The beneficial effects of pomegranate (Punica granatum L.) consumption on human health: a review

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Agnese Di Napoli 1,2, Federico Germani 1, Francesco Parisi 2, Pietro Zucchetti 1

1 Istituto Italiano di Permacultura, Scagnello (CN), Italy
2 DNA Prolife Srls Unipersonale, Borgo San Lorenzo (FI), Italy

Corresponding author: Agnese Di Napoli, Istituto Italiano di Permacultura, Loc. Gambaldo n.1 Via Torino, 12070 Scagnello (CN), Italy. E-mail: agnesedinapoli@outlook.com

Abstract

The pomegranate (Punica granatum L.) is a small tree or shrub, which is grown in large parts of the world. The medicinal properties of this plant are known since ancient times and are due to the phytochemical constituents found in the plant. The purpose of this review is to describe the health benefits of pomegranate, which are reported in the scientific literature. We performed a literature search, using the PubMed database. We utilised this database to find the research articles published between 2000 and 2021, showing the medicinal properties of oral intake of pomegranate. We included 55 research articles and we found 11 beneficial effects of pomegranate consumption on human health. The effects of this plant comprise those on diabetes, the cardiovascular system, oxidative status, the nervous system, cancer, colitis, metabolic syndrome and obesity, arthritis, the reproductive system, parasitic infections and skin health. Cardiovascular, antioxidant and antidiabetic activities are well reported in the scientific literature and the beneficial properties of pomegranate may be exerted by polyphenols found in the plant. This review describes the health
benefits of oral intake of pomegranate, which are mentioned the scientific literature. The most commonly reported beneficial activities of this plant are antioxidant, cardiovascular and antidiabetic effects. The polyphenol constituents of pomegranate may be responsible for its health properties. Future research is needed to define the beneficial effects of oral intake of this plant and the phytochemical compounds implicated in these activities.

**Keywords:** Pomegranate, Health benefits, Antioxidant, Cardiovascular, Antidiabetic

**Impact statement:** The consumption of pomegranate (*Punica granatum L.*) exerts beneficial effects on human health, such as cardiovascular, antidiabetic and antioxidant activities.

1. Introduction

The pomegranate (*Punica granatum L.*) is a shrub or small tree widely spread in Iran and South Asia and commonly cultivated in many parts of the world (e.g., the Mediterranean region, South Africa, North and South America, Australia, Japan and China) (Magangana et al., 2020; Viuda-Martos et al., 2010). "Punica" comes from the latin words "Punicum malum", which mean "the Carthaginian apple". The latin word "granatum" means "seeded" (Grieve, 1931). *P. granatum* belongs to the Myrtales order and is considered a member of the family Lythraceae or Punicaceae (Kandylis and Kokkinomagoulos, 2020). The plant can reach minimum and maximum heights of 1 and 10 meters, respectively, and can live up to 300 years (Levin, 2006). The pomegranate leaves are elongated and bright-green. The orange-red flowers are flashy and have a bell-shaped calyx. The pomegranate fruit is round, ranges from 8 to 18 cm in diameter, has a leathery rind and a calyx at the top. Fruit skin colour changes from green to yellow to red. The edible seeds and juice are enclosed in arils, which are located inside the fruit (Grieve, 1931; Jurenka, 2008; Levin, 2006; Zarfeshany et al., 2014) (Fig. 1).

The pomegranate is characterized by high nutritional value due to metabolites found in different parts of the plant, such as flowers, leaves, peel, seeds, juice, roots and bark. Sugars (e.g.,
fructose and glucose), organic acids (e.g., citric acid), dietary fibres, proteins, lipids and bioactive compounds are mainly found in pomegranate (Bar-Ya’akov et al., 2019). Various phytochemicals are present in different parts of the plant and are considered responsible for its therapeutic effects, which are known since antiquity (Longtin, 2003). Phytoestrogens and punicic acid are contained in seeds (Shabbir et al., 2017; Zarfeshany et al., 2014) (Fig. 2). The pomegranate is a rich source of polyphenols. The main flavonoids include anthocyanins, luteolin, kaempferol and quercetin. Anthocyanins, which are plant pigments, are found in peel, juice, flowers and leaves. Ellagitannins and gallotannins are hydrolyzable tannins (e.g., punicalagin, ellagic acid, punicalin and gallic acid) present in every part of the plant (Fig. 3). Alkaloids are mainly found in roots and bark (Bar-Ya’akov et al., 2019; Sreekumar et al., 2014).

