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A COMPREHENSIVE REVIEW ON BIOLOGICAL PROPERTIES AND IMPORTANT FINDINGS OF POMEGRANATE

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Abstract

The pomegranate fruit is made of white to deep purple seeds that are enclosed in a white, spongy, astringent membrane, also known as pericarp, covered by a thick red skin and a crownshaped calyx. It contains a variety of beneficial ingredients, including flavonoids, ellagitannin, punicalagin, ellagic acid, vitamins, and minerals. Pomegranates possess numerous health benefits, and their use in disease treatment has been widely recognized since antiquity. This fruit was known to exhibit several biological properties, including anti-inflammatory, antibacterial, antioxidant, and anticancer activities. This review summarizes the information about bioactive compounds of pomegranate and its nutritional studies highlighting the potential role of whole pomegranate biological properties and biological Applications. To study the mechanisms involved, to develop industrial processes for the development of nutraceutical or functional food product.

Keywords: *Punica granatum* L, Hexahydroxydiphenic acid, ellagitannins, ABTS and DPPH.

1. Introduction

The pomegranate (Punica granatum L.), since ancient times, has been a crop exploited by humankind; it belongs to the *Punicaceae* family that grows in tropical and subtropical regions. Its name is derived from the Latin Malum granatum, which means "granular apple". The tree is having a twisted and thorny trunk, elongated green with smooth surfaces leaves and petals of orange or crimson coloration. It adapts very well to variable climatic conditions; the fruit is globose in the shape of 6-12 cm in diameter. The coloration of the pomegranate peel varies from yellow, green, and pink, which in turn can go to intense red and dark purple. According to the previous literature studies show that the edible portion comprises 50% of the total weight and the remaining 50% corresponds to the peel. In turn, the edible portion is comprised of juice (78% w/w) and seeds (22% w/w). A pomegranate fruit with longitudinal cuts, to exhibit all the components analyzed below, it consists of peel, arils, and seeds. The pomegranate plant is native to Iran, cultivated

in Tunisia, Turkey, Spain, Egypt, Morocco, the United States, China, India, and the Near and East Asia. Estimated global pomegranate production was around 3.8 million metric tons in 2017, with India being the largest pomegranate producer with an estimated 234,000 ha and a production of 2.84 million metric tons. India cultivates seventeen types of pomegranates such as "Bhagwa", "Ganesh", "Mridula", "Maskat", " Red Jodhpur", "Jalore seedless" and "Red ruby", among others.

According with the literature pomegranate have a great therapeutic effect, for example, antioxidant and antitumor capacity, with different extracts obtained from distinct parts of the plant, these biological activities are due to the presence of bioactive compounds called "Tannins". Tannins are naturally occurring compounds, distributed in the plant kingdom. The main function of tannins is to be the plant defense against microorganisms and animal attacks, due to their astringent capacity and ability to form complexes with proteins and polysaccharides. Tannins are a large family of phytochemicals, with molecular weights between 500 and 3000 Da¹. They are classified into four groups: complex tannins, condensed tannins, gallotannins, and ellagitannins. One of the remarkable groups within the tannin family, the so-called ellagitannins, formed from gallotannins, by the oxidative coupling at carbon 6 of two gallovl units, forming a hexahydroxydiphenic acid (HHDP) unit and generating a monomeric ellagitannin. Ellagitannins contain one HHDP group which after spontaneous hvdrolvsis dehydrates, followed by lactonization thus forming ellagic acid. Ellagitannins are abundant in some fruits and seeds such as pomegranates, black raspberries, raspberries, strawberries, walnuts, and almonds. Punicalagin is the main ellagitannin in pomegranate peel and its content can reach 65.75% of the total polyphenols in pomegranate peel. Punicalin can be derivate from the punicalagin, and both punicalagin and punicalin after hydrolysis reach to ellagic acid under

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J. Funct. Mater. Biomol. 7(2) (2023) pp 668 – 675

specific reaction conditions².

Usually, consumption of pomegranate is as fresh fruit; however, industrial interest has increased the consumption of other pomegranate products such as alcoholic beverages, juices, jams, and jellies. Furthermore, the industrial application has led to an increase in the production of waste material (shells and seeds), triggering a potential risk of contamination for the environment and encouraging the search for environmentally friendly alternatives that take advantage of the bioactive effect of the components present in the waste material.

This article analyzes and discusses the benefits of pomegranate parts: aril, seed, and peel in terms of their bioactive composition and compounds biological properties. The studies conducted with this fruit, the main conclusions are about the high added value, have estimated the degree of valorization of these by-products and their effect on their use in health for advances in food, medicine, cosmetics, and pharmacy due to their bioactive source compounds. This paper emphasizes the work with the pomegranate peel since it represents 50% of the total weight, considered agro-industrial waste and implies a greater environmental problem, this can be an opportunity for the generation of new industrial applications in food, pharmaceuticals, or/and cosmetics³.

