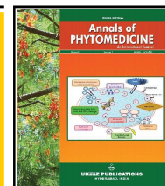


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Pomegranate and its wild genotypes: Nutraceutical opportunities and challenges

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Abstract

The great possibilities of bioactive from fruits and their by-products to maintain or improve health, is increasing the interest in finding new products with positive pharmacological effects. Pomegranate and its wild genotypes play great role as a functional food of interest due to its multiple beneficial bioactive components which exerts protective role towards various degenerative diseases. Furthermore, pomegranate and its different parts such as arils, peel, membrane and seeds contain different bioactive compounds such as ascorbic acid, anthocyanins, gallic acid, ellagic acid, punicalagin, quercetin, etc., which have higher bioactivity due to potential to reduce free radical generation and ability to prevent generation of various diseases. Not only commercial cultivars of pomegranate, but different parts of wild genotypes also possess wide antioxidant potential and antimicrobial activity against food borne pathogens like *Staphylococcus aureus*, *Enterobacter aerogenes*, *Salmonella typhi*, *Klebsiella pneumonia*, *Escherichia coli*, etc. In this review, we highlight different studies on the bioactive compounds of pomegranate and its wild genotypes parts specifically linking them through antioxidant activity with increasing therapeutic effects.

1. Introduction

In the past few years, the natural antioxidants particularly of plant origin has been gaining growing attention as food additives. Antioxidants are generally classified into two types as natural and synthetic antioxidants. The potential toxicity of synthetic antioxidants have given plant products considerable attention toward natural alternatives, which can act as antioxidants to defend against various diseases caused by free radicals. Polyphenols are natural antioxidants present in different concentrations in various parts of pomegranate fruit known as dietary antioxidants and their total dietary intake reported could be as 1 g/day, which is a lot higher than other phytochemicals (Scalbert *et al.*, 2005). Phenolics are the plants; secondary metabolite possessing an aromatic ring bearing one or more than one hydroxyl groups, together with their functional derivatives. Phenolic compounds originate from one of the most important classes of secondary metabolites in plants and classified on the basis of chemical structure (aromatic ring) as well as the pathway by which they are synthesized (*e.g.*, phenyl propanoid, which produces tannins) (Das and Gezici, 2018). Plants have a large range of phenolic derivatives including simple phenols, benzoic acid derivatives, phenylpropanoids, flavonoids, stilbenes, tannins and lignans. Polyphenols as total dietary intake (1 g/day) is

10 times higher than the intake of vitamin C and 100 times higher than the intakes of vitamin E and carotenoids (Scalbert *et al.*, 2005). In recent years, significant progress has been made in curing the cardiovascular diseases and today it is well established that some polyphenols administered as supplements or with food, improve health condition as indicated by a number of biomarkers closely linked with cardiovascular risk.

Pomegranate fruit comprise of four different parts: the non-edible exocarp and mesocarp (peel) and also the edible endocarp which contains the seed, forming the arils. All fruit parts constitute different compounds in varying concentration (Table 1). The pomegranate fruit should be considered as functional food because it has useful compounds in different parts of the fruit that have functional and medicinal effects (Viuda-Martos *et al.*, 2010). Different parts of pomegranate contains different bioactive polyphenolic compounds such as anthocyanins in arils (delphinidin, cyaniding, pelargonidin-3-glucosides and 3,5-diglucosides), hydrolysable tannins in peel (ellagitannins such as punicalagin, punicalin, pedunculagin, granatin A, granatin B) and punicalic acid in seeds (conjugated fatty acids), therefore whole fruit extract can be the interesting dietary supplements (Lansky and Newman, 2007). This fruit has also got various medicinal properties due to presence of various bioactive compounds as well as phenolic antioxidants. Extracts of different parts of the fruit seem to have medicinal benefits (Lansky and Newman, 2007). Pomegranate extracts are being used to treat several parasitic and microbial infections. The seed as well as peel extracts of cultivated and wild form of pomegranate were reported to have important anti-bacterial activities against various micro-organisms (Devi *et al.*, 2011) including microbial activities against *Staphylococcus aureus*, *Listeria monocytogens*, *Escherichia coli* and *Yersinia*

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enterocolitica (Al-Zoreky, 2009). Biological properties of peel (flavedo) are mainly associated with presence of flavonoids and hydrolysable tannins. Polyphenols utilization under permissible limits in products is likely to generate beneficial health effects.

Polyphenols can be used for the development of various nutraceutical/functional foods as well as for the enrichment of various food products. The present review includes the literature pertaining to these studies under the following heads and sub heads.

Table 1: Nutritional value of pomegranate fruit and its by-products

Parameters	Units/100g	Pomegranate (raw)	Pomegranate juice	Pomegranate peel powder	Pomegranate seed powder
Water	g	77.93	85.95	13.70	5.82
Energy	kcal	83.00	54.00	-	-
Protein	g	1.67	0.15	3.10	13.66
Total lipids	g	1.17	0.29	1.73	29.60
Carbohydrate (by difference)	g	18.70	13.13	80.50	13.12
Fiber (total/crude)	g	4.00	0.10	11.22	39.36
Total sugars	g	13.67	12.65	-	-
Calcium (Ca)	mg	10.00	11.00	342.00	229.20
Iron (Fe)	mg	0.30	0.10	6.11	10.88
Magnesium (Mg)	mg	12.00	7.00	56.00	-
Phosphorus (P)	mg	36.00	11.00	120.00	481.10
Potassium (K)	mg	236.00	214.00	150.00	434.40
Sodium (Na)	mg	3.00	9.00	68.00	33.03
Zinc (Zn)	mg	0.35	0.09	1.08	5.54
Copper (Cu)	mg	0.16	0.02	0.65	3.82
Selenium (Se)	mg	0.0005	0.0003	1.07	0.23
Manganese (Mn)	mg	0.12	0.10	0.86	2.26
Vitamin A (ERA)	mg	-	-	0.181	0.089
Thiamin (B ₁)	mg	0.07	0.02	0.141	0.930
Riboflavin (B ₂)	mg	0.05	0.02	0.09	0.146
Niacin (B ₃)	mg	0.29	0.23	-	-
Pantothenic acid (B ₅)	mg	0.38	0.29	-	-
Pyridoxine (B ₆)	mg	0.08	0.04	-	-
Folate (B ₉ , DFE)	µg	38.00	24.00	-	-
Vitamin C (ascorbic acid)	mg	10.20	0.10	13.26	3.02
Vitamin E (α-tocopherol)	mg	0.60	0.38	413	1.35
Fatty acids (total saturated)	g	0.12	0.08	23.04	8.1 (seed oil)
Fatty acids (total monounsaturated)	g	0.09	0.06	20.76	8.6 (seed oil)
Fatty acids (total polyunsaturated)	g	0.08	0.05	56.20	82.0 (seed oil)

DFE: Dietary folate equivalent; ERA: Equivalent to retinol activity

Source: USDA (2020); Omer *et al.* (2019); Rowayshed *et al.* (2013).

