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Therapeutic efficacy of *Punica granatum* peel in the prevention of hypertension

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ABSTRACT

Pomegranate is scientifically known as *Punica granatum*, extensively cultivated in India that generates million tons of fruit waste mainly peel and pomace annually. Pomegranate peel is a rich source of bioactive compounds as compared to other part of the fruit. Major bioactive compounds present in the peel are ellagic acid, gallic acid, punicalagin, tannins, flavonoids etc. that have the potential to provide many therapeutic applications such as antihypertensive, anti-aging, anti-cancer, anti-inflammatory properties and many more. Hypertension is connected with many diseases such as cardiovascular disease, type 2 diabetes, anti-inflammatory, end stage renal disease, cerebrovascular disease and metabolic syndrome. Finding from several studies exhibits that the presence of bioactive compounds in the pomegranate peel acts as antioxidant which helps to reduce the risk of hypertension by inhibiting the activity of serum angiotensin converting enzyme which eventually decreased the systolic blood pressure. Pomegranate fruit as whole is also known as heart healthy fruit, due to its anti-hypertensive activity which ultimately improves the heart health. Overall this review explores the antihypertensive activity of *P. granatum* peel.

KEYWORDS

Punica granatum, Fruit Waste, Antioxidant, Hypertension, Bioactive Compounds

HOW TO CITE THIS ARTICLE

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High blood pressure or hypertension is one of the major consequences of cardiovascular diseases which include stroke, myocardial infarction and heart failure; cerebrovascular diseases, type 2 diabetes, end stage renal disease and metabolic syndrome, these diseases are the major cause of death and infirmity around the globe. Prevalence of hypertension is about 15% throughout the world which is expected to increase up to 30% by 2025. To avoid the occurrence of these diseases it is necessary to control the blood pressure of the patient either by lifestyle modification, medication or both. Several controlled study indicated that 5 mmHg decline in diastolic blood pressure, reduce the risk of cardiovascular diseases up to 15 to 40% respectively. According to seventh report of joint national committee on prevention, detection, evaluation and treatment of high blood pressure (JNC - 7), initiation of cardiovascular disease is due to the double increment of blood pressure of 20/10 mmHg. JNC - 7 also defined prehypertension at 120 mmHg ≤ systolic blood pressure (SBP) < 140 mmHg and/or 80 mmHg ≤ diastolic blood pressure (DBP) < 90 mmHg. Prehypertension is a medical condition in which development of hypertension in future is 2 fold higher that can be a risk factor for the progression of several other diseases.

It is a major public health issue as many people are unaware because it is mostly asymptomatic at initial stage. Finding suggested that through the intervention, progression of prehypertension can be reduced. Several anti-hypertensive drugs has been introduced, still hypertension remains the major medical problem. This is why the focus has been shifted on products from natural sources to treat the high blood pressure (Asgary *et al.,* 2013, Stowe, 2011). Pomegranate is one the famous edible fruit deliberated as ornamental fruit for Mediterranean people which provide broad application in traditional medicine since ancient times. It is enduring and drought-lenient plant, growing in arid and semiarid regions. They are extensively cultivated in Iran, India and the Mediterranean countries like Turkey, Spain, Morocco, Egypt and Tunisia. Pomegranate is considered as berry but belonging to its own botanical family *Lythraceae* subfamily *Punicaceae*, containing single genus *Punica*, with one main species known as *P. granatum* (Zarfeshany *et al.*, 2014). All parts of the pomegranate plant like peel, juice, seed, flower, bark, leaf and root contains ample amount of phytochemical compounds including flavonoids (e.g. anthocyanins, catechins, quercetin, and rutin), other types of polyphenols, ellagitannins, antioxidants, water soluble vitamins and minerals which provides many therapeutic activities against different types of disorders. Pomegranate contains a juicy volume but the major portion of the fruit is peel, around 50% of fruit weight, 40% arils and 10% seeds. The peel consists of two parts; outer hard structure is called pericarp and the inside soft structure is mesocarp in which the arils are attached (Ranjha *et al.,* 2021, Asgary *et al.,* 2013, Viuda-Martos *et al.,* 2010).