2. Experimental

Pomegranate peel

Worldwide, the pomegranate juice industry produces approximately 1.9 million metric tons of pomegranate peel, which constitutes approximately 50% of the total weight of the fruit. Pomegranate skin is inedible, because in the sensory and organoleptic characteristics dominate the bitter and astringent flavors, and a firm and dry texture.

From the report that pomegranate peels are a rich source of dietary fiber, especially insoluble fiber, 27.11 and 32.51% on a dry weight basis. The pigmentation of the peel is another characteristic that differentiates the varieties, the coloration encompasses yellow, green, and pink shades (which can reach deep red and purple). The intensity of the colors is influence by the chemical structure and concentration of each anthocyanin pigment. Phytochemically speaking pomegranate peel is characterized by the presence of phenolic compounds, high molecular weight, complex polysaccharides, flavonoids such as catechin, epicatechin, quercetin, procyanidins, and anthocyanins such as delphinidin-3delphinidin-3,5-diglucoside, glucoside, cvanidin-3pelargonidin-3glucoside, cyanidin-3,5-diglucoside, glucoside, and pelargonidin-3,5-diglucoside. 2 hydroxycinnamic acids (caffeic and p-coumaric acids) also have identification. In addition to containing appreciable amounts of microelements that have demonstrate important activities such as antimutagenic, antioxidant, apoptotic, and antimicrobial potential⁴.

The method of extraction of any of the abovedescribed compounds present in pomegranate peel is one of the determining variables for their efficient recovery. K. Sheela et.al.

Maceration. Soxhlet extraction. and hvdro distillation are the methods considered conventional for the recovery of bioactive compounds. However, in recent years, technologies such as ultrasound and microwave-assisted extraction have been employed, which are "green" technologies, due to the reduction of solvents and short extraction times. It has reported that in ultrasoundassisted extraction of polyphenols from pomegranate peel using 10 min as extraction time the results indicate that the extraction kinetics are accelerate, and the recovery of polyphenols present in the peels increases. On the other hand, microwave-assisted technology reduces the treatment time by sixty times compared to conventional technologies obtained 1.7-fold higher yields in 4 min compared to the conventional method. The extract obtained reached 94.91% antioxidant activity, attributed to the concentration of punicalagin present in the sample whose concentration is 143.64 mg on a dry basis.

Pomegranate peel fermentation is another reported technology that produces industrially valuable secondary metabolites but is environmentally friendly due to the reduced or low amount of waste generated by this alternative process. Sepulveda et al., (2018) obtained a yield of 47 mg of polyphenols/g of pomegranate peel, from pomegranate peel extracts, by fermentation in a solid medium, the biodegradation of the ellagitannins of the peel was performed to obtain ellagic acid; Ascacio-Valdés et al., evaluated the fungal biodegradation of punicalin, recovered from pomegranate peel, several enzymatic activities were tested (xylanase, xylanase, β-glucosidase, polyphenol oxidase, tannase, and ellagitannin hydrolyzing activities). The results indicated that ellagitannase is the enzyme responsible degradation for the of ellagitannins and ellagic acid with an enzymatic activity of 200.04 U/L5.

2.1 Biological properties of pomegranate peels

Since ancient times pomegranate peel extract has been use by people of Egyptian culture for the treatment of common ailments such as inflammation, diarrhea, and infertility recent research has demonstrated other types of biological activities.

2.1.1. Antioxidant Activity

During cellular metabolic processes, there are reactive oxygen species, such as superoxide anion (hydrogen peroxide (H_2O_2) and hydroxyl radical (HO^-) , which cause diseases such as cancer and cardiovascular diseases, induced by factors such as exposure to ionizing factors and xenobiotics; the toxic effects of reactive oxygen species depend on their ability to damage important and sensitive biological substrates such as RNA, DNA, lipids, and plasma membrane proteins. Pomegranate peel has anti-proliferative effects against breast cancer cell lines demonstrated that the pomegranate peel extracts inhibited the growth of prostate cancer cells, as these extracts could induce apoptosis of this type of cancer. Likewise, anti-carcinogenic capacity has also in colon cancer cell lines ^{6,7}. The compared pomegranate seed, peel, and leaf extracts, showing that the antioxidant capacity of pomegranate peel, seed, and leaf extracts was 55.3%,

35.7%, and 16.4% respectively, such results were attributed to the phenolic content of the peel extract, which was found to be 2.8 times higher than pomegranate leaf extract; reported the highest pomegranate peel extract removal activity of (DPPH) 2,2-diphenyl-1-picrylhydrazyl and 2,2'-azino-bis [3-ethylbenzothiazoline-6-sulfonic acid] (ABTS), among mango, kinnow, banana and loquat fruits⁸(figure 1).



