



Review

Pomegranate (*Punica granatum*): a functional superfruit with therapeutic properties

Granada (*Punica granatum*): una superfruta funcional con propiedades terapéuticas

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ABSTRACT

The Pomegranate (*Punica granatum*) is a fruit that contains innumerable chemical compounds with a high biological value distributed in the bark, carpel membranes, juice (arils) and seeds. The Pomegranate known as a super fruit because of its proven antioxidant power and its health benefits that help slow down the aging process, maintain healthy skin, reduce blood pressure thus fighting heart disease, promote blood circulation, and prevents some types of cancer. The pomegranate has a high content of calcium, magnesium, potassium, and phosphorus (0.01%, 0.012%, 0.236%, and 0.036% respectively), which are part of various enzymes that help prevent alterations in the metabolism of fats and carbohydrates. The purpose of this work was to compile the various investigations on the therapeutic properties of the compounds of the pomegranate.

Keywords: *Punica granatum*; antioxidants; phenolic compounds; gallic acid.

RESUMEN

La granada (*Punica granatum*) es un fruto que contiene innumerables compuestos químicos de alto valor biológico distribuidos en la corteza, las membranas del carpelo, el jugo (arilos) y las semillas. La granada es conocida como una súper fruta por su probado poder antioxidante y sus beneficios para la salud que ayudan a retrasar el proceso de envejecimiento, a mantener una piel sana, a reducir la presión sanguínea combatiendo así las enfermedades cardíacas, a promover la circulación sanguínea y a prevenir algunos tipos de cáncer. La granada tiene un alto contenido de calcio, magnesio, potasio y fósforo (0,01%, 0,012%, 0,236% y 0,036% respectivamente), que forman parte de diversas enzimas que ayudan a prevenir las alteraciones en el metabolismo de las grasas y los carbohidratos. El propósito de este trabajo fue recopilar las diversas investigaciones sobre las propiedades terapéuticas de los compuestos de la granada.

Palabras clave: *Punica granatum*; antioxidantes; compuestos fenólicos; ácido gálico.

1. Introduction

Pomegranate (*Punica granatum*) is the fleshy fruit from the pomegranate tree, which grows in tropical and subtropical areas of the world. The seeds are embellished with a juicy, refreshing, and sweet-and-sour-flavored pulp (Stover and Mercure, 2007). In the world of finance, the main exporters of pomegranate are India, Egypt, Turkey, with 21.2%, 14.3% and 14.2%, respectively, where Peru is located in the eighth place with 3% of world exports (Records, 2019) According to the statistical data of the last years the great increase

exponentially in Peru, passed from 928.2 t in the year 2000 to 46 382.9 t in 2018, registering an annual average rate of 24.3%. Being 2011 (4,526 t) the beginning of large-scale production in the country, and consolidated in 2018 (46,382.9 t), as a result of high global demand for this fruit, could become the star of Peruvian agroexports, following the route of the blueberries.

According to Minagri (2018) in Peru, the departments that contribute to the national production are; Ica with 84.9% in 2018, complementing the commercial production

Arequipa (6.6%), Lambayeque (4%) and Lima provinces (3%), with a joint contribution of 13.6%, in this way the 5 remaining regions (Ancash, Apurimac, La Libertad, Moquegua and Tacna) contributed with 1.5%. Consequently, the importing countries of Peruvian pomegranate are the Netherlands (50.7%), Russian Federation (16.9%), United Kingdom (8.4%), Canada (3.5%), etc. To the extent that campaigns are promoted to disseminate the nutritional and health benefits of this fruit, its consumption will likely grow, as is happening with blueberries and to a lesser extent with aguaymanto and other fruits with antioxidant properties. All components of the Pomegranate, peel, juice, flower, and seed, offer a large number of health benefits' such as the elimination of water and salts through the kidneys so it is considered an excellent diuretic achieving an adequate hydro saline balance of the body (Ragab, 2019). Not to mention its components help in the treatment and prevention of cancer (Fellah, 2018). The most important derivative of the pomegranate is its juice, without a doubt the most studied part with multiple references in scientific literature worldwide (Lucci *et al.*, 2015; Murthy, 2017). The food industry currently needs antioxidants, polyphenols, and other functional nutrients from natural sources to be applied in the development

of new products (Iqbal *et al.*, 2008; Fructuoso *et al.*, 2014). The objective of this research is to provide information regarding the composition and related health benefits of the pomegranate (Lansky and Newman, 2007).