2. Antioxidant potential

Generally, plants and plant products are rich sources of natural antioxidants including vitamins (ascorbic acid, vitamin A and α-tocopherols), carotenoids and phenolic compounds. The recent interest in the bioactivity of the flavonoids from plant sources is due to the potential health benefits of the phenolic compounds as important dietary antioxidants. They exist in the form of vitamins, minerals, anthocyanins, phenols and tannins in various foods including wild pomegranate as well in cultivated pomegranate (Table 2). Reactive oxygen species (ROS) toxic effects depend on its ability to destroy important and sensitive biological substrates, such as DNA, RNA, proteins, and membrane lipids. ROS include superoxide radicals, lipoperoxides, hydrogen peroxide and hydroxyl free radicals. Pomegranate peel's antioxidant function is related to its phenolic compounds in the form of anthocyanins, gallotannins, ellagitannins, gallagyl esters, hydroxybenzoic acids, hydroxycinnamic acids, and dihydroflavonol. Pomegranates have the highest concentration of punicalagin and studies have shown that

punicalagin has the properties of antioxidants, antifungal and antibacterial. Pomegranate punicalagin alpha and beta forms are polyphenolic hydrolysable tannins, and 2,3-(S)-hexahydroxydiphenoyl-4,6-(S, S)-gallagyl-D-glucose isomers (Ismail *et al.*, 2012). Ascorbic acid is an antioxidant naturally found in fruits and vegetables which play an important role in the prevention of various diseases. Ascorbic acid content in the range of 9.23 to 22.48 mg/100 g has been observed in various wild pomegranate genotypes grown in Kashmir valley and in HP (Wani *et al.*, 2014; Thakur *et al.*, 2018). Pande and Akoh (2009) have reported ascorbic acid content as 1.4 to 4.2 and 20.3 to 37.3 mg/100 g (FW) in seeds and peels of six pomegranate cultivars. However, Barros *et al.* (2014) have reported vitamin C content in pomegranate peel as 0.21 ± 0.1 mg/g (ascorbic acid equivalent/g of freeze dried peel). Sorour *et al.* (2014) have reported ascorbic acid content in fresh pomegranate fruit peel and seeds as 1.44 and 0.16 mg/100 g, respectively. In Ganesh and Mridula cultivars, Hota and Dahiya (2017) reported ascorbic acid content as 10.52 and 13.81 mg/100 g, respectively.

Table 2: Range of various phytoconstituents in different parts of pomegranate fruit

Type	Fruit part	Ascorbic acid (mg/100 g)		Activity/Health effects
Wild	Arils	10.52 - 13.81		<ul style="list-style-type: none"> •Acts as antioxidant •Can remove superoxide and hydroxyl radicals
Cultivated		1.40 - 29.41		
Cultivated	Flavedo	1.44 - 37.30		<ul style="list-style-type: none"> •Essential for the biosynthesis of collagen •Natural antioxidant, potent reducing agent that efficiently quenches potentially damaging free radicals produced by normal metabolic respiration of the body. Prevent initiation and progression of several chronic and acute diseases
Wild	Arils	Anthocyanins (mg/100 g)		<ul style="list-style-type: none"> •Water soluble pigment responsible for red color of arils acts as free radicals scavenger •Dietary antioxidants that help prevent neuronal diseases, cardiovascular diseases, cancer, diabetes, inflammation, and many other diseases
Cultivated		9.65 - 22.15		
		3.40 - 180.70		
Wild	Arils	Total phenols (mgGAE /100 g)		<ul style="list-style-type: none"> •Polyphenols are reducing agents and together with other dietary reducing agents, such as vitamin C, vitamin E and carotenoids, they protect the body's tissues against oxidative stress. •Flavonoids protect cell constituents against oxidative damage through scavenging of free radicals. •The bioactivity exerted by these compounds has been associated with reduced risk of severe diseases.
		84.64 - 103.97		
Cultivated	Pulp	164.4 - 2380.0		<ul style="list-style-type: none"> •Commonly referred to as antioxidants, they may prevent various diseases associated with oxidative stress, due to antioxidant potential as well as their antimicrobial properties, anti-inflammatory activity, anticancerous, antitumor activity and reduces coronary heart diseases.
	Flavedo	18.0 - 5990.0		
	Seeds	2.0 - 89.2		
	Albedo	177.4-0 - 2149.00		
Wild	Arils	Total flavonoids (/100 g)		
		(mg QuE)	(mg CE/RE)	
		31.75 - 41.89	-	
Cultivated	Pulp/juice	5.4 - 99.20	84.0 - 458.0	
	Flavedo	1.2 - 821.0	5640	
	Seeds	1.50 - 11.2	760 - 6460	
	Albedo	162.0 - 706.0	-	

GAE: Gallic acid equivalent; QuE= Quercetin equivalent, CE=Catechin equivalent, RE=Rutin equivalent.

Sources: Gill *et al.* (2000); Scalbert *et al.* (2005); Pande and Akoh, (2009); Ardekani *et al.* (2011); Thakur *et al.* (2011); Shiban *et al.* (2012); Zaouay *et al.* (2012); Al-Rawahi *et al.* (2013); Mansour *et al.* (2013); Rowayshed *et al.* (2013); Ali *et al.* (2014); Barros *et al.* (2014); Sorour *et al.* (2014); Mphahlele *et al.* (2014); Wani *et al.* (2014); Fernandes *et al.* (2015); Li *et al.* (2015); Ambigaipalan *et al.* (2016); Li *et al.* (2016); Asadi- Gharneh *et al.* (2017); Hota and Dahiya (2017); Derakhshan *et al.* (2018); Thakur *et al.* (2018)

2.1 Anthocyanins

Anthocyanins are a sub-class of flavonoids that are responsible for the brilliant red, blue and purple colour of most of the fruits and vegetables. These occur in various chemical forms, both colored and uncolored, according to pH. Though they are extremely unstable in the aglycone type (anthocyanidins), once they are in plants, they are resistant to conditions of light, pH and oxidation which are likely to degrade them. Glycosylation, usually with a glucose at position 3, and esterification with various organic acids (citric and malic acids) and phenolic acids avoid degradation. In addition, the development of complexes with other flavonoids (copigmentation) helps to stabilize anthocyanins (Manach *et al.*, 2004). Gill *et al.* (2000) have reported 30.60 mg/100 ml of total anthocyanins content in fresh arils of Wonderful cultivar. They further reported that anthocyanins were composed of delphinidin-3-5-diglucoside, cyanidin-3,5-diglucoside, delphinidin-3-glucoside, cyanidin-3-diglucoside and pelargonidin-3-glucoside with the concentrations of 4.29, 5.30, 7.60, 12.83 and 0.59 mg/100 ml, respectively. Zaouay *et al.* (2012) and Asadi-Gharneh *et al.* (2017) have proclaimed the

wide range of anthocyanins content from 5.40 to 180.70 mg per 100 g in different pomegranate Persian and cultivars grown in Tunisia. However, anthocyanins content of wild pomegranate fruits ranging from 9.65 to 22.15 mg/100 g from different locations of Himachal Pradesh (HP) and Kashmir has been observed by Wani *et al.* (2014) and Thakur *et al.* (2018).