Fig 1: Benefits of *Punica granatum* peel 2.1.2 Antimicrobial activity

Pomegranate peel extracts have been studied as effective agents to treat or prevent different infections different pathogens consumption caused by of pomegranate peel extract by oral gavage with 100 mL (300 mg/kg) showed that it is possible to reduce up to 75%, 20 days post-infection, Giardia lamblia cyst counts in male Swiss albino mice (Mus musculus) likewise. experimental groups with pomegranate peelingestion showed protection to infection 10 days after initiation of supplementation. Similar studies with pomegranate peel extract have resulted in coccidiosis caused by the pathogen Eimeria *papillata* have attenuated inflammation and injury of the jejunum, as well as decreased cyst production⁹.

Similarly, in vitro studies have shown inhibition effects on pathogenic bacteria, specifically against gram-positive bacteria, *i.e.*, Propionibacterium acnes, Staphylococcus aureus, and Bacillus subtilis. Similarly, showed that punicalagin from crude peel extract of (*P. granatum* L.) inhibited the growth of cariogenic Streptococcus mutans after 6 h of exposure to 1.56, 3.125, 6.25 mg/mL crude peel extract, biofilms of S. mutans biofilms were reduced by 94.76, 96.6 and 90.97% respectively, this finding proposes that pomegranate peel extract has the potential to prevent dental caries; it has been reported that punicalagin from pomegranate by-products inhibit the growth of pathogenic clostridia and Staphyloccocus aureus.

Furthermore, it has been reported in the literature that methanolic extracts of pomegranate peel are significantly effective against bacterial strains such as Shigella dysenteriae serotype 2, Salmonella typhimurium, and *Escherichia coli*; together, according to another study in mice, decreased pathogenicity was reported for infections caused by Citrobacter rodentium bacteria similar to *E. coli* that infects mice, is a model to study bacterial pathogenesis and the health benefits of food additives and their impact on the microbiota because it replicates aspects of the enteropathogenic bacterial infections in humans, such as gastrointestinal pathogens. This finding indicates that pomegranate polyphenols may be a source of beneficial compounds for the treatment of intestinal disturbances.

addition, antifungal activity studies In of methanolic extracts of pomegranate peel have been evaluate in against Penicillium expansum, Penicillium digitatum, and Botrytis cinerea. The viabilitv of B. *cinerea* conidia. incubated for 20 h. result inhibited with 12 g/L and strongly reduced by 94 and 80% at 1.2 g/L, respectively, compared to the control demonstrated that pomegranate peel extracts could inhibit the growth of Trichophyton mentagrophytes, T. rubrum, Microsporum canis, and *M. gypseum fungi* at the conidial and hyphal stages, with MIC (Minimum Inhibitory Concentration) values of 125 mg/mL and 250 mg/mL, respectively, for each genus¹⁰.

2.1.3 Antiviral activity

In recent years, the popularity of pomegranate has been increasing due to its proven antiviral effects. One of the compounds within the pomegranate peel responsible for its antiviral properties has been gallic acid. Gallic acid (GA), known as 3,4,5-trihydroxy benzoic acid, is a phenolic compound obtained found within fruits and vegetables, especially pomegranate conducted a study evaluating the effects of GA on Hepatitis C virus (HCV) expression examined using an HCV sub genomic replicon cell culture system expressing HCV non-structural (NS) proteins. GA down-regulated NS5A-HCV (~55%) and HCV-RNA $(\sim 50\%)$ protein expression levels in a time-dependent manner compared to levels in untreated cells. Thus, GA treatment showed to decrease cellular oxidative stress by reducing the production of reactive oxygen species ROS, which disfavors HCV. Therefore, GA is a promising adjuvant in HCV therapy. Furthermore, GA does not induce cytotoxicity at concentrations of 100 and 600 mg/mL¹¹.