1.1 Composition of the pomegranate

Table 1 shows the proximal composition of the edible and inedible portion of the pomegranate such as bark, root, leaves, flowers, and fruits, which are phenols 2.4 to 9.3 g/l, anthocyanins 0.815 to 7.760 g/l, of juice and polyphenols which give it its bright color, as well as essential vitamins (folate and vitamin K) (Madrigal *et al.*, 2009). The bark and root of the pomegranate contain flavonoids and amino (Alu'datt, 2017). In the leaves, flowers and peels are found tannins, flavones, gallic and ursolic acid which are the most abundant along with quercetin, ellagitannins, luteolin, and apigenin. The seeds make up 12 to 20% of the total weight of the fruit, 99% of the oil extracted from them are triglycerides, 80% is octadecatrienoic acid and in smaller percentages are the sterols, steroids, and cerebrosides. The matrix of the seeds contains hydroxycinnamic acids and lignin derivatives with high antioxidant power.

Table 1
Percentage composition of the pomegranate (g / 100 g)

Values (g / 100 g)	USDA (2009)	de Lama and Tezén (2017)	Calín-Sánchez y Carbonell-Barrachina (2012)
PROXIMAL			
Water	77.93 g	72.6-86.4 g	80.97 g
Energy	83 kcal	-	68 kcal
Proteins	1.67 g	0.05-1.6 g	0.95 g
Total Lipids	1.17 g	0.9 g	0.30 g
Ashes	0.53 g	0.36-0.73 g	-
Carbohydrates (By Difference)	18.7 g	15.47-19.6 g	17.17 g
Total Dietary Fiber	4 g	3.4-5 g	0.6 g
Total Sugars	13.67 g	-	16.57
VITAMINS			
Vitamin C, Ascorbic Acid	10.2 mg	4-4.2 mg	6.1 mg
Thiamine	0.067 mg	-	-
Riboflavin	0.053 mg	0.012-0.03 mg	-
Niacin	0.293 mg	0.18-0.30 mg	-
Vitamin E, Alpha -Tocopherol	0.6 mg	-	0.60 mg
Vitamin K	16.4 mcg	-	4.6 ug
MINERALS			
Calcium	10 mg	3-12 mg	4.6 mg/L
Iron	0.3 mg	0.3-1.2 mg	3 mg/L
Magnesium	12 mg	-	65.8 mg/L
Phosphorus	36 mg	8-37 mg	-
Potassium	236 mg	-	933 mg/L
Sodium	3 mg	-	25.9 mg/L
Zinc	0.35 mg	-	4.4 mg/L
Copper	0.158 mg	-	2.1 mg/L
Manganese	0.119 mg	-	1.9 mg/l

2. All parts of the pomegranate are beneficial to our health

2.1 Pomegranate shell

The peel of the pomegranate (30-40% of the whole fruit) which can be considered an industrial waste product (non-toxic) and non-valuable is one of the most important sources of biologically active compounds compared to an edible pulp (Ragab, 2019). According to (Xie, 2019) phenolic compounds (a class of bioactive phytochemicals) are mainly concentrated in the rind portion of the pomegranate fruit, the main phenolic compounds being flavonoids (anthocyanins, anthoxanthins, tannins, and phenolic acids) (Singh *et al.*, 2018; Yan, 2017). As can be seen in Figure 1 shows the external parts of the pomegranate, indicating which were studied for their clinical benefits, for example:

2.1.1 Antidiabetic power

When our body cannot regulate the sugar concentration in the blood, it is called diabetes. The anti-diabetic capacity of pomegranate husk extract was demonstrated in a study where a solution of pomegranate husk extract and α -amylase enzyme was mixed, the same was done with α -glucosidase. The result was that all samples inhibited both the α -amylase enzyme and the α -glucosidase by 50% (Šavikin and Živković, 2018). Also, Gharib and Kouhsari (2019) they concluded that all this process is attributed to gallic and ellagic acid-reducing blood glucose and increased plasma insulin level, which indicates a high rate of diabetes prevention, this was verified in diabetic lab rats used for the study.