2.2 Total phenols

Phenolic compounds are those that have a minimum of one aromatic ring connected to one or more hydroxyl groups. There are several thousands of polyphenolic compounds that occur as secondary metabolites of plants. Phenolic compounds such as flavonoids, phenolic acids and tannins are considered to be major contributors to the antioxidant capacity of plants. Polyphenols antioxidant activity is characterized by their phenolic structure and the ability to delocalize unpaired electrons has the strongest activity (Croft, 2006). These antioxidants also possess diverse biological activities, such as anti-inflammatory, anti-atherosclerotic and anti-carcinogenic activities as reported in literature. These activities may be related

to their antioxidant activity. Two types of major polyphenolic compounds are present in pomegranate fruit extract are anthocyanins (delphinidin, cyanidin and pelargonidin), which contribute fruit and juice its color and hydrolysable tannins (punicalin, pedunculagin, punicalagin, gallagic and ellagic acid esters of glucose), which account for 92 per cent of the antioxidant activity of the whole fruit (Gill *et al.*, 2000). Total phenols content as 84.64 to 116.30 mg GAE/100 g in wild pomegranate fruit arils from different locations of HP has been reported in previous studies (Thakur *et al.*, 2011; Thakur *et al.*, 2018). Different workers have reported total phenols content in different cultivated pomegranate cultivars in the broad range from 164.4-2380.0 mg GAE/100 g (Pande and Akoh, 2009; Derakhshan *et al.*, 2018). Peel of this fruit is rich source of various polyphenolic compounds. Rowayshed *et al.* (2013) have reported total polyphenolic content of pomegranate peel powder as 1.40 per cent on dry weight basis. They further reported that polyphenol fractions in pomegranate peel powder contain catechins (868.4 mg/100 g), gallic acid (125.8 mg/100 g), caffeic acid (60.46 mg/100 g), ellagic acid (44.19 mg/100 g), p-coumaric (17.64 mg/100 g) and resorcinol (12.50 mg/100 g). A very high total phenols content as 5990 mg GAE/100 g in fresh pomegranate peel has also been reported by Al-Rawahi *et al.* (2013), whereas, Fernandes *et al.* (2015) have reported total phenols content as 20.39 to 33.87 mg GAE/g in peel and 16.76 to 21.49 mg GAE/g in capillary membrane (pellicle) of pomegranate fruit. Li *et al.* (2016) have reported total phenolic fraction in peel of five pomegranate cultivars as gallic acid (0.18 to 0.41 mg/g dw) and ellagic acid (2.68 to 7.07 mg/g dw). Ambigaipalan *et al.* (2016) have reported total phenolic content as 21.18 mg GAE/g in divider membrane, 17.74 mg GAE/g in mesocarp and 9.38 mg GAE/g in outer layer of peel of pomegranate fruit. Pande and Akoh (2009) have reported total polyphenolic content in seeds of pomegranate fruits as 89.2 mg GAE/100 g (FW). However, Li *et al.* (2016) have reported total phenolic fraction as gallic acid (0.02 to 0.03 mg/g dw) and ellagic acid (0.05 to 0.02 mg/g dw) in seeds of five pomegranate cultivars.

2.3 Total flavonoids

Flavonoids are the most abundant plant polyphenols occurring in fruits with a strong antioxidant activity. Flavonoids also consists water soluble pigments that are present in the plant cell vacuoles. They have basic structural unit $C_6-C_3-C_6$, comprises two phenyl rings together with one heterocyclic ring fused. They are divided into 6 subclasses: flavonols, flavones, isoflavones, flavanones, anthocyanidins, and flavanols (catechins and proanthocyanidins) (Manach *et al.*, 2004). These are reported to be active against various bacterial disease, oxidation, viral diseases and algesia. These are widely distributed as essential secondary metabolites in plants and have many health benefits due to active against free radicals (Das and Gezici, 2018; Nooreen *et al.*, 2018). Pande and Akoh (2009) have reported individual flavonoid content as 92.1 to 99.2 mg/100 g (FW) quercetin equivalent in pulp of 6 pomegranate cultivars, whereas, Ardekani *et al.* (2011) have reported total flavonoids content ranging from 0.84 to 2.14 mg CE/g in pulp extract of nine Persian pomegranate cultivars. Mphahlele *et al.* (2014) have reported a little higher amount of total flavonoids content (3.35 to 4.58 mg CE/ml) in juice extracted from Wonderful cv. of pomegranate fruit. Thakur *et al.* (2018) have reported total flavonoids content of wild pomegranate fruits ranging from 31.75 to 41.89 mg QuE/100 g from

4 different locations of HP. A very low amount of flavonoids content as 0.054 to 0.335 mg QuE/ml has been reported in ten Chinese pomegranate cultivars by Li *et al.* (2015). Pande and Akoh (2009) have reported individual phenolic content as 66.7 to 77.1 and 10.6 to 11.2 mg QuE/100 g (FW) in peel and seeds of 6 pomegranate cultivars. Total flavonoids as 56.40 ± 2.70 mg RE/g in methanolic extract of pomegranate peel have been reported by Shibani *et al.* (2012). Total flavonoids in pomegranate peel as 1.2 to 2.9 mg QuE/100 g (dw) have been reported by Mansour *et al.* (2013), whereas, Fernandes *et al.* (2015) have reported range of total flavonoids content as 492.0 to 821.0 mg QuE/100 g in peel and 162.0 to 706.0 mg QuE/100 g in capillary membrane (pellicle) of pomegranate fruit. Ali *et al.* (2014) have reported higher total flavonoids content in pomegranate seed as 64.6 ± 0.68 (methanol extract) and 7.60 ± 0.25 mg RE/g (ethyl acetate extract on dry weight basis). Fernandes *et al.* (2015) have reported range of total flavonoids content as 1.50 to 2.90 mg QuE/100 g in seeds of pomegranate fruit.

2.4 Antioxidant properties

The disease prevention mechanism is attributed to the antioxidant properties of polyphenolic compounds. So far no literature on antioxidant activity of wild pomegranate fruit has been reported, however, in commercial cultivars it has been reported widely (Table 3).