The pomegranate is consumed mainly as fruit, fresh juice, concentrated syrup, jelly, sauce, jam, tea infusion and plant extracts (e.g., capsules and tablets) (Zarfeshany et al., 2014). The consumption of pomegranate has spread worldwide and many research studies have reported experimental evidence on the health benefits of this plant. In this review, we perform a literature search to find the beneficial effects of oral consumption of pomegranate. This study can help improve our knowledge of the health properties of this plant and its use for preventing and treating different conditions.

2. Methods

We used the PubMed database (www.ncbi.nlm.nih.gov/pubmed) to find previous research studies, which described the beneficial effects of pomegranate consumption. We set the following PubMed options: article type (books and documents, clinical trial and randomized controlled trial), language (English) and publication date (2000 to 2021). We entered six keywords into the database: "Punica granatum", "pomegranate", "Punica granatum therapeutic effects", "Punica
granatum health benefits”, "Punica granatum medicinal properties” and “Punica granatum therapeutic properties”.

After performing the search by keywords, we read the titles and abstracts of the articles and we chose those related to the beneficial effects of pomegranate consumption on human health. Then we read them carefully and we selected the appropriate research articles.

3. Results

Overall, we found 125 research studies, carrying out the literature search, and we selected 55 articles, which were suitable for defining the beneficial properties of pomegranate consumption. We describe 11 health effects of oral intake of pomegranate, which are reported in previous research studies. Our results show that oral consumption of pomegranate exerts beneficial effects on the nervous system, oxidative stress, the reproductive system, colitis, cancer, the cardiovascular system, diabetes, obesity and metabolic syndrome, parasitic infections, arthritis and skin health (Table 1).

3.1. Neuroprotective activity

A study by Siddarth et al. (2020) showed that daily consumption of pomegranate juice over a period of 1 year can exert beneficial effects on visual memory in a sample of 200 aging individuals. Another study found that maternal intake of pomegranate juice exhibits neuroprotective effect in a cohort of 55 newborns with intrauterine growth restriction (IUGR) (Matthews et al., 2019). Bellone and colleagues (2019) showed that pomegranate polyphenol supplements enhance functional and cognitive outcomes, examining 16 stroke rehabilitation patients.

3.2. Antioxidant activity

A previous study by Urbaniak et al. (2018) found that daily oral intake of pomegranate juice increases total antioxidant capacity (TAC) in 19 athletes (i.e., rowers). Mazani and colleagues
(2014) demonstrated that consumption of pomegranate juice limits oxidative damage after exhaustive exercise. Previous research showed that punicalagin present in pomegranate juice has antioxidant activity in 12 human placenta in vivo and in vitro (Chen et al., 2012). Other studies demonstrated that consumption of probiotic pomegranate juice improves antioxidant activity in women with polycystic ovary syndrome (PCOS) (Esmaeilinezhad et al., 2019; Esmaeilinezhad et al., 2020). A study by Heber et al. (2007) found that oral consumption of ellagitannin-rich pomegranate extract exerts antioxidant effects in a cohort of 22 overweight individuals. Another study found that oral intake of pomegranate extract reduces oxidative stress in overweight or obese individuals (Hosseini et al., 2016). Gouda and colleagues (2016) showed improved antioxidant activity in human plasma and urine after daily consumption of polyphenol-rich pomegranate juice in a sample of 35 healthy individuals. Other two studies showed the antioxidant activity of pomegranate juice in diabetic individuals (Rosenblat et al., 2006; Sohrab et al., 2017). Ghoochani and colleagues (2016) found the antioxidant activity of pomegranate juice in a cohort of 38 patients with osteoarthritis (OA), while other two studies demonstrated that consumption of pomegranate extract has antioxidant activity in samples of six (Balbir-Gurman et al., 2011) and 55 (Ghavipour et al., 2017) patients with rheumatoid arthritis (RA). Previous studies showed that drinking pomegranate juice three times per week improved the oxidative status, testing 41 (Barati Boldaji et al., 2020) and 101 (Shema-Didi et al., 2012) individuals undergoing hemodialysis. A research work by Shema-Didi and colleagues (2013) studied 27 patients and found an improvement in oxidative status during a single dialysis session. Another study demonstrated that pomegranate polyphenol extract has beneficial effects on oxidative stress in a cohort of 27 hemodialysis patients (Wu et al., 2015). Guo and colleagues (2008) found increased antioxidant activity after daily oral intake of pomegranate juice in elderly individuals and this activity was probably exerted by polyphenols contained in the plant. Hamoud et al. (2014) showed an improvement of oxidative status in individuals with hypercholesterolemia after consumption of pomegranate extract or placebo pills during statin therapy. A study by Kanlayavattanakul et al. (2020) demonstrated the antioxidant activity of phenolic-enriched pomegranate peel extract in vitro.
3.3. Effects on the reproductive system