2.1.2 Anti-alzheimer's properties

Alzheimer's is a neurodegenerative disease that causes problems with memory, thought and behavior, and is characterized by a reduction in the level of the neurotransmitter acetylcholine. He claims (Wu, 2019) that pomegranate husk extract exhibits anti-neurodegenerative properties through enzyme inhibition tests that are associated with the development of neurodegenerative disorders. Tyrosinase (Tyr), is a key enzyme in the synthesis of melanin, the formation of neuromelanin (an enzyme associated with hypertension and Parkinson's) and acetylcholinesterase (AChE), the results successfully showed maximum inhibition of these enzymes, gallic acid inhibits AChE and punicalagin for tyrosinase as main compounds of this bioactive (Setiadhi *et al.*, 2019).

2.2 Pomegranate flower

Pomegranate flowers have more antioxidant activity than leaves (Fellah, 2018; Yisimayili, 2019; Zhang *et al.*, 2011). The decoction stops the bleeding and the purging. It has medicinal properties such as infusion of the sprouts that are used to cure chronic diarrhea, especially in children (Liu, 2018; Jafri *et al.*, 2000).

The alcoholic extract of pomegranate flowers has a powerful free radical scavenging, antioxidant activities thanks to anthocyanins and hepatoprotective. It can protect against oxidative damage to lipids and proteins, and to increase/maintain the levels of antioxidant molecules and enzymes in vivo (Abdolahi, 2018; Zhang *et al.*, 2011).

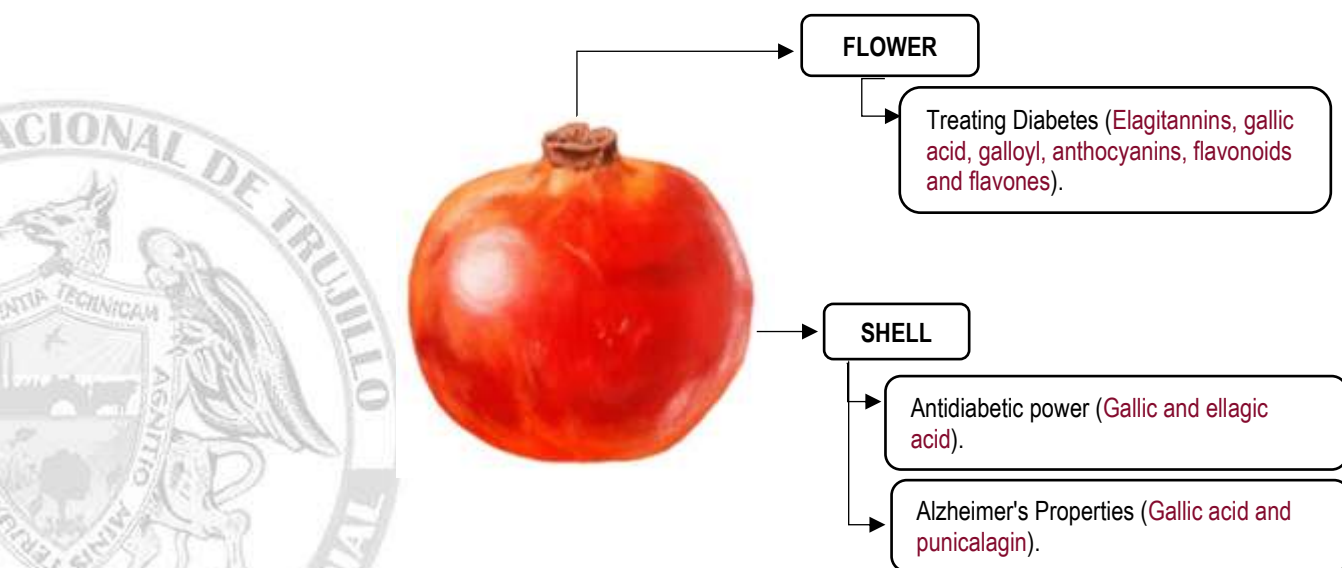


Figure 1. Description of the external parts of the Pomegranate.