2.4.1 DPPH (2,2-Diphenyl-1-picrylhydrazyl) radical scavenging activity

DPPH (2,2- Diphenyl-1-picrylhydrazyl) radical is one of the few stable organic nitrogen radicals, which bears a deep purple colour. This assay is based on the measurement of the reducing ability of antioxidants toward DPPH. Antioxidant assays are based on measurement of loss of DPPH colour at 515 nm after reaction with test compound (Prior *et al.*, 2005). DPPH antioxidant activity of wild pomegranate fruits ranging from 32.11- 40.72 per cent from different locations have been reported by various researchers (Thakur *et al.*, 2018). Whereas, Akhavan *et al.* (2015) have also reported lower range of antioxidant activity as 18.8 to 46.8 per cent in pomegranate juices from 10 different Iranian cultivars. Kulkarni (2005) has reported antioxidant activity of pomegranate pith and capillary membrane as 3.35 ± 0.04 per cent, 92.1 ± 0.32 per cent and 94.5 ± 0.02 per cent in chloroform, ethyl acetate and methanol extracts, respectively. Orak *et al.* (2012) have reported DPPH free radical scavenging activity of pomegranate peel extract as 77.02 to 86.36 per cent and in seed extract as 12.07 to 12.65 per cent. A high antioxidant activity in fresh pomegranate fruit peel and seeds as 90.22 and 91.83 per cent, respectively has been observed by Sorour *et al.* (2014). However, Derakhshan *et al.* (2018) have reported antioxidant activity in different parts of pomegranate fruit ranging from 45 to 58 per cent and 26 to 54 per cent in ethanolic extract of peel and seeds, respectively.

2.4.2 FRAP (Ferric reducing anti-oxidant power) assay

FRAP measure the reducing capability based upon ferric ion and assay is based on the rapid reduction in ferric-tripyridyltriazine (Fe^{3+} TPTZ) by antioxidants present in the samples forming ferrous-tripyridyltriazine (Fe^{2+} TPTZ), a blue-colored product (Benzie and Strain, 1996). The reaction detects compounds with redox potentials <0.7 V (the redox potential of Fe^{3+} -TPTZ), so FRAP is a reasonable screen for the ability to maintain redox status in cells and tissues.

Table 3: Range of various antioxidant properties of different parts of pomegranate fruit

Type of fruit	Fruit part	Antioxidant activity (%)	Mechanism
Wild pomegranate	Arils	32.11 - 40.72	<ul style="list-style-type: none"> •DPPH radical is one of the few stable organic nitrogen radicals, which bears a deep purple colour. •This assay is based on the measurement of the reducing ability of antioxidants toward DPPH. •Antioxidant assays is based on measurement of DPPH colour loss at 515 nm after reaction with test compound.
Cultivated pomegranate	Juice	18.8 - 46.80	
	Flavedo	45.0 - 90.22	
	Albedo	3.35 - 94.50	
	Seeds	12.07 - 91.83	
Wild pomegranate	Arils	FRAP ($\mu\text{mol Fe}^{2+}/100 \text{ g}$) 19.37 - 27.65	<ul style="list-style-type: none"> •FRAP measure the reducing capability based on the rapid reduction in ferric-tripyridyltriazine (Fe^{3+} TPTZ) by antioxidants present in the samples forming ferrous-tripyridyltriazine (Fe^{2+} TPTZ), a blue-colored product. •FRAP is a reasonable screen for the ability to maintain redox status in cells and tissues. Reducing power appears to be related to the level of hydroxylation and extent of conjugation in polyphenols.
Cultivated pomegranate	Juice	13.6 - 46782.0	
	Flavedo	82.11 - 282.666	
	Seeds	0.72 - 20.70	
	Wild pomegranate	Arils	
Cultivated	Juice	13.26 - 38.23	
	Flavedo	10.86 - 68.55	
	Seeds	2.10 - 12.06	
	Wild pomegranate	Arils	Reducing power (OD at 700nm) 0.256 - 0.365
Cultivated	Juice	0.090 - 0.290	
	Flavedo	1.01 - 1.89	
	Seeds	0.16 - 0.45	

Source: Guo *et al.* (2003); Kulkarni (2005); Prior *et al.* (2005); Hajimahmoodi *et al.* (2008); Ardekani *et al.* (2011); Orak *et al.* (2012); Sorour *et al.* (2014); Akhavan *et al.* (2015); Anahita *et al.* (2015); Basiri (2015); Gupta, (2015), Aloqbi *et al.* (2016); Thakur *et al.* (2018); Derakhshan *et al.* (2018)

Reducing power appears to be related to the degree of hydroxylation and extent of conjugation in polyphenols. FRAP mechanism is totally electron transfer conducted in acidic pH and rely on hypothesis that redox reactions proceed so rapidly that all reactions are complete within 4 and 6 minutes. Fast reacting phenols that bind the iron or breakdown to compounds with lower or different reactivity are best analyzed with short reaction time (Prior *et al.*, 2005). Thakur *et al.* (2018) have reported antioxidant activity as per ferric reducing antioxidant power of wild pomegranate fruits ranged from 19.37 to 27.65 $\mu\text{M Fe}^{2+}/100 \text{ g}$ from 4 different locations of HP. Antioxidant activity as 279.33 to 467.82 micromol Fe^{2+}/g (FRAP value) in pulp of nine Persian pomegranate cultivars has been reported by Ardekani *et al.* (2011). Akhavan *et al.* (2015) have also reported FRAP in pomegranate aril juice from 10 different Iranian cultivars as 13.6 to 25.9 $\text{mmol Fe}^{2+}/100 \text{ ml}$. However, Guo *et al.* (2003) have reported antioxidant activity of pomegranate pulp, peel and seeds as 3.10 ± 0.12 , 82.11 ± 4.01 and $0.72 \pm 0.05 \text{ m mol}/100 \text{ g}$ as ferric reducing power (on wet weight basis). Hajimahmoodi *et al.* (2008) have reported the antioxidant activity of ten Persian pomegranate cultivar hydroextracts. They further reported the highest FRAP value in pulp and peel in Sour alac (143.9 ± 4.2 micromol/g hydro extract) and Sweet white peel (2826.66 ± 252.75 micromol/g hydro extract) cultivars. Anahita *et al.* (2015) have also

reported ferric reducing antioxidant power of pomegranate juice, seeds and juice with seeds as 32 ± 5.1 , 20 ± 2.8 , and $47 \pm 5.5 \text{ mmol Fe}^{2+}/\text{l}$, respectively. Basiri (2015) has also reported ferric reducing antioxidant power of pomegranate seeds as 20.70, 4.07 and 2.22 $\mu\text{mol Fe}^{2+}/100 \text{ g}$ in water extract, acetone extract and ethyl acetate extract of seeds, respectively.