Table 1. Principal bioactive compounds present in different parts of the pomegranate fruit

Fruit Components	Bioactive Compounds	References
Peel	Anthocyanin, Ellagic acid, Gallic acid, Catechin, Quercetin, Rutin, Punicalin, Delphinidin, Punicalagin, Linoleic acid, Caffeic acid, Chlorogenic acid, Coumaric acid Tannin, Luteolin, Pelletierine alkaloids, Qunic acid, Epicatechin, Epigallocatechin-3-gallate, Kaempferol, Kaempferol-3-O-glycoside, Kaempferol-3-O-rhamnoglycoside, Naringin, Cyanidin, Pelarginidin, Delphinidin, Corilagin, Casuarinin, Gallagyldilacton, Pedunculagin, Tellimagrandin, Granatin A, Granatin B.	Prakash *et al.,* 2011, Jacinto, 2018)
Seed	Anthocyanin, Ellagic acid, Gallic acid, Catechin, Quercetin, Rutin, Punicalin, Punicalagin, Coniferyl, Sinapyl, Cinnamic acid, Genistein, Linoleic acid, Caffeic acid, Tannin, Luteolin, Pelletierine alkaloids, Ellagic acid, 3,3'-Di-O-methylellagic acid, 3,3'.4'-Tri-O-methylellagic acid, Punicic acid, Stigmasterol, β-Sitosterol, Daucosterol, Camesterol, 17-α-Estradiol, Estrone, Testosterone, Estriol, γ-tocopherol, Ursolic acid, Oleanolic acid, Genistein, Daidzein	
Juice	Anthocyanin, Ellagic acid, Gallic acid, Catechin, Quercetin, Rutin, Kaempferol, Punicalin,Cinnamic acid,Delphinidin, Punicalagin, Linoleic acid, Caffeic acid, Tannin, Luteolin, Pelletierine alkaloids, Quinic acid, Caffeic acid, Chlorogenic acid, *p*- Coumaric acid, Catechin,Epicatechin, Epigallocatechin-3-gallate, Cyanidin-3-O-glucoside, Cyanidine-3,5-di-Oglucoside, Delphinidin-3-O-glucoside, Delphinidin-3,5-di-Oglucoside, Pelargonidin-3-O-glucoside, Pelargonidin-3,5-di-Oglucoside, α-tocopherol , Corilagin, Casuarinin, Gallagyldilacton	

Peel of the pomegranate is deliberated as agro-industrial waste but it is a good source of bioactive compounds such as tannins (punicalin, punicalagin, pedunculagin, gallic acid and casuarinin), alkaloids, flavonoids (catechin, epicatechin, epigallocatechin-3-gallate, flavan-3-ol, kaempferol, kaempferolerol-3-O-glucoside, kaempferol-3-O-rhamnoglycoside, luteolin, luteolin 7-O-glucoside, Naringin, pelargonidin, prodelphindin, quercetin and rutin) and organic acids which possesses many health benefits. Several studies also indicated that pomegranate peel comprises greater antioxidant activity as compared with flower, leaf, seed and juice (Malviya *et al.*, 2014).

Bioactive Compounds Present in Different Parts of Pomegranate

Bioactive compounds is also called as phytochemical compounds which are particularly found in variety of foods and have the ability to regulate the metabolic processes, resulting in better health advancement. These compounds are mostly found in plant sources such as whole grains, fruits and vegetables, which is when included in the diet in considerable amount provides health benefits beyond the elementary nutrition. Bioactive compounds present in different part of pomegranate are listed below in (table 1).

Anti-Hypertensive Activity of Pomegranate

Anti-hypertensive activity of pomegranate is very effective which acts in various mechanisms due to the presence of polyphenols. In a dose dependent manner it was observed that polyphenols from juice of pomegranate reduce the risk of hypertension through the reduction of serum angiotensin-converting enzyme (ACE) up to 36% which in turns decrease the systolic blood pressure by 5%. It was detected that juice provides protection against vascular diseases which might correlated with the inhibition of oxidative stress and serum ACE activity (Wang *et al*., 2010). A study conducted on small randomized human trials indicated that 50 ml consumption of pomegranate juice provides 1.5 mM of total polyphenols to the patient having severe carotid artery stenosis encouraged the reduction of carotid intermediate thickness (IMT) and also decrease the systolic blood pressure (Aviram *et al*., 2004). Several polyphenols like punicalagin, which is the main compound of the peel increase the synthesis of endothelial nitric oxide (NO) that provides relaxing sensation in the endothelium through the stimulation of endothelial NO synthase (eNOS) that acts as vasodilator which ultimately reduce the blood pressure (Nigris *et al.*, 2007). In a study pomegranate juice is given to the hypertensive patient for about two weeks, showed the significant reduction by 36% of ACE activity due to the antioxidant property of the juice. It was observed that antioxidant therapy used to control the blood pressure in hypertensive patient, because of the oxygen species that contributes to the contraction of endothelium and increase the vascular resistance which in turns decreases the blood pressure.