It shows strong anti-Alzheimer's activity and can be considered potentially useful as a source of natural anti-AChE and anti-BuChE compounds. According to studies carried out on the pomegranate flowers of 7 varieties, the results showed the activities of cholinesterase against the two types: acetylcholinesterase (AChE) and butyrylcholinesterase (BuChE), with the flowers showing greater anti-AChE activity than the leaves. On the other hand, they show that while the brain's AChE activity decreases continuously, BuChE increases continuously during the progression of the disease (Giacobini, 2004). To date, one therapeutic strategy for the continued management of ellagic acid is the use of agents with the ability to effectively inhibit AChE and BuChE (Mohamed and Rao, 2011).

2.3 Pomegranate juice

Pomegranate juice has recently received a great deal of attention for its health benefit mainly due to its high polyphenol content and related antioxidant capacity (Murthy, 2017). Pomegranate juice (PJ) is the major contributor to the intake of pomegranate containing 85% water, 10% total sugars, 1.5% pectin, ascorbic acid, and

polyphenols (Aviram *et al.*, 2000). As can be seen in Figure 2 shows the internal parts of the pomegranate, indicating which were studied for their clinical benefits, for example:

2.3.1 Anti-cancer properties

In recent years, countless clinical trials have been conducted on the anti-cancer properties of the pomegranate (Núñez-Sánchez *et al.*, 2014). The investigations have shown that pomegranate juice has protective properties against prostate cancer. For prostate-specific antigen (PSA) there was a 14.7% increase in patients who received a dietary supplement consisting of pomegranate, a good source of polyphenols (Thomas *et al.*, 2014). Pomegranate juice, extracts, and whole fruit powder are usually given to patients with early to mid-stage cancer are also used as antidepressants (Valdés *et al.*, 2017).

2.3.2 The pomegranate, an ally against prostate cancer

This disease is the second leading cause of death among men (Lee *et al.*, 2012). In vitro studies have found that pomegranate fruit extract (PFE) and ellagic acid (EA) regulates the expression of the pro-apoptotic genes, Bax and Bak, in the prostate tumor cells (Malik and Mukhtar, 2006).