2.4.3 Metal chelating activity

It measures the chelating activity of ferrous ions by extracts. The inhibition percentage of ferrozine- Fe^{2+} complex formation is measured spectrophotometrically at 562 nm (Orak *et al.*, 2012 and Gupta, 2015). Orak *et al.* (2012) have reported metal chelation capacity of extracts of different parts of four pomegranate cultivars ranging from 13.26 to 38.23 per cent (in juice extracts), 2.10 to 12.06 per cent (in seed extracts) and 10.86 to 68.55 per cent (in peel extracts). They further reported that mean value of metal chelating capacity of different extracts was 37.22 per cent in peel extract, 7.15 per cent in seed extract and 16.19 per cent in juice extract of four pomegranate cultivars. Metal chelating activity as 14.00 per cent in Spanish pomegranate cultivars has been observed by Aloqbi *et al.* (2016). Thakur *et al.* (2018) have reported metal chelating activity of wild pomegranate fruits ranging from 10.45 to 12.57 per cent among 4 different locations of HP.

2.4.4 Reducing power

The reducing power of a compound is related to its electron transfer ability and may therefore, serve as a significant indicator of its potential antioxidant activity. The increased absorbance of reaction mixture at 700 nm indicates the reduced power (Orak *et al.*, 2012). Substances having a reduction potential react with potassium ferricyanide forming potassium ferrocyanide which further reacts with FeCl_3 to form an intense prussian blue complex having maximum absorbance at 700 nm (Gupta, 2015). The reducing power of a compound is related to its electron transfer ability and may therefore serve as a significant indicator of its potential antioxidant activity. Thakur *et al.* (2018) have reported reducing power of wild pomegranate fruits varying from 0.256 to 0.365 (absorbance at 700 nm) from 4 different locations of HP. However, Orak *et al.* (2012) have reported reducing power of different parts of four cultivars as 1.01 to 1.89 (in peel extracts), 0.10 to 0.19 (in juice extracts) and 0.16 to 0.45 (in seed extracts), whereas, by taking the mean values they further reported that the reducing power of peel extract is 4.70 fold higher than seed extract and 10.50 fold higher than juice extract. A wide range of reducing power ranging from 0.090 to 0.290 (in terms of absorbance at 700 nm) has been reported in various Spanish pomegranate cultivars (Aloqbi *et al.*, 2016).

3. Traditional utilization

Pomegranate fruit plant is widely used in curing various ailments. The evidence of these are also mentioned in various texts as use in traditional medicines including the traditional Indian medicine as Ayurveda, Unani and Greek documents for the cure of numerous diseases and ailments as vermifuge bactericide, stimulant, hair dye, to improve the symptoms of respiratory illness (asthma, bronchitis) and inflammation, fever, bleeding disorders (Reddy *et al.*, 2007). The hydroethanolic extract of the whole fruit in the traditional Cuban medicine, was also used to treat respiratory diseases. The parts of pomegranate as peel have also been used since ancient times in the Middle East as textiles colorant because of peel high phenolic and tannin contents (Li *et al.*, 2006). Aqueous pomegranate peel extract (dried peel decocted in water) is obtained by traditionally is used to treat diarrhea, aphthae, dysentery and ulcers (Lansky and Newman, 2007). However, not only the commercial cultivars but its wild genotypes had various therapeutic properties. The utilization of wild pomegranate fruits which is also known as *daru*, is traditionally lies in drying the arils of fruits to prepare a souring product known as *anardana* used in Ayurvedic and Unani medicines (Devi *et al.*, 2011). *Anardana* is dried arils from sour wild pomegranate fruits and mainly used as acidulent in Northern Indian styled chutney with various ingredients such as salt, mint, *etc.*, and other culinary preparations in North India as a replacement of acidic amchur (dried green mango powder). The acidic product *anardana* is also used in preparing digestive candies. The rind or peel of wild pomegranate fruit also has good medicinal value and is used by India's herbal industry on very small scale. However, its conventional uses include preparation of ink for school children to write on Takhti, in dyeing leather, for making FYM (Murtaza and Ahmad, 2017). Devi *et al.* (2011) have found wild pomegranate fruits (*Daru*) are rich in antioxidants, has antibacterial properties and has been found useful in treating dental health. Therefore, ongoing studies should focus on developing new pomegranate

derived products to benefit from these constituents throughout a healthy life cycle.

4. Nutraceutical opportunities/properties

ROS (Reactive oxygen species) created from interaction with ionizing radiation or xenobiotics during normal cellular metabolic processes are well-recognized concausal factors in many chronic diseases, including cardiovascular diseases and cancer. The lethal effects of ROS might be dependent on their capability to damage appropriate and sensitive biological substrates, such as DNA (deoxyribonucleic acid), RNA (Ribonucleic acid), proteins and membrane lipids and they include various radicals such as superoxide radicals (O_2^-), lipoperoxides, hydrogen peroxide (H_2O_2) and hydroxyl free radicals (OH^\cdot). The use of therapeutic agents as anti-oxidative and anti-proliferative in the form of phytonutrients and nutraceuticals from various fruits and vegetables had opened a new potential way for protecting, preventing and cure of certain malignancies due to reservoir of natural antioxidants (Ismail *et al.*, 2012). In these way pomegranate and its wild genotypes byproducts plays important role since ancient times due to high pharmacological potential of each parts as used in ayurveda. There are many studies on the reported evidence of health benefits of various pomegranate parts on humans as well as on animals in recent times (Table 4). Aviram *et al.* (2000) analyzed the effect of pomegranate juice consumption by healthy males in 2 human studies. In the first study aged 20-35 years were supplemented with 50 ml pomegranate juice/day (1.5 mmol total polyphenols) for 2 weeks and in subsequent study, for ≤ 10 weeks, three subjects were supplemented with increasing doses of pomegranate juice (20-80 ml/day, equivalent to 0.54-2.16 mmol total polyphenols/day). The study shows that juice had strong antiatherogenic effects in healthy males lying on preventive lipoprotein oxidation due to decreased low-density lipoprotein susceptibility toward aggregation as well as retention and improved activity of serum paraoxonase by 20 per cent. The study shows that potent antioxidative capacity of juice against lipid peroxidation may be the innermost link for the antiatherogenic effects of juice on lipoproteins, macrophages and platelets. In another study by Esmailzadeh *et al.* (2004) have reported the effect of pomegranate juice (concentrated) intake (40 g) on lipid profiles of diabetic patients (type II) with hyperlipidemia (≥ 200 mg/dl total cholesterol or triglycerides). After completion of the study (8 weeks) decrease were noticed in total cholesterol level (5.43%), low-density lipoprotein cholesterol level (9.24%), total/High-density lipoprotein cholesterol proportion (7.27%) as well as LDL/HDL proportion (11.76%). Pomegranate juice has higher content of flavonoids and phenols including tannin which have many health benefits including significant antiatherosclerotic activity. Kaplan *et al.* (2001) have prepared concentrated pomegranate juice, by squeezing the whole fruit and diluted in water as 6.25 ml of concentrated juice in 1 liter of water. This solution was fed to the mice an average of 5 ml/day (0.875 mmol equivalent of total polyphenols/d). The study revealed that mice with highly developed atherosclerosis pomegranate juice supplementation decreased macrophage oxidative stress, macrophage cholesterol flux furthermore even attenuated the progress of atherosclerosis. Afaq *et al.* (2005) have reported fruit extract of pomegranate provide clear indication of anti skin tumor-promoting effects in CD-1 mouse due to strong anti-inflammatory along with antioxidant properties of the extract