Previous studies showed that pomegranate juice consumption ameliorates symptoms and comorbidity of PCOS (e.g., levels of testosterone, metabolic syndrome parameters and cardiovascular risk factors) (Abedini et al., 2021; Esmaeilinezhad et al., 2019; Esmaeilinezhad et al., 2020). Chen and colleagues (2012) found that oral intake of pomegranate juice can prevent placental diseases. Another study demonstrated that pomegranate extract is useful in the treatment of idiopathic central precocious puberty (ICPP) together with gonadotropin-releasing hormone (GnRH) analog therapy, examining a cohort of 210 patients (Liu and Tang, 2017).

3.4. Anticolitis activity

Kamali and colleagues (2015) showed that oral intake of pomegranate peels aqueous extract can improve clinical response in patients with ulcerative colitis. In this study, the Lichtiger colitis activity index (LCAI) was used to evaluate symptoms in a sample of 62 individuals aged 18-65 years. Patients were given pomegranate extract or placebo for four weeks. This study is characterized by a small sample size and is not informative about the mechanisms through which this plant has anti-ulcerative colitis effect, but represents the first experimental evidence that pomegranate can exert this effect in humans. Other research works should confirm these findings.

3.5. Anticancer activity

Previous studies demonstrated that consumption of pomegranate juice and extracts can ameliorate clinical outcomes in prostate cancer, examining samples of 92 (Paller et al., 2013) and 42 (Pantuck et al., 2006) patients. Another study found that this activity can be exerted by polyphenol metabolites (i.e., dimethyl ellagic acid and urolithin glucuronides) (González-Sarrías et al., 2010). González-Sarrías and colleagues (2018) showed that oral intake of pomegranate extracts has a beneficial effect in a cohort of 45 patients with colorectal cancer by decreasing endotoxemia. Other two studies found that pomegranate extracts can regulate microRNAs and gene expression in colorectal cancer tissues (Nuñez-Sánchez et al., 2015; Nuñez-Sánchez et al., 2017). A preliminary
study showed that oral intake of pomegranate juice can be effective on the prevention of breast cancer by decreasing serum sex hormone levels (Kapoor et al., 2015).