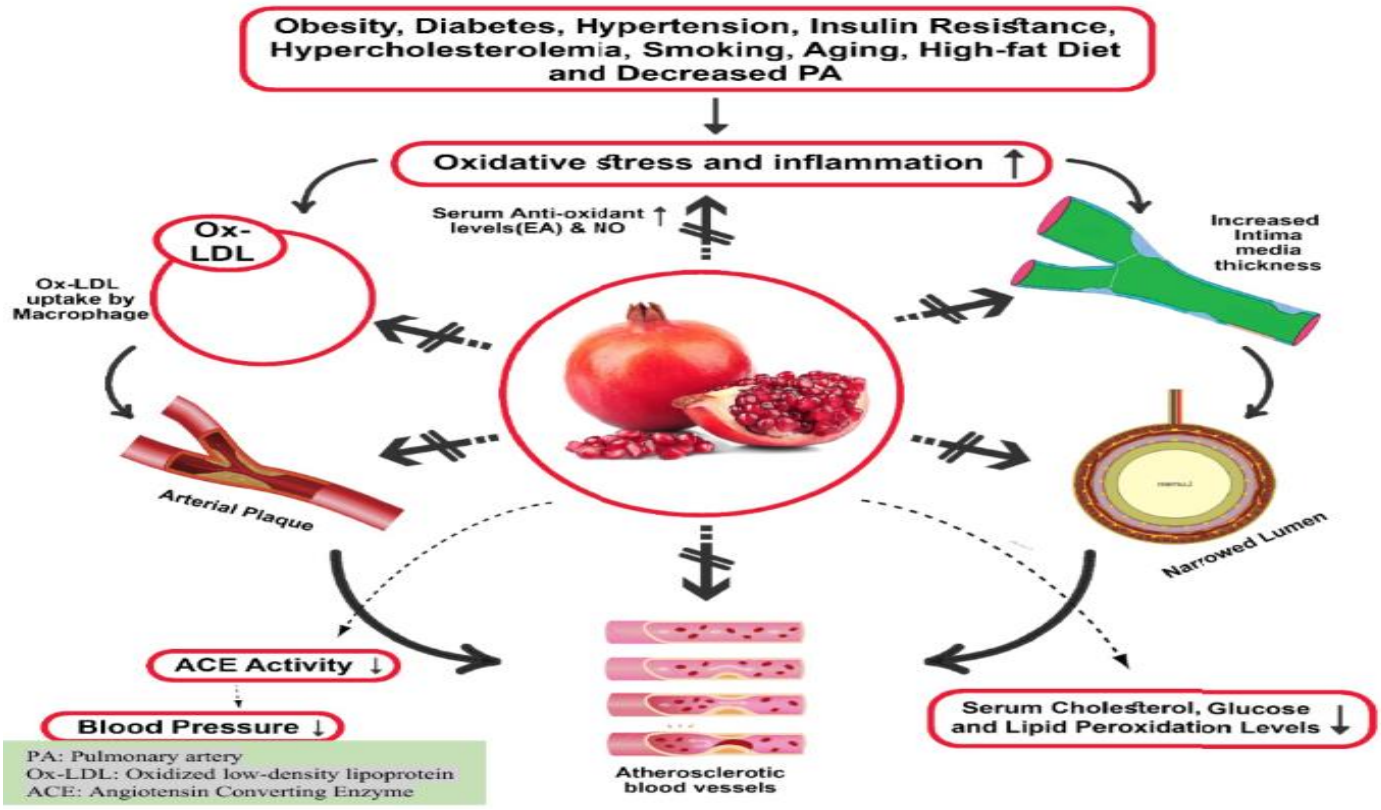

Fig 1. Effect of pomegranate on CVDs (Ranjha *et al.*, 2020)

Additional possibility of the reduction of serum ACE activity by pomegranate juice is related to the effect of cytochrome P-450 enzymes which breakdowns the ACE inhibitory drugs and lowers the activity of serum ACE, thus regulate the blood pressure (Aviram and Dornfeld, 2001). Figure 1 illustrated the effect of pomegranate on cardiovascular disease. Several studies indicated that highest polyphenols was found in peel as compared to juice and seed, but there is no study reported on anti-hypertensive activity of pomegranate peel, only the consumption of juice was detected which prevent the hypertension in some extent. Main focus of this review is to detect the anti-hypertensive activity of peel in future researches.

Conclusion

This review concluded that different parts of pomegranate contain various bioactive compounds that have many beneficial health effects. Researches indicated that highest polyphenolic content was found in the peel which is considered as waste and discarded. It is also proved by several studies that pomegranate juice provides antihypertensive effect by reducing the ACE activity, all the antioxidants and phenolic compounds which is present in juice are also present in the peel in greater extent so the anti-hypertensive activity of peel may also obtained in future research.

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