An important finding within the antiviral capacity of pomegranate peel has been against the influenza virus, this capacity has been attributing to the inhibition of influenza virus RNA replication. Punicalagin compounds have inhibitory activity at concentrations up to 40 mg/mL and are the most active in blocking viral RNA replication. Recently, SARS-CoV2 emerged as a highly contagious pathogen, causing the pandemic disease COVID-19, with a case fatality rate of 3%. Currently, there are no antiviral drugs available to cure patients with COVID-19. One expectation for the current situation is to resort to secondary metabolites extracted from fruits and vegetables, as they have antiviral properties against COVID-19. Punicalin and punicalagin have been reported to have an attenuating effect on the ability of Sglycoprotein, involved in virus binding to specific receptors on host cells, in addition, angiotensin-converting enzyme2 (ACE2) also demonstrated that the bioactivity of pomegranate peel extracts can be attributed to urolithin A, which is a natural compound from the gut microbiome of humans, produced in the colon after microbiome-mediated transformation of natural polyphenols, which are contained in products such as pomegranate. What is

J. Funct. Mater. Biomol. 7(2) (2023) pp 668 - 675

attributed to pomegranate peel extracts and urolithin A is a significant effect in blocking the S-glycoprotein-ACE2 contact. Another study reported the affinities and interactions between gallic acid, ellagic acid, punicalagin, and punicalin from pomegranate peel extract on four protein targets selected according to the process of virus entry into a host cell¹². The targets were SARS-CoV-2 spike glycoprotein, angiotensin-converting enzyme two, furin, and SARS-CoV-2 transmembrane serine protease. The results showed that punicalagin and punicalin influence significant interactions with target proteins, thus they have considered alternatives for *in vivo* evaluations (Table 1).

Fruit Part	Metabolites	Refs.
Peel	Esteroles, γ - tocopherol and δ -tocopherol and α -tocopherol, punicalagin, flavonoids such as catechin and epicatechin	(<u>Elfalleh et al.,2011</u>) (<u>Muñiz-Márquez et al.,</u> <u>2021</u>)
Peel and juice	Anthocyanins, delphinidin-3- glucoside, delphinidin-3,5- diglucoside, cyanidin-3- glucoside, cyanidin-3,5- diglucoside, pelargonidin-3- glucoside and pelargonidin- 3,5-diglucoside.	(Noda et al., 2002) (<u>Fischer et al., 2011</u>)
Seed & seed oil	Amino acids, nucleosides, phenolic acids, flavones, and coumarins, Vitamin E, palmitic, stearic, oleic, linoleic,	(<u>Li et al., 2020</u>) (<u>Tian et al., 2013</u>).
Seed oil	and punicic acids Steroids, testosterone, b- sitosterol, and campesterol. hydroxybenzoic acids (gallic acid) and ellagic acid) and 2 hydroxycinnamic acids (caffeic acid and p- coumaric acid).	(Abbasi, Rezaei, & Rashidi, 2008; Eikani, Golmohamma d & Homami, 2012)

2.1.4 Other health benefits

On the other hand, pomegranate peel has other beneficial health effects, such as anti-inflammatory and anti-allergic effects. The inflammatory response contains the activation of white blood cells, the release of immune system chemicals, and the production and release of inflammatory mediators and prostaglandins. Lox and Cox are the two most important enzymes for arachidonic acid prostaglandins which generate metabolism. and cyclooxygenases (COX) and lipoxygenases (LOX), which are the inflammatory mediators. The cyclooxygen-ase (COX) and lipoxygenase (LOX) inhibitory activity of a flavonoid present in pomegranate peel, identified as (2E)-3- (4-hydroxy-3-pentylphenyl)-1- (2-hydroxy-4,5-di (E)prop-1-enyl) phenyl) prop-2-en-1-one (Sudheesh et al., 2018). This is attribute to the polyphe-nolic nature of the compound, which operates as a free radical scavenger or inhibitor, or proceeds as a primary oxidant thereby inhibiting inflammation. According to research, an antiallergic effect demonstration, mention that pomegranate peel extracts standardized to contain 13% w/w ellagic acid inhibited the release of β -hexosaminidase from antigen-stimulated rat basophilic leukemia (RBL-2H3) cells, the results indicated that the standardized pomegranate peel extract possessed marked inhibitory activity with IC50 values of 20. 9 and 4.3 g/mL, respectively, which elucidated that pomegranate extracts standardized to obtain 13% w/w can function therapeutically with anti-allergic effects13.

Another biological property that has been reported about the pomegranate peel, is its antidiabetic and hypolipidemic activity, as they have given effective results in in vitro studies; this could be due to the pres-ence of bioactive compounds such as alkaloids, flavo-noids, saponins, and tannins, which may act in inhibiting α -glucosidase and increasing glucose uptake.

Likewise, pomegranate peel extract has demonstrated the ability to combat degenerative diseases, incited by oxidative stress, such as Alzheimer's dementia, as its activity improve learning and long-term memory.

