *Aspergillus flavus* CECT 2686, *Aspergillus parasiticus* CECT 2947, *Gibberella fujikuroi var. fujikuroi* CECT 2987 (syn. *Fusarium verticillioides*), *Alternaria alternata* CECT 20560, *Botryotinia fuckeliana* CECT 20754 (Syn. *Botrytis cinerea*) (Rosas-Burgos et al., 2017). The comparative results regarding the isolation with the three classical extraction methods (aqueous, methanol and ethyl acetate) shows that pressurized water extraction method may also be successfully used, limiting the residue and the toxic remains from the methanol and ethanol extraction (Derakhshan et al., 2018). In 2006, Wang isolates a new compound from the pomegranate leaves, named pomegranatate 1, togheter with ellagic acid, derivates of ellafic acid 3,3′,4′-tri-O-methylellagic acid and phyllanthusiin E (Wang et al., 2006). Traditional Iranian medicine frequently uses pomegranate flowers for its therapeutic effects and gallic acid was first synthetized from two local genotypes, 'Ghojagh' and 'Golnar', and its content was 25.94% for 'Ghojagh' and 15.19 mg gallic acid equivalents per gram of dry powder (Hajimahmoodi et al., 2013). Studies have shown that the antioxidative capacity of pomegranate juice is stronger than the one in red wine or green tea, possible as a result of the presence of hydrolysable tannins from rid, anthocians and ellagic acids and its derivates (Gil et al., 2000).

IV. Flavonoids

Widespread in the biochemical structure of plants, flavonoids are classified in flavones, flavonols, flavanones, flavanonols, chalcones, isoflavonoids (mainly isoflavones), anthocyanins (anthocyanidins) and bioflavonoids (dimer of flavones, flavonols and flavanones) (Cai et al., 2004).

The extract from the whole fruit of pomegranate (aqueous extract, ethyl acetate extract and ethanol extract) has 30 % more favonoides than the peel extracts. Research showed that there is a correlation between the total antioxidant activity and the high flavonoids content and the type of extraction (Masci et al., 2016). The same research evidentiates that, in general, the extracts from the whole fruit have a higher bioactive potential than the ones obtained from the peel. Although there are differences between varieties and cultivars (Maroc) regarding the content in polyphenols, the value of correlation (R2=0.9) between flavonoids and the oxidative capacity of pomegranate juice showed that flavanoides are one of the most important compounds that contribute to the oxidative capacity of the species (Hmid et al., 2018). Compared to the apple juice, the content of flavonoids is almost double, from 92 mg/L in apple to 174 mg/L in pomegranate, being highly recommended for its antioxidant activity, especially for older people (Guo et al., 2008).

The antioxidant and anti-bacterian effect of flavonoids was reported as a result of the identification of chelating capacity of the iron and/or copper ions that launches the hypothesis that flavonoids can prevent the cellular damage caused by the free radicals. Therefore, a comparison of antioxidant activities of juice, peel and seed of pomegranate and inter-relationships with the total phenolic, tannin, anthocyanic and flavonoid contents was carried out (Oral et al., 2012). A good correlation evidentiated that in pomegranate juice, only flavonoids (r = 0.410) are the ones that contribute to the chelating capacity of metals, and, similarly, in the seed extract, the total content of flavonoids and the correlation value (r = 0.623) is also responsible for the chelating capacity of metals.

Catechin, gallocatechin and procyanidin B were identified using chromatography-mass spectrometry (LC-MS) analysis in the peel of a Tunisian cultivar of *Punica granatum* var. *Nana* (Wafa et al., 2016). Catechin was found in peel in concentrations that varied from 76.5 mg/100 g and 12.66 mg/100 mg in varieties from India and China (Singh et al., 2016; Song et al., 2016). Research identified the presence of flavonols, quercitin and rutin (Shams Ardekani et al., 2009), flavonones and flavones (Newwar et al., 1994) in pericarp. Anthocians, flavonones, flavones, flavonols and isoflavonols were identified in the flower extracts of two Tunisian cultivars (Fellah et al., 2018), while Al-Rwahi isolated Kaemferol 3-orutinoside, kaempferol derivatives, isorhamnetin and hexahydroxydiphenoyl -glucosideacetyl glucoside derivatives. (Al-rawahi et al., 2014)

A study on nine Spanish cultivars (Fernandes et al., 2017) identified a total content of flavonoids between 20.8 and 189 mg QE/100 ml juice, where two cultivars 'Katirbasi' and 'CG8' have shown the highest level, and 'Parfanka', 'Wonderful 2' and 'Cis 127' with the lowest level of total flavonoids. All the values in the study were slightly higher than the ones obtained in the Turkish varieties - 38.78 and 45.50 mg QE/100 ml aqueous extract (Orak et al., 2012).