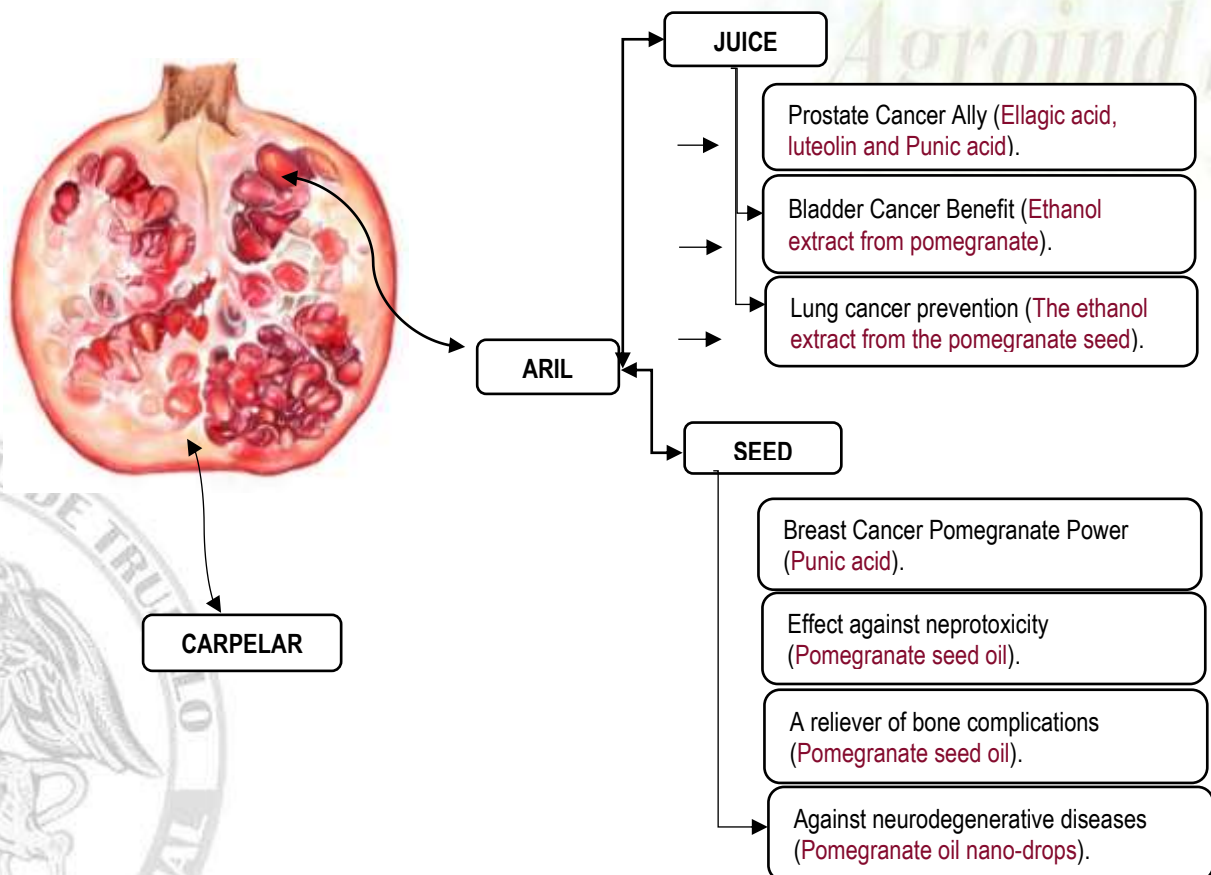


Figure 2. Description of the internal parts of the pomegranate.

Also, [Melgarejo \(2019\)](#) that in vivo using transgenic rats for model prostate adenocarcinoma (TRAP) showed that both pomegranate juice and ellagic acid inhibited prostate tumor growth, proliferation, and progression.

The components of pomegranate juice: ellagic acid (EA), luteolin (L) and puniceic acid (PA) have been found to significantly suppress prostate tumor growth ([Wang *et al.*, 2012](#)). Phenolic compounds were found to exert anti-angiogenic activity and anti-proliferative effects, and induced apoptosis in prostate tumors. Therefore, the pomegranate is an effective chemotherapeutic agent for the treatment of prostate cancer.

2.3.3 Bladder cancer benefits

Bladder cancer is one of the most widespread lethal malignancies of the urinary tract, with poor outcomes for patients with advanced stages of the disease ([Fahmy *et al.*, 2016](#)). Pomegranate is known to be a highly significant functional food playing a crucial role in the treatment of bladder cancer ([Masci *et al.*, 2016](#)). According to [Lee *et al.*, \(2013\)](#) reported that pomegranate ethanol extract (PEE) suppressed tumor cell proliferation of urothelial bladder carcinoma (UBUC). Besides, [Wu *et al.* \(2016\)](#) the study also showed that the ethanol extract has anti-proliferative and apoptotic activities.

2.3.4 Lung cancer prevention

Lung cancer has been identified as the most common cancer worldwide, with about 1.8 million new cases in 2012. They demonstrated ([Banerjee, 2019](#); [Modaeinama *et al.*, 2015](#)) that pomegranate ethanol extract (PPE) and seed extract possessed antioxidant properties and inhibited the growth and proliferation of A549 cells in vitro. Cellular lung carcinoma treatment with pomegranate leaf extract (PLE) inhibited cell invasion and migration via cell cycle arrest in the G2/M phase, reduced matrix metalloproteinase expression, and reduced mitochondrial membrane potential. Taken together, these studies suggest that pomegranate has potent chemotherapeutic properties that exert anti-cancer activities on lung carcinoma by inducing apoptosis, inhibiting cell growth and proliferation, and thereby preventing the migration and progression of lung cancer ([Khan *et al.*, 2007](#)).

2.4 Pomegranate seed

Generally, pomegranate seeds are considered a loss of pomegranate juice production. However,

according to studies seed oil contains 65-80% of conjugated fatty acids, especially puniceic acid ([Gasmi and Sanderson, 2010](#)). As can be seen in Fig.2 these bioactive compounds have a beneficial effect on health and help prevent a variety of diseases, including cancer ([Nemazifard, 2016](#)).