2.2 Pomegranate peel applications

The high demand for products made from pomegranate may pose an environmental problem as it involves the disposal of vast amounts of peel. It is neces-sary to explore the opportunity area that this waste has in the industrial sector, given that pomegranate peel is a source of bioactive compounds that have a wide range of biological properties that are being valued and studied by different research groups, examples of which were detailed earlier in the paper to expand the applications that can be obtained from waste such as pomegranate peel, several researchers have been working on the search for useful products, in addition to making their uses more attractive to each specific audience and obtaining econom-ic benefits. The following is a description of different applications in which the use of pomegranate peels and/or their components can be exploit.

J. Funct. Mater. Biomol. 7(2) (2023) pp 668 - 675

2.2.1 Applications in food products

Currently, animal health and nutrition directions are using fruit peels as animal feed. Such peels also contain a significant amount of minerals and nutrients necessary for healthy animal development and are rich in carbohydrates, crude fiber, crude protein, and ash. Currently, there is a wide variety of viable applications as stabilizers, feed preservatives, and quality enhancers of pomegranate peel extract components. The following is a description of work in which the efficacy of pomegranate peel extracts in feed matrix application has evaluated.

Biopolymer films developed in recent decades for their use in food, as they as considered as a barrier that pro-tects food from environmental factors such as oxygen, ultraviolet light, water vapor, pressure, and heat. Research has indicated that pomegranate peel extracts can improve the functional characteristics of chitosan, zein, and gelatin-based materials for film formation as food coatings collaborated with a fish gelatin film, in which they added pomegranate peel extract and used a control without extract. The result showed that the films with pomegranate peel extracts significantly improved, the antioxidant properties of the films in ABTS and DPPH radical scavenging activity tests14-16. This is due to the compounds present punicalagin, ellagic acid, and other flavonoids such quercetin, kaempferol, and luteolin glycosides as possessing phenolic hydroxyl groups that transfer hydroxyl groups to free radicals, thus quenching these harmful species and consequently, an antioxidant capacity response occurs, The reported on the efficacy of encapsulated pomegranate peel extract in improving the shelf life of hazelnut paste by inhibiting its oxidation, the results indicated that the maximum en-capsulation efficiency was 99.80%. Other contributions in the literature applied to the encapsulation of pome-granate peel extracts provided, who evaluat-ed microencapsulation conditions with maltodextrin, showing that after 90 days of storage at 4°C, there were no significant differences in phenolic content. Evaluated the use of cookies as a food matrix, where they observed that pomegranate peel extracts encapsulated from orange juice residues are ideal for supplementing the matrix with functional metabolites, however, baking the cookie resulted in losses in phenolic content of 65 and 76% of the encapsulated extract and crude extract17.

3. Aril

In the pomegranate fruit, the edible part is the arils which constitute 52% of the total weight of the fruit, comprising 78% juice and 22% seeds. According with "Aril" definition is a tegument, attached to the hilum that totally or partially envelops the seed; years later, the concept changes to pulpy structures that grow from parts of the ovule, or funiculus, after fertilization, and that cov-er part or all the seed. Arils have a transparent, pink, red, or whitish coloration and are separated by membranous walls and white tissue, aril coloration, total soluble sol-ids, and acidity are commonly used in the evaluation of fruit quality to meet industry requirements. The arils are constituted by a juicy and fleshy edible layer that devel-

ops from the outer epidermal cells of the seed, which are largely elongated in a radial direction. Arils are mainly composed of water, sugars, and pectins, they are an excellent source of minerals such as potassium, phosphorus, calcium, iron, manganese, zinc, and copper; it also presents a considerable content of fiber and vitamin C; in addition, they are rich in anthocyanins which are watersoluble pigments, flavonoids that are present in several edible fruits and plants, specifically pomegranate and berry. Such compounds are glycosides made up of aglycones, the most common of which are delphinidin, pelargonidin, peonidin, petunidin, cya-nidin, and malvidin. The presence of other metabolites has also been reported, such as phenolic acids, main-ly ellagic acid, and gallic acid, which belong to the hydroxybenzoic acids; in addition, the presence of chlorogenic acid, caffeic acid, and p-coumaric acid, which are part of the hydroxycinnamic acids, has also been demonstrated 18-20.

4. Seed

4.1 Biological properties of the seed

The properties possessed by the pomegranate seed, are due to the punicic acid, recent studies have elucidated the possibilities of application since the bioactive properties help the human body to fight cancer, heart disease, diabetes, and obesity. The pomegranate seed extract has demonstrated in vitro and in vivo studies, the antiatherogenic effect of punicic acid to prevent the dangerous accumulation of harmful cholesterol, LDH (low-density cholesterol) in the arteries, in that study 51 peo-ple were treated with 800 mg of pomegranate seed oil twice a day for 4 weeks, the results showed a significant decrease in the level of high-density lipoproteins. Now, another biological property present in pomegranate seed is the pro-female fertility effects, attributed to its constit-uent, βsitosterol, which acts as a non-estrogen receptor-mediated mechanism. In addition, β -sitosterol plays a vi-tal role in the maintenance of bones, the central nervous system, and in the cardiovascular system21. Type two di-abetes disease has been on the rise over the last 20 years, affecting more than 415 million people worldwide. This disease diagnosed, through increased blood sugar levels, urinating very frequently at night, losing weight without intending to, being constantly hungry, and having very dry skin, among others; attributed to an abnormality in insulin secretion. It is worth mentioning that is, also, influenced by genetic elements, however other environ-mental factors such as low physical activity, high caloric intake, and increasing obesity, reflect current trends, which are conducive to the prevalence of such disease22-26.