(anthocyanins, ellagitannins and hydrolyzable tannins). They reported that extract application resulted in a substantial decrease of ODC and cyclooxygenase-2 skin edema, hyperplasia, epidermal ornithine decarboxylase activity and protein expression, which are classic markers of tumor and inflammation promotion. In another study, anti-inflammatory and antioxidant substances prevent the probability of delayed wound healing. In general, various active substances of pomegranate can act as antibacterial, anti-inflammatory and have strong antioxidant activity. The increased dosage of standardized extract of pomegranate (40 % ellagic acid) ointments shows important effects of collagen formation and 10 per cent this standardized extract ointment is helpful for the healing of second-degree burns in rats (Lukiswanto *et al.*, 2019). Different

studies have also reported role of pomegranate extract in preventing as well as reducing pathogenic dental bacteria which leads reduction in the risk of gingivitis, plaque and periodontal disease. Hajifattahi *et al.* (2016) have reported that pomegranate petal hydroalcoholic extract (50% water and 50% ethanol) had high inhibitory antibacterial effect on very common oral bacteria, such as *Streptococcus salivarius*, *S. sanguinis*, *S. mutans*, *S. sobrinus* and *Enterococcus faecalis*. The maximum antibacterial effect observed against *S. mutans* with minimum inhibitory concentration of 3.9 mg/ml and showed maximum zone of inhibition zone against *S. sanguinis* and minimum against *E. faecalis*. The bioactive compound in various parts of pomegranate has also shown antiviral properties that modulate respiratory infections and influenza by inhibition of

Table 4: Nutraceutical potential of pomegranate fruit and its by-products extracts

Type/Health status	Fruit part/Extract used/ Dose/Time (days)	Health effects/Source
Humans: Healthy men	Pomegranate juice (fruit squeezed and enzymatically treated with pectinase to yield juice); 50 ml/d for 14 d and 20-80 ml/d for <70 d.	Reduced LDL susceptibility to aggregation and retention; increased activity of serum paraoxonase (esterase which protect against lipid peroxidation) by 20 % (Aviram <i>et al.</i> , 2000).
Mice: Apolipoprotein E-deficient with atherosclerosis	Pomegranate juice (6.25 ml concentrated juice was diluted in one litre of water); 5 ml/d for 60 d.	Reduction in macrophage oxidative stress, macrophage cholesterol flux and attenuated the development of atherosclerosis (Kaplan <i>et al.</i> , 2001).
Humans:Diabetic patients (Type II) with hyperlipidemia	Concentrated pomegranate juice; 40 g/d for 56 d.	Decrease in total cholesterol (5.43%), LDL-cholesterol (9.24%), LDL/HDL-cholesterol (11.76%) and total/HDL-cholesterol (7.27%) (Esmailzadeh <i>et al.</i> , 2004).
Humans:Diabetic patients (Type II)	Pomegranate juice (Juice obtained by squeezing fruits then filtration, pasteurization, concentration); 50 ml/d for 90 d.	Decreased lipid peroxidation levels and cellular uptake of oxidized LDL (Rosenblat <i>et al.</i> , 2006).
Humans:Active healthy men	Pomegranate juice; 500 ml/d for 15 d.	Potent anti-inflammatory, anti-muscle damage and anti-thrombocytopenia. Decreased systolic blood pressure, creatinine and muscle damage parameters (Achraf <i>et al.</i> , 2017).
Albino Wistar rats: Diabetic	Aqueous flower extracts (500 g air-dried flowers powder were extracted with water in soxhlet for 6 h); 250 mg/kg/d for 21 d.	Reduction in total cholesterol, triglycerides, LDL-cholesterol, Increase: HDL-cholesterol (Bagri <i>et al.</i> , 2009).
Mice: CD-1 mice	Pomegranate fruit extract (freeze dried extract of arils squeezed in 70% acetone (1:20 by w/v); 2 mg for 48 h.	Possesses antiskintumor-promoting effects in CD-1 mouse (Afaq <i>et al.</i> , 2005).
Humans: Ulcerative colitis patients	<i>Punica granatum</i> peel aqueous extract (1 kg peel powder mixed/ liter of boiling water for 6 h and concentrated to 100 mg extract); 6g/d for 28 d.	Decreased Lichtiger colitis activity index, effective in complementary management of UC (Kamali <i>et al.</i> , 2015).
Humans: Women patients with dyslipidemia	Pomegranate peel extract (500 mg dried 80% ethanolic extract encapsulated along with rice flour 50 mg); 500 mg/d for 56 d.	Decrease in systolic blood pressure, LDL and total cholesterol; increase in HDL-cholesterol (Haghighian <i>et al.</i> , 2016).
Humans: Diabetes mellitus type-2 patients	Pomegranate peel extract (vacuum oven dried 70 % ethanolic extract); 500 mg/d for 56 d.	Attenuated the systolic and diastolic blood pressure in type-2 diabetic patients, hypolipidemic, hypoglycemic, antioxidative potential (Grabez <i>et al.</i> , 2019).
Humans: Overweight and obese patients	Whole pomegranate fruit extract; 1000 mg/d for 30 d.	Anti-inflammatory effect; decreases body weight, serum glucose, total cholesterol, LDL; Increases HDL (Hosseini <i>et al.</i> , 2016)
Male albino rats	Whole pomegranate fruit extract; 10 % (twice/d) for 14 d.	Accelerates the healing of deep second-degree burn wound (Lukiswanto <i>et al.</i> , 2019)