3.6. Cardiovascular effects

Previous studies demonstrated that oral consumption of pomegranate juice lowers triglycerides and blood pressure and improves high-density lipoprotein cholesterol (HDL-C) (Barati Boldaji et al., 2020; Shema-Didi et al., 2014) and atherosclerosis (Shema-Didi et al., 2012) in patients undergoing hemodialysis. Wu and colleagues (2015) showed that pomegranate polyphenol extract is able to decrease blood pressure in hemodialysis patients, while Jafari et al. (2020) found that consumption of pomegranate peel extract and vitamin E can improve endothelial function in these patients. A previous study demonstrated that oral intake of concentrated pomegranate juice can lead to a reduction of total and low-density lipoprotein cholesterol (LDL-C) in diabetic hyperlipidemia (Esmailzadeh et al., 2004). Other two research works found that oral intake of pomegranate juice decreases blood pressure, studying 60 diabetic patients (Sohrab et al., 2019) and 30 individuals with metabolic syndrome (Moazzen and Alizadeh, 2017). Mirmiran et al. (2010) demonstrated the beneficial activity of pomegranate seed oil on serum lipids in a sample of 45 individuals with hyperlipidaemia. Another study found that oral intake of pomegranate extract pills has anti-atherogenic activity in subjects with hypercholesterolemia undergoing statin therapy (Hamoud et al., 2014). Mathew and colleagues (2012) demonstrated that individuals who consumed a drink with ellagitannin-rich pomegranate extract displayed inhibition of postprandial improvement in systolic blood pressure after eating a high fat meal, testing a cohort of 19 healthy males. A previous study showed the cardiovascular protective effect of urolithin present in pomegranate extract in a sample of 49 subjects with obesity or overweight (González-Sarrías et al., 2017). Hosseini and colleagues (2016) demonstrated the beneficial effects of pomegranate extract on cardiovascular system in individuals with overweight or obesity. Lynn and colleagues (2012) found that pomegranate juice has a beneficial effect on blood pressure and Razani and colleagues (2017) showed that pomegranate juice has a therapeutic effect in ischemic heart disease. Another
study demonstrated that oral consumption of pomegranate juice exerts health benefits on myocardial ischemia in a sample of 45 individuals with ischemic coronary heart disease (Sumner et al., 2005). Abedini and colleagues (2021) showed that pomegranate juice can prevent cardiovascular diseases, lowering triglycerides and blood pressure and raising HDL-C in a cohort of 42 PCOS patients. A study by Esmaeilinezhad et al. (2020) found that consumption of synbiotic pomegranate juice lowers blood pressure, total cholesterol and LDL-C, while improves HDL-C in a sample of 92 individuals with PCOS.

3.7. Antidiabetic activity

Previous studies showed the beneficial effects of oral intake of pomegranate juice in diabetic patients. Sohrab and colleagues (2019) found that consumption of pomegranate juice improves cardiovascular parameters in a cohort of 60 diabetic patients, lowering diastolic and systolic blood pressure. A study by Banihani et al. (2014) evaluated the effect of pomegranate juice consumption on glucose control in a sample of 85 diabetic patients and found decreased fasting serum glucose and insulin resistance and improved pancreatic β-cell function. Sohrab and colleagues (2018) showed improvement of the inflammatory status (i.e., nuclear factor kappa B (NF-kB) and sirtuin1 (SIRT1) levels) in diabetic individuals, who were given pomegranate juice. Other two research works found an improvement of oxidative status in diabetic patients (Rosenblat et al., 2006; Sohrab et al., 2017). Kerimi and colleagues (2017) demonstrated in a sample of 16 healthy individuals that pomegranate juice consumption can lower blood glucose levels after a bread meal through α-amilase inhibition by punicalagin and polyphenol metabolites, such as urolithins, can regulate glucose metabolism about 3-6 hours after the meal. A previous study by Hosseini et al. (2016) found that pomegranate extract reduces blood levels of insulin and glucose in individuals with overweight or obesity. Another study showed that pomegranate seed oil can ameliorate diabetic parameters in a cohort of 52 individuals with obesity and type 2 diabetes mellitus (T2DM) (Khajebishak et al., 2019). Esmaeilinezhad and colleagues (2019) demonstrated that individuals with PCOS who consumed synbiotic pomegranate juice showed improved glycemic
control, testing 92 patients. A study by Banihani et al. (2020) found that oral intake of pomegranate juice exerts beneficial effects in a sample of 89 diabetic patients, lowering cortisol levels.

3.8. Effects on metabolic syndrome and obesity

Previous studies showed that pomegranate juice consumption ameliorates metabolic syndrome, examining samples of 23 (Kojadinovic et al., 2017) and 30 (Moazzen and Alizadeh, 2017) individuals. Other two studies found that pomegranate juice (González-Ortiz et al., 2011) or extract (Hosseini et al., 2016) has beneficial effects in overweight or obese individuals. González-Ortiz and colleagues (2011) studied a sample of 20 obese participants. Esmaeilinezhad and colleagues (2019) showed reduced weight, waist circumference and body mass index (BMI) in women with PCOS drinking synbiotic pomegranate juice.