Studies have reported hypolipidemic activity, i.e., reduction of blood lipid levels, attributed to the punicic acid contained in the pomegranate seed described earlier in this paper demonstrated the beneficial effects of punicic acid in human hepatoma cells; the conclusions mention the significant decrease in the secretion of apolipoprotein B100, a component of low-density lip-oprotein. Furthermore, in the same study, they worked with Otsuka Long Evans Tokushima Fatty rats, which is an exclusive line of rats to study type 2 diabetes with obesity, and it

J. Funct. Mater. Biomol. 7(2) (2023) pp 668 - 675

was observed that the rats remained thin when pomegranate seed oil was added to the diet, be-cause fat cells could undergo programmed cell death, re-ducing glycemic values when exposed to punicic acid from the seed oil. In another study with patients suffering from obesity with type 2 diabetes, performed supplemen-tation with capsules containing 3 g of pomegranate seed oil daily for 8 weeks, showing that blood glucose de-creased significantly at the end of the study27-29.

Regarding the anticarcinogenic properties exert-ed by pomegranate seed, Kohno et al. (2004) reported that pomegranate seed oil is rich in conjugated linolenic acids, and these compounds can inhibit or reduce the in-cidence of multiple colon adenocarcinomas. According to another similar study, Hora et al. (2003) determined the chemopreventive efficacy of skin cancer in mice induced by topical exposure to 7,12-dimethylbenzanthracene and 12-O-tetrade-canoylphorbol 13-acetate (TPA). From figure 2 the results indicated that mice treated with 5% pomegranate seed before each TPA exposure had significantly decreased tumor incidence and multiplicity, demonstrating the potential of pomegranate seed oil as a chemopreventive agent30-35.



Fig 2: Biological Properties of pomegranate seed

4.2. Applications of the seed

Concerning the biological activities that pomegranate seeds contain, studies have demonstrated the capacity they possess and their therapeutic and nutraceutical applications.

The main use of pomegranate seed is oil extraction, which has a wide range of applications, from food preservation to food production. Being the best natural source of punicalagin and punicic acid the nutritional value of pomegranate is quite commendable. It exhibits antioxidant, hepatoprotective, anticancer, and neuroprotective properties considered high value that can help improve health36.

During the last decades, studies have shown, how pomegranate seed oil, has been beneficial application as feed for animal production, meat, and milk, since the demonstration that this oil, enriches the products derived from these animals, to give a higher quality to the product as food, reported how by supplementing goat feed with pomegranate seed oil, milk fat content increased without affecting protein content. Regarding the evaluation of the acid profile observed an increase fatty in monounsaturated fatty acids, polyunsaturated fatty ac-ids, and conjugated linoleic acids, and a decrease in saturated fatty acids37-38.

Recently, seed oils are receiving increasing interest due to their high yield of both hydrophilic and lipophilic phytochemicals, as they have the potential for nutritional, pharmaceutical, and cosmetic purposes. Considering the valuable lipophilic compounds, which are present in the oil extracted from the pomegranate plant the demand has increased; due to the biological properties present such as: anti-inflammatory, antimicrobial, antioxidant, and antiseptic.

Squalene and phytosterols are bioactive compounds widely used in cosmetics for skin protection, showing advantages for the skin as an emollient, antioxidant, and moisturizing agent, so oils rich in these compounds are essential in the pharmaceutical and cosmetic industry. From the different fruit seed oils including pomegranate seed, watermelon, melon, sea buckthorn, red currant, Japanese quince, grape, gooseberry, and apple, indicated that the oil extracted from pomegranate seed contained (86.2%) and 2.0 mg/g squalene. This shows that according to the lipophilic compound profile pomegranate seed oils are a valuable source of bioactive compounds for the cosmetic and pharmaceutical industries39.