RNA replication (Ismail *et al.*, 2012). Moradi *et al.* (2017) have observed anti-influenza A viruses activity of the pomegranate (70% ethyl alcohol) extracts by using of MDCK cell line and MTT (3-[4,5-dimethylthiazol-2-yl]-2,5-diphenyltetrazolium bromide) method. The extract anti-influenza A virus activity could be possibly to its phenolic compounds. The pomegranate extract antiviral activity may be related with the existence of hydrolysable tannins along with polyphenols, specifically punicalagin and gallagic acid (Reddy *et al.*, 2007). In patients with type 2 diabetes mellitus, Grabez *et al.* (2019) reported the effects of pomegranate peel extract (70 % ethanol) intake on plasma lipid profile, fatty acid levels and blood pressure. They reported extract significantly lowered both systolic and diastolic blood pressure. However, plasma levels of triglycerides, low-density lipoprotein cholesterol/high-density lipoprotein cholesterol ratio (LDL-C/HDL-C) were significantly decreased, while the level of HDL-C was increased. Haghghian *et al.* (2016) have observed a positive effect of pomegranate peel extract (500 mg daily for 8 weeks) consumption in improving cardiovascular risk factors in obese women with dyslipidemia. The most common type of inflammatory bowel diseases is Ulcerative colitis, is characterized by inflammation and ulceration of the mucosal layer of the colon. Kamali *et al.* (2015) have observed *P. granatum* peel extract seems to be effective in complementary management of ulcerative colitis through consumption of *P. granatum* peel aqueous extract (equivalent to 6 g of dry peel/day) for four weeks. Hosseini *et al.* (2016) have observed that pomegranate extract may reduce complications linked with obesity as is great source of antioxidants and when 1000 mg of pomegranate extract supplemented in individuals with obesity and overweight daily for 30 days resulted in a considerable decrease in serum levels of glucose, insulin, total cholesterol, LDL-C and increased HDL-C significantly.

5. Antibacterial activity

The pomegranate peel is reported to have several health benefits due to the presence of various constituents like tannins, flavonoids, alkaloids and organic acids (Malviya *et al.*, 2014). The antimicrobial activities of phenolic compounds have involved the multiple modes of action like degradation of cell wall, interaction with the composition and disruption of cytoplasmic membrane, precipitation of membrane proteins resulting in microbial cell lysis (Ismail *et al.*, 2012). The range of antibacterial activity reported in literature has been mentioned in Table 5. Duman *et al.* (2009) have reported that extract of pomegranate arils show remarkable antibacterial activities against all the tested bacterial strains (*Pseudomonas aeruginosa*, *Staphylococcus aureus*, *Escherichia coli*, *Enterococcus faecalis*, *Rhodotorula rubra*, *Candida albicans*). Devi *et al.* (2011) have compared antibacterial activity of different parts (peel, white membrane and seeds) of pomegranate with wild pomegranate and reported that all parts showed significant inhibition zone against *Streptococcus* sp., *Lactobacillus* sp., *Staphylococcus* sp., and *Proteus* sp. Nuamsetti *et al.* (2012) have reported antibacterial activity against *Bacillus subtilis*, *Staphylococcus aureus*, *Escherichia coli* and *Salmonella typhimurium* in different extracts (hot water, 95% ethanol and acetone) of pomegranate peels and arils by agar well-diffusion method. They further reported that Gram-positive bacteria were generally more sensitive to the extracts than Gram-negative ones, as highest inhibition zones were recorded for *E. coli* as 30.3 mm in acetone extract, followed by ethanol (29.0 mm) and

hot water extract (27.0 mm), whereas, for *S. aureus* highest inhibition zones as 34.0 mm in ethanol extract have been observed. Malviya *et al.* (2014) have tested antibacterial activity of pomegranate peel extracts against four bacterial strains like *Staphylococcus aureus*, *Enterobacter aerogenes*, *Salmonella typhi*, *Klebsiella pneumoniae* and reported that extracts show remarkable antibacterial activities against all the tested bacterial strains. The antibacterial activity of peel of pomegranate may be due to the presence of broad spectrum antimicrobial compounds that act against both Gram positive and Gram negative bacteria. However, Abdolahi *et al.* (2018) have reported that flower extract of pomegranate also shows antimicrobial activities against *Escherichia coli*, *Staphylococcus aureus*, *S. epidermidis*, *Enterococcus faecalis*, *Pseudomonas aeruginosa*, and *Klebsiella pneumonia*.

6. Challenges in utilization and limitations

Pomegranate fruit arils usually used for table purpose since medial time by peoples. But other parts didn't receive any commercial attention due to difficulty of its astringency because of high tannin content as well polyphenolic compounds. Pomegranate peel is still underutilized in food systems because astringency is the key restrictive factor in its exploitation as food regardless of its exceptional nutritional as well as ethnopharmacological potential. The harsh sensation of pomegranate peel depends on the formation of tannin-salivary protein complexes. Tannins undergo precipitation in the oral cavity as they are exposed to histatins and proline rich proteins. With the production of precipitated tannins and salivary proteins, especially salivary glycoprotein complexes, haze formation is further enhanced (Kallithraka *et al.*, 2001; Dinnella *et al.*, 2009). Despite the complexity of its astringency, however, dietary use of pomegranate peel is increasingly seen as of immense value. By virtue of its nutritional composition, peel could be realistically utilized as a important ingredient in food products (Viuda-Martos *et al.*, 2010) to easily supplied macro as well as micro-nutrients such as minerals, vitamins, β -carotene, polysaccharides and fibre (Rowayshed *et al.*, 2013; Omer *et al.*, 2019). However, wild pomegranate fruit characteristics totally differs that of commercial pomegranate fruit due to its specific growing conditions as well as in terms of production of highly acidic fruits rich in organic acids which have thick flavedo. Although, it is widely found growing in natural habitat of Himachal Pradesh, Uttarakhand, Jammu and Kashmir, which also lead to wide variation in its fruit characteristics. Due to highly acidic nature of wild pomegranate cannot be used for table purpose and its traditional utilization lies in the dried seeds along with pulp (arils) which is known as *anardana*. The fresh arils of wild pomegranate contain high level of organic acid (3.88 % as citric acid) (Thakur *et al.*, 2018) and it has been used in Indian traditional chutneys and other dishes as souring agent but its fruits commercial potential yet to be tapped besides *anardana* production. A number of formulations of *anardana* have been used as ayurvedic medicines in the treatment of dysentery, diarrhea etc. But at commercial scale wild pomegranate arils powder has not got popularize, because of the sensitivity of powder to oxidation due to the presence of high oil content in the seed portion of arils which shortens its shelf life. Besides this some value added products from arils have been already standardized (Thakur *et al.*, 2017; Thakur *et al.*, 2017a; Thakur *et al.*, 2018a; Thakur *et al.*, 2018b). However, like cultivated pomegranate peel,

Table 5: Antimicrobial activity of fruit and its by-product extracts by agar well diffusion method against various micro-organisms

Type of fruit/ Fruit part used	Extract preparation	Micro-organism	Antimicrobial activity (Inhibition zone mm)
Pomegranate peel	5 g powdered peel dissolved in 80% methanol and left in dark at room temperature for 1 h prior to filtration (Whatman no. 1) and centrifugation at 8654 g for 10 min at 5°C. Then extract was membrane filtered (0.45 µm) followed by concentration under reduced pressure at 40°C. Dried extract were then dissolved in 80% methanol (10 mg/ml) (Al-Zoreky, 2009).	<i>Listeria monocytogenes</i> (ATCC 7644) <i>Staphylococcus aureus</i> (MRSA) <i>Bacillus subtilis</i> (ATCC 6633) <i>Escherichia coli</i> (ATCC 10536) <i>Pseudomonas aeruginosa</i> (ATCC 9027) <i>Yersinia enterocolitica</i> (ATCC 23715)	20 16 17 16 18 19
Pomegranate (Eksi variety) arils	Arils of fruits (about 100 g lots) were hand-separated and frozen at -20°C. Three replicates were maintained for each analysis, each replicate composed of six pomegranate fruits. Arils from each cultivar were thawed at room temperature and then homogenized in a food processor. Slurries were used to prepare fruit extracts for antimicrobial activity tests (Duman <i>et al.</i> , 2009).	<i>Pseudomonas aeruginosa</i> <i>Staphylococcus aureus</i> <i>Escherichia coli</i> <i>Enterococcus faecalis</i> <i>Rhodotorula rubra</i> <i>Candida albicans</i>	20.7 17.7 26.0 15.7 22.0 23.7
Pomegranate peel		<i>Streptococcus</i> sp. <i>Lactobacillus</i> sp. <i>Staphylococcus</i> sp. <i>Proteus</i> sp.	27 25 25 23
Pomegranate white membrane	Crude solvent extract was prepared by taking 50 g of dried powder sample and extracted by Soxhlet distillation apparatus using methanol. The solvent was removed under reduced pressure in a rotary evaporator until the residue become completely dry (Devi <i>et al.</i> , 2011).	<i>Streptococcus</i> sp. <i>Lactobacillus</i> sp. <i>Staphylococcus</i> sp. <i>Proteus</i> sp.	26 24 25 23
Pomegranate seeds		<i>Streptococcus</i> sp. <i>Lactobacillus</i> sp. <i>Staphylococcus</i> sp. <i>Proteus</i> sp.	25 24 24 20
Wild pomegranate (Daru) peel		<i>Streptococcus</i> sp. <i>Lactobacillus</i> sp. <i>Staphylococcus</i> sp. <i>Proteus</i> sp.	28 26 28 24
Wild pomegranate (Daru) white membrane	Crude solvent extract was prepared by taking 50 g of dried powder sample and extracted by Soxhlet distillation apparatus using methanol. The solvent was removed under reduced pressure in a rotary evaporator until the residue become completely dry (Devi <i>et al.</i> , 2011).	<i>Streptococcus</i> sp. <i>Lactobacillus</i> sp. <i>Staphylococcus</i> sp. <i>Proteus</i> sp.	28 26 27 23
Wild pomegranate (Daru) seeds		<i>Streptococcus</i> sp. <i>Lactobacillus</i> sp. <i>Staphylococcus</i> sp. <i>Proteus</i> sp.	25 24 25 22
Pomegranate arils	50 g of blended peels or arils were mixed with 100 ml of 95% ethanol followed by shaking at room temperature for 18 h and then filtration. The filtrates were concentrated under reduced pressure with a rotary evaporator at 40°C and this crude extract were kept at 4°C until use (Nuamsetti <i>et al.</i> , 2012).	<i>Bacillus subtilis</i> <i>Staphylococcus aureus</i> <i>Escherichia coli</i> <i>Salmonella typhimurium</i>	24.3 20.7 23.7 19.7
Pomegranate peel		<i>Bacillus subtilis</i> <i>Staphylococcus aureus</i> <i>Escherichia coli</i> <i>Salmonella typhimurium</i>	31.0 34.0 29.0 26.3
Pomegranate (Ganesh variety) peel	20 g of ground peel soaked in 100 ml of methanol in the shaking incubator (200 rpm), followed by incubation (37°C) for 24 h. After filtering extract with Whatman No. 1 filter paper, filtrate was stored at 4°C (Malviya <i>et al.</i> , 2014).	<i>Staphylococcus aureus</i> <i>Enterobacter aerogenes</i> <i>Salmonella typhi</i> <i>Klebsiella pneumoniae</i>	24.5 18.2 18.3 11.3
Pomegranate flower	The powdered flowers (10g) were mixed with 100 ml of the ethanol (70%) followed by shaking in rotary (200 rpm for 24 h) at room temperature. After extract filtration with Whatman No. 1 filter paper, filtrate was evaporated to dryness at 40°C in a rotary evaporator and then the extract was freeze-dried (Abdolahi <i>et al.</i> , 2018).	<i>Escherichia coli</i> <i>Staphylococcus aureus</i> <i>Staphylococcus epidermidis</i> <i>Enterococcus faecalis</i> <i>Pseudomonas aeruginosa</i> <i>Klebsiella pneumonia</i>	10 13 19 11 8 11

wild pomegranate peel has also unique astringent taste which is rich source of phenolic and fibre besides minerals. Astringency is the major limiting factor due to which its commercial value is not tapped yet, besides its small scale use by Indian herbal industry. Extract of pomegranate peel can generate toxicity when supplemented excessively above threshold limits. As there are many antinutrients factors in plants based foods which directly or indirectly shows adverse effects on nutrients bioavailability when consumed in excess, but adequate processing methods may lead to reduction in their content before consumption (Hamid *et al.*, 2017). As the use of peel from pomegranate and its extracts for functional and nutraceutical (enrichment/fortification) purposes in food products is on the rise, the toxicological issues deserves the utmost consideration.

7. Conclusion

Based on research on various therapeutic properties over the last decade on different parts of pomegranate and clinical trials, it seems to be a promising food with well-defined remedial benefits. The antioxidant capacity of pomegranate and its parts are linked to the presence of bioactive compounds, such as phenolic compounds. The bioactive compounds associated with pomegranate and its fruit parts such as phenolic acids (gallic acid), flavonoids (anthocyanins) and tannins may possess a strong tools for protective and possibly therapeutic interventions against various human diseases. In addition to that, the possible use of pomegranate extracts as a therapy or adjunct for the prevention and treatment of several disease processes, such as diabetes, cardiovascular disease, atherosclerosis, inflammation, microbial infection, obesity, male infertility, Alzheimer underscores the need for more clinical research. Therefore, current studies should focus on developing novel pomegranate derived products utilizing it's all parts to gain from these bioactive constituents throughout a healthy life cycle.

Conflict of interest

The authors declare that there are no conflicts of interest in the course of conducting the research. All the authors had final decision regarding the manuscript and decision to submit the findings for publication.

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