2.4.1 The power of the pomegranate against breast cancer

Breast tumors are the second leading cause of death among women worldwide and are found to be more common in less developed regions ([Chen *et al.*, 2015](#)). Pomegranates have proven to be a promising therapeutic agent against breast tumors ([Rocha *et al.*, 2012](#)).

Studies revealed powerful antioxidant activity of pomegranate seed extract of the Italian variety "Dente di Cavallo" through different mechanisms of action, as well as anti-proliferative activity in the human breast cancer cell line ([Lucci *et al.*, 2015](#)). The effect of puniceic acid inhibits the growth of both an insensitive estrogen line of breast cancer cells (MDA-MB-231) with 92% and an estrogen-sensitive cell line (MDA-ER α 7) with 96%, compared to untreated cells ([Grossmann *et al.*, 2010](#)).

2.4.2 Effect against nephrotoxicity

Applied scientific research in laboratory rats found that pomegranate seed oil was able to protect the kidney against gentamicin nephrotoxicity, improving kidney function, all by reducing urine protein and glucose, reducing serum urea and creatinine, decreasing malondialdehyde (MDA) as an indicator of lipid peroxidation and also increasing thiol content as a protective factor ([Borouhaki *et al.*, 2014](#)).

2.4.3 A reliever of bone complications

Studies on rats have shown that the consumption of 5% granda seed oil (PSO) in the diet has beneficial properties on bone tissue about age ([Mditshwa *et al.*, 2013](#)). It has anti-inflammatory properties and helps against osteoporosis and powerful anti-oxidants both in vitro and in VIVO ([Spilmont *et al.*, 2013](#)).

2.4.4 Pomegranate seed against neurodegenerative diseases

Neurodegenerative diseases are fatal disorders that affect a large number of individuals in our society. Therefore one of the researches is based on the pomegranate oil nano-drops whose specific size generates a strong clinical effect, according to studies the Nano-PSO applied to asymptomatic

mice and already sick mice results in a significant delay of the disease, reduces lipid oxidation and neuronal loss (Mizrahi *et al.*, 2014). This is because Pearl Seed Oil (PSO) protects cellular lipids from oxidative stress, indicating a strong neuroprotective effect, as lipids and protein oxidation are known to be important features of all neurodegenerative diseases (Haider *et al.*, 2011).

3. Critical appraisal

The analysis based on studies about the benefits that the pomegranate offers us is complex. However, it has been possible to demonstrate in multiple articles of experimental investigation, the functional properties of the pomegranate. The information obtained in these articles is directed towards the investigation of innovative methods of treatments using this fruit as an ally to fight inflammatory cardiovascular neurodegenerative diseases, obesity, diabetes, and to delay the effects of cancer. The statistics show us that the health benefits found concerning the pomegranate have been on the rise over the last 6 years. Researchers are currently showing interest in studying the healing properties of this fruit, however, the lack of a research article that compiles in a single document the health benefits provided by the pomegranate. As expected, that future research will focus more on the non-marketed raw materials of the pomegranate helping to complement the experimental studies already conducted.

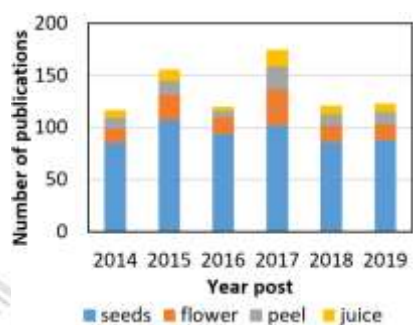


Figure 3. Publications of scientific articles on the pomegranate (*Punica granatum*) information obtained from the Scopus database (search criteria: ARTICLE TITLE, ABSTRACT, KEYWORDS: "Pomegranate" and type of DOCUMENT TYPE: "ALL").

4. Conclusions

The pomegranate (*Punica granatum*) has been defined as a functional food because of its great quantity of antioxidants, which are mostly unknown by those who consume it. For this reason, the scientific studies carried out on this fruit show us its high content of bioactive

compounds and polyphenols that are found in all its parts, mainly in the juice and its peel, which shows that the pomegranate is the fruit that has the most beneficial properties for humans, boosting the immune system and providing the necessary antioxidants used as a natural medicine to prevent bone complications, diabetes, hypertension and help delay the various types of cancer, improving the quality of life of the population.

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