The efficacy of pomegranate seed in foods has also been evaluated, as the compounds present; Cam et al., (2013) conducted a study to improve the functional properties of ice cream by adding pomegranate seed oil as a substitute for milk fat at levels of 2.0 and 4.0% (w/w), thereby increasing the conjugated fatty acid content in ice cream, indicating that ice cream could be incorpo-rated into the market as functional ice cream. In a similar study, pomegranate seeds fractionated through a sieve with a particle size of 0.15 mm and then added to a bar-type product, resulting in 84% recovery of punicic acid. These data elucidate that the incorporation of a seed powder fraction used as a vehicle for the consumption of punicic acid, allowing its use in a functional food formu-lation, in addition to fructifying the residual material40.

According to the results reported yogurt enriched at 0.5% with pomegranate seed powder indicated similar pH and nutritional values to control yogurt, however, the content of conjugated linoleic acid grades and antioxidant capacity was significantly higher by pre-senting 69.22% and 61.55% respectively. In pomegranate seed extract to chicken and veal meatballs when cooked by different methods such as oven, charcoal roasting, broiling, and frying. Pomegranate seed extract had an in-hibitory effect on amine formation, observed in charcoal-roasted and fat-fried veal meatballs by 39% and 46%, re-spectively, which are common methods of cooking meat-balls, while 49% inhibition in chicken meatballs for fat frying.

Another finding, within the applications that have been studied with pomegranate seed oil, was made, where the antioxidant capacity against oxidative deterioration of sunflower and canola oils during storage was evaluated, and the results indicated that 7% pomegranate seed oil can be an alternative against oxidative deterioration because of its antioxidant capacity, compared to synthetic antioxidants.

J. Funct. Mater. Biomol. 7(2) (2023) pp 668 – 675

4 Conclusions

In summary, despite the experimental review paperwork focused on pomegranate fruit (Punica granatum L.) production in Mexico is widely be-cause of its adaptability to climatic conditions. The pom-egranate has been studied for applications of biological activities since several scientific studies have reported the presence of various bioactive compounds such as el-lagitannins as punicalagin, punicalin, punicic acid, and ellagic acid, which have beneficial effects on human health and have been evaluated by in vitro and in vi-vo assays. In this review article on biological properties and biomedical applications of whole pomegranate in ac-tivity and fruits of maintaining a strategic distance from poisonous impetus.

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Conflict of Interest: NIL

References

- [1] Chen, J.; Liao, C.; Ouyang, X.; Kahramanog'lu, I.; Gan, Y.; Li, M. Antimicrobial Activity of Pomegranate Peel and Its Applications on Food Preservation. J. Food Qual. 2020, 2020, 8850339.
- [2] Vuc^vic['], V.; Grabež, M.; Trchounian, A.; Arsic['], A. Composition and Potential Health Benefits of Pomegranate: A Review. CPD 2019, 25, 1817– 1827.
- [3] Dhumal, S.S.; Karale, A.R.; Jadhav, S.B.; Kad, V.P. Recent Advances and the Developments in the Pomegranate Processing and Utilization: A Review. J. Agric. Crop Sci. 2014, 1, 1–7. 17. Tereso, A.; Carreto, L.; Baptista, M.; Almeida, M.A. Interstitial Lung Disease Induced by Crizotinib in Non-Small-Cell Lung Cancer. Acta Med. Port. 2019, 32, 236– 239.
- [4] Bartling, B.; Hofmann, H.-S. Reduced proliferation capacity of lung cells in chronic obstructive pulmonary disease. Z.Gerontol. Geriat. 2019, 52, 249– 255.
- [5] Kolb, M.; Vašáková, M. The natural history of progressive fibrosing interstitial lung diseases. Respir. Res. 2019, 20, 57.
- [6] Abegunde, D.O.; Mathers, C.D.; Adam, T.; Ortegon, M.; Strong, K. The burden and costs of chronic diseases in low-income and middle-income countries. Lancet 2007, 370, 1929–1938.
- [7] Obi, J.; Mehari, A.; Gillum, R. Mortality Related to Chronic Obstructive Pulmonary Disease and Comorbidities in the United States, A Multiple Causes of Death Analysis. COPD J. Chronic Obstr. Pulm. Dis. 2018, 15, 200–205.
- [8] Peery, A.F.; Crockett, S.D.; Barritt, A.S.; Dellon, E.S.; Eluri, S.; Gangarosa, L.M.; Jensen, E.T.; Lund, J.L.; Pasricha, S.; Runge, T.; et al. Burden of Gastrointestinal, Liver, and Pancreatic Diseases in the

United States. Gastroenterology 2015, 149, 1731–1741.e3.