3.9. Antiparasitic activity

A study by El-Sherbini et al. (2010) demonstrated the antiparasitic activity of pomegranate extract against Trichomonas vaginalis in vitro and in vivo. Another study showed the beneficial effects of pomegranate extract against Cryptosporidium parvum in calves (Weyl-Feinstein et al., 2014). These works provide experimental evidences of the antiparasitic effect of this plant in animals, humans and in vitro. However, other research studies are required, due to small sample sizes and the need of data replication of these findings. The mechanisms through which pomegranate extracts exert antiparasitic activity should be explained.

3.10. Antiarthritic activity

Previous studies found that pomegranate juice or extract can be beneficial for OA (Ghoochani et al., 2016) and RA (Balbir-Gurman et al., 2011; Ghavipour et al., 2017) by improving the oxidative status. Balbir-Gurman and colleagues (2011) demonstrated the effects of this plant extract in a small cohort of six postmenopausal females with RA, evaluating clinical symptoms and serum oxidative status. The study by Ghavipour et al. (2017) evaluated the effect of pomegranate extract in a sample of 55 patients with RA and found an improvement in clinical symptoms and
blood inflammatory and oxidative stress parameters. Ghoochani and colleagues (2016) studied the health benefits of pomegranate juice in a cohort of 38 OA patients. They demonstrated that this plant can ameliorate clinical symptoms and serum oxidative stress and OA biomarkers.

3.11. Effects on skin health

Previous studies showed that oral intake of pomegranate juice, extract and extract rich in ellagic acid can protect the skin from ultraviolet (UV) radiation (Henning et al., 2019; Kasai et al., 2006). Henning and colleagues (2019) found that consumption of pomegranate juice and extract can improve minimal erythema dose (MED) and reduce melanin concentration in a sample of 74 healthy females. They also demonstrated that pomegranate consumption alters the skin microbiota, but they could not evaluate if the microbiota modification is involved in the UV protection. The study by Kasai et al. (2006) demonstrated the beneficial effect of oral intake of ellagic acid-enriched pomegranate extract in a cohort of 37 healthy women through assessment of melanin, erythema and luminescence values. Kanlayavattanakul and colleagues (2020) demonstrated that phenolic-enriched pomegranate peel extract has beneficial effects against skin hyperpigmentation in vitro through enhanced antioxidant activity.

4. Discussion

In this review, we conducted a literature search to find the health benefits of oral intake of pomegranate. Overall, we show 11 beneficial effects of this plant, including those on the nervous system, oxidative status, colitis, cancer, the cardiovascular system, diabetes, parasitic infections, arthritis, metabolic syndrome and obesity, the reproductive system and skin health.

Our results show that the most commonly reported health property is antioxidant activity, which is described in 20 previous research studies. The beneficial effects of pomegranate on the cardiovascular system is also well reported in the scientific literature and 18 studies showed this plant health benefit. The antidiabetic activity of pomegranate was examined in 10 studies (Table 1). Diabetes is a risk factor for cardiovascular diseases (Leon and Maddox, 2015) and previous
research studies found that oxidative stress is involved in these conditions (Kattoor et al., 2017; Maritim et al., 2003; Sugamura and Keaney, 2011). In this review, we show that oral intake of pomegranate can ameliorate diabetes (Rosenblat et al., 2006; Sohrab et al., 2017) and cardiovascular parameters (Barati Boldaji et al., 2020; Hamoud et al., 2014; Shema-Didi et al., 2012; Shema-Didi et al., 2014) by improving the oxidative status. These beneficial effects may be mediated by pomegranate phenolic compounds and metabolites (Chen et al., 2012; González-Sarrías et al., 2017; Gouda et al., 2016; Guo et al., 2008; Heber et al., 2007; Kanlayavattanakul et al., 2020; Kerimi et al., 2017; Mathew et al., 2012; Wu et al., 2015). Most of the research studies focused on the beneficial properties of pomegranate juice instead of this plant extracts.