V. Anthocyanins

Anthocyanins, class of flavonoids, are responsible for the colours that can vary from orange to blue in flowers, leaves, fruits, seeds or other tissues. Most of the times, carotenoids and anthocyanins are present together in the same tissue or organ, which gives increased a intensity and a variety of colours, next to the pH and the metal ions that are present (Tanaka et al., 2008). In pomegranate, anthocyanins are the main class of pigments and are responsible of the aril and peel colour, depending on the complex of glicosides that are present. Only 3-glicosides and 3,5-diglucosides of cyanidin, delphinidin and pelargonidin, are identify in peel, the species having a high concentration of anthocyanins in comparation to other fruits (Masci et al., 2016). Research on the anthocyanins content in the fruit skin identified only cyaniding and pelargonidin derivates (Tanaka et al., 2008). The increased interest for the anthocyanins in pomegranate comes from their role in the antioxidant activity: preventing the formation of free radicals by chelating iron and scavenging of free radicals (Fischer et al., 2011). The total content of anthocyanins varies depending on the cultivar, the maturation stage and the type if exposure, an increase of anthocyanins concentration being reported in the last stage of fruit ripening (Fernandes et al., 2017) (Figure 2).

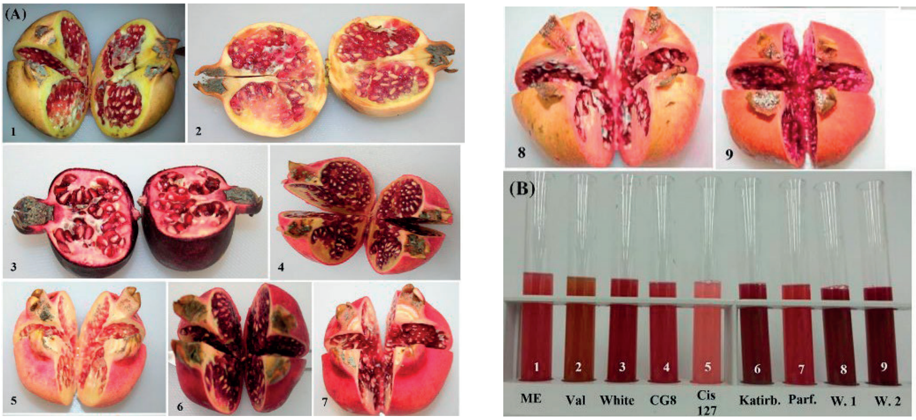

Figure 2. Pomegranate fruits (a) and juices (b) of nine cultivars grown in Spain: 1 - Mollar de Elche, 2 -Valenciana, 3 - White, 4 - CG8, 5 - Cis 127, 6 - Katirbasi, 7 - Parfianka, 8 - Wonderful 1, 9 - Wonderful 2 (Fernandes et al., 2017)

3,5-diglucosides predominate in the early ripening stage and delphinium based derivates are mostly found, while in the later ripening stages, the concentration of monoglicosides raises, and cyanidin based derivates become predominant (Gil et al., 1995).

Research by Fischer et al. (2011) has revealed a series of anthocyanins in the peel of some unknown Peruvian cultivars: the most representative - delphinidin 3,5 diglucoside (10.8 mg/kg), followed by cyanidin 3,5-diglucoside (157.8 mg/kg), pelargonidin 3,5-diglucoside (145.8 mg/kg), delphinidin 3-glucoside (13.3 mg/kg), cyanidin hexoside (1.7 mg/kg) and cyanidinpentoside (1.4 mg/kg), cyanidin 3-glucoside (41.2 mg/kg) pelargonidin 3-glucoside (56.7 mg/kg), cyanidin 3-rutinoside (18.4 mg/kg).

They reported that there still are molecular structures that are not identified in this species, as cyanidin 3-rutinoside and cyanidin-pentoside were not mentioned in the literature at the time of the study. Antocians were not found in the aril and peel of green or immature fruits, and seed analysis evidentiated the presence of delphinidin 3-glucoside, cyanidin 3-glucoside, delphinidin 3,5-diglycoside, cyanidin 3,5-diglucoside, pelargonidine 3,5-diglucoside and pelargonidine 3-glucoside (Sreekumar et al., 2014)

The activity of delphinidin, cyanidin, and pelargonidin on H_2O_2 induced lipid peroxidation in rats and the values of 0.7, 3.5, and 85 íM, respectively, showed that this three antocianidini contribute to the antioxidant activity of the pomegranate fruit, delphinidin being considered the main constituent that gives the juice the inhibitory effect on H_2O_2 –induced lipid peroxidation. (Noda et al., 2002).

VI. Fatty acids

Fatty acids are present in different concentrations in pericarp (Jurenka, 2008; Moorthy et al., 2013), in leaf (1.7 ± 0.96%) (Yan et al., 2017), fruit peel (1.2%), seeds (4.8%), whole fruit (1.4%) (Sharma et al., 2018) and juice (Liu et al., 2009). The quantity of oil/kg of seeds varies not only depending on the genotype but also on the extraction method (Abbasi, 2008). The saponification point of pomegranate oil is 188.9 and the high breakdown rate of pomegranate oil can be attributed to the high trans-fatty acid content (El-Nemr et al., 1990). Although pomegranate seeds have a low content of polyphenols (Singh et al., 2016), the oil extracted from them has multiple nutraceutic uses, having a high content of phytosterol and punicic acid. In the majority of industrial extraction processes used for processing pomegranate, the seeds are discarded, despite the fact that these are an important source of polyunsaturated fatty acids, sugars, proteins and other bioactive compounds (Yoshime et al., 20169). Recent studies on pomegranates from Iran, Turkey, Spain and China evidentiated the antioxidant activity of pomegranate oil, and the composition of fatty acids gained interest for further research. In the oil obtained from the seeds, 83.6% of the fatty acids are saturated and 16.3% unsaturated

(Momeni et al., 2021). The lipid content of seeds varies between 140-270 g/kg dry weight, hence they are rich in lipid (Lansky & Newman, 2007). Johanningsmeier & Harris (2011) mentioned that the oil extracted from the seeds of 15 Turkish cultivars contains α-eleostearic, linoleic, oleic, catalpic, palmitic, stearic, β-eleostearic, gadoleic, arachidic, and behenic acids and punicinic acid represents between 70-76% or the oil composition (Johanningsmeier and Harris, 2011).

The average content of seeds is between 37-143 g/kg fruit, depending on the ripening stage, culture conditions, geographic location and cultivar (Fernandes et al., 2017). A consistent variability between genotypes was identified in a study on pomegranates from Puglia, Italy, the values being between 10.7 % ('ModTri') and 26.8% ('Ako') in case of sweet genotypes and between 4.9% ('SouTri') and 17.4% ('Wond') for the sour genotypes (Ferrara et al., 2014). Pomegranate oil contains phyto-estrogens, which are very similar with the ones produced by the human body (Abbasi et al., 2008). Van Elswijk et al. (2004) isolated from the pomegranate oil steroidal estrogens (g-tocopherol, 17-a- oestradiol, stigmasterol, β-oestriol sitosterol and testosterone) and non-steroidal compounds (compestrol, coumestrol) (van Elswijk et al., 2004).

VII. Alkaloids

The presence of alkaloids was reported in the fruit peel, seeds, bark and in the whole fruit (Sharma et al., 2018), but their identification begins in 1994, when an unusual alkaloid was isolated from pomegranate leaves: N-(20,50 -dihydroxyphenyl)-pyridinium chloride (Schmidt et al., 2005). In 2016, a new alkaloid was discovered, pyrrolidine, isolated from the rid of *Punica granatum*. Pyrrolidine was tested on MDR *Klebsiella pneumonia* and it had efflux inhibition activity at a concentration of 6 mg (Rafiq et al., 2016). The four most studied alkaloids isolated from *Punica granatum* are pelletierine, pseudopelletierine, isopelletierine and methylisopelletierine, the one with the best anthelmintic activity being pelletierine (Wibaut et al., 1954). Piperidine alkaloids were isolated from the roots of different pomegranate cultivars (Jurenka, 20018). Pelletierine, pseudopelletierine, isopelletierine and methylisopelletierine are considered the most importants alkaloids found in *Punica granatum*.

CONCLUSIONS

An analysis of over 100 scientific papers or research from literature highlights the importance of pomegranate for human health and we selected over 70 for this paper. Having a wonderful taste, either sweeter or sour, the pomegranate fruit and its derivates (molasses, juice, concentrate) have a remarkable antioxidant activity compared to other fruits and have a capacity to reduce free radicals. Worldwide, pomegranate is an edible species that still needs to be studied regarding its chemical compounds that are still not totally identified.

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