- [9] Hall, E.H.; Crowe, S.E. Environmental and Lifestyle Influences on Disorders of the Large and Small Intestine: Implications for Treatment. Dig. Dis. 2011, 29, 249–254.
- [10] Lansky, E.P.; Newman, R.A. Punica granatum (pomegranate) and its potential for prevention and treatment of inflammation and cancer. J. Ethnopharmacol. 2007, 109, 177–206.
- [11] Viuda-Martos, M.; Fernández-López, J.; Pérez-Álvarez, J.A. Pomegranate and its Many Functional Components as Related to Human Health: A Review. Compr. Rev. Food Sci. Food Saf. 2010, 9, 635–654.
- [12] Viladomiu, M.; Hontecillas, R.; Lu, P.; Bassaganya-Riera, J. Preventive and Prophylactic Mechanisms of Action of Pomegranate Bioactive Constituents. Evid.-Based Complement. Altern. Med. 2013, 2013, 789764.
- Padini,A.C.;Marder,M.;Viola,H.;Wolfman,C.
 ;Wasowski,C.;Medina,J.H.FlavonoidsandtheCentral NervousSystem: From Forgotten Factors to Potent Anxiolytic Compounds. J. Pharm. Pharmacol. 2010, 51, 519–526.
- [14] Zand, R.S.R.; Jenkins, D.J.A.; Diamandis, E.P. Steroid hormone activity of flavonoids and related compounds. Breast Cancer Res. Treat. 2000, 62, 35–49.
- Sisein, E.A. Biochemistry of Free Radicals and Antioxidants. Sch. Acad. J. Biosci. 2014, 2, 110–118. 30. Preiser, J.-C. Oxidative Stress. JPEN J. Parenter. Enter. Nutr. 2012, 36, 147–154
- [16] Neha, K.; Haider, M.R.; Pathak, A.; Yar, M.S. Medicinal prospects of antioxidants: A review. Eur. J. Med. Chem. 2019, 178, 687–704.
- [17] Joshua Loke, W.S.; Lim, M.Y.; Lewis, C.R.; Thomas, P.S. Oxidative Stress in Lung Cancer. In Cancer; Elsevier: Amsterdam, The Netherlands, 2014; pp. 23–32. ISBN 978-0-12-405205-5.
- [18] Bhattacharyya, A.; Chattopadhyay, R.; Mitra, S.; Crowe, S.E. Oxidative Stress: An Essential Factor in the Pathogenesis of Gastrointestinal Mucosal Diseases. Physiol. Rev. 2014, 94, 329–354.
- [19] Shaygannia,E.;Bahmani,M.;Zamanzad,B.;Rafieian Kopaei,M.AReviewStudyonPunicagranatumL.J.Evid. BasedComplement. Altern. Med. 2016, 21, 221– 227.
- [20] Aviram, M.; Kaplan, M.; Rosenblat, M.; Fuhrman, B. Dietary Antioxidants and Paraoxonases Against LDL Oxidation and Atherosclerosis Development. In Atherosclerosis: DietandDrugs; von Eckardstein, A., Ed.; Handbook of Experimental Pharmacology; Springer: Berlin/Heidelberg, Germany, 2005; Volume 170, pp. 263–300. ISBN 978-3-540-22569-0.
- [21] Francenia Santos-Sánchez, N.; Salas-Coronado, R.; Villanueva-Cañongo, C.; Hernández-

Carlos, B. Antioxidant Compounds and Their Antioxidant Mechanism. In Antioxidants; Shalaby, E., Ed.; IntechOpen: London, UK, 2019; ISBN 978-1-78923-919-5.

- [22] Benchagra, L.; Berrougui, H.; Islam, M.O.; Ramchoun, M.; Boulbaroud, S.; Hajjaji, A.; Fulop, T.; Ferretti, G.; Khalil, A. Antioxidant Effect of Moroccan Pomegranate (Punica granatum L. Sefri Variety) Extracts Rich in Punicalagin against the Oxidative Stress Process. Foods 2021, 10, 2219.
- [23] Estrada-Luna, D.; Martínez-Hinojosa, E.; Cancino-Diaz, J.C.; Belefant-Miller, H.; López-Rodríguez, G.; Betanzos-Cabrera, G. Daily supplementation with fresh pomegranate juice increases paraoxonase 1 expression and activity in mice fed a high-fat diet. Eur. J. Nutr. 2018, 57, 383–389.
- [24] Aviram, M.; Rosenblat, M.; Gaitini, D.; Nitecki, S.; Hoffman, A.; Dornfeld, L.; Volkova, N.; Presser, D.; Attias, J.; Liker, H.; et al. Pomegranate juice consumption for 3 years by patients with carotid artery stenosis reduces common carotid intima-media thickness, blood pressure and LDL oxidation. Clin. Nutr. 2004, 23, 423–433.
- [25] Asgary, S.; Javanmard, S.; Zarfeshany, A. Potent health effects of pomegranate. Adv. Biomed