Anticancer activity of pomegranate is found in seven research studies and this effect may be attributed to pomegranate polyphenol metabolites (González-Sarrías et al., 2010) (Table 1). Previous research has focused on the activity of pomegranate against prostate (González-Sarrías et al., 2010; Paller et al., 2013; Pantuck et al., 2006), colorectal (González-Sarrías et al., 2018; Nuñez-Sánchez et al., 2015; Nuñez-Sánchez et al., 2017) and breast (Kapoor et al., 2015) cancers. The health benefits of pomegranate on the reproductive system and the beneficial effects of this plant on obesity and metabolic syndrome are reported in five studies (Table 1). In this review, we show that the effects of pomegranate on the reproductive system (Chen et al., 2012; Esmaeilinezhad et al., 2019; Esmaeilinezhad et al., 2020) and obesity or overweight (Heber et al., 2007; Hosseini et al., 2016) can be mediated by improved oxidative status. Polyphenols may exert the beneficial activity on the reproductive system (Chen et al., 2012) and overweight (Heber et al., 2007).

Only few studies reported the beneficial effects of pomegranate consumption on the nervous system, arthritis and skin health (three studies), colitis (one study) and parasitic infections (two studies) (Table 1). The antiarthritic activity is mediated by the antioxidant effects of pomegranate (Balbir-Gurman et al., 2011; Ghavipour et al., 2017; Ghoochani et al., 2016) and phenolic compounds and metabolites, which are present in this plant, may be beneficial for skin health (Henning et al., 2019; Kanlayavattanakul et al., 2020; Kasai et al., 2006).
Future research is required to define the potential health benefits of pomegranate consumption and the phytochemicals involved in these activities. Limitations of this review are the following: most of the research studies utilise small sample sizes, only published articles are included and personal selection criteria are used.

5. Conclusions

This review describes the main beneficial properties of pomegranate consumption previously reported in the scientific literature. We show 11 health benefits of this plant, which include positive effects on the cardiovascular system, oxidative status, diabetes, the nervous system, colitis, cancer, metabolic syndrome and obesity, parasitic infections, arthritis, the reproductive system and skin health. The most commonly reported health properties of oral intake of pomegranate are antioxidant, cardiovascular and antidiabetic activities and polyphenols present in this plant may exert the beneficial effects on human health. Future studies are needed to clarify the health benefits of pomegranate and the mechanisms underlying these activities, as we are still unsure of the potential impacts of this plant and its bioactive compounds on human health.

Abbreviations

- **BMI**: body mass index
- **GnRH**: gonadotropin-releasing hormone
- **HDL-C**: high-density lipoprotein cholesterol
- **ICPP**: idiopathic central precocious puberty
- **IUGR**: intrauterine growth restriction
- **LCAI**: Lichtiger colitis activity index
- **LDL-C**: low-density lipoprotein cholesterol
- **MED**: minimal erythema dose
**NF-kB**: nuclear factor kappa B

**OA**: osteoarthritis

**PCOS**: polycystic ovary syndrome

**RA**: rheumatoid arthritis

**SIRT1**: sirtuin1

**T2DM**: type 2 diabetes mellitus

**TAC**: total antioxidant capacity

**UV**: ultraviolet

**Declarations**

**Funding**

No funding was received for conducting this study.

**Conflict of interest**

The authors declare that there is no conflict of interest.

**Availability of data and material**

All data and material are available upon request.

**Code availability**

Not applicable

**Authors’ contributions**

ADN, FG, FP and PZ contributed to the study conception and design. Literature search was performed by ADN. The first draft of the manuscript was written by ADN and all authors
commented on previous versions of the manuscript. All authors read and approved the final manuscript.

**Ethics approval and consent to participate**

Not applicable

**Consent for publication**

Not applicable

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**FIGURE LEGENDS**
Fig. 1 The pomegranate. A botanical representation of pomegranate ("Punica granatum" by Adriana Morgante Giornetti)

Fig. 2 Punicic acid. 2D structure image of punicic acid. Retrieved from https://pubchem.ncbi.nlm.nih.gov/compound/5281126#section=2D-Structure

Fig. 3 Ellagic acid. 2D structure image of ellagic acid. Retrieved from https://pubchem.ncbi.nlm.nih.gov/compound/5281855#section=2D-Structure
Figure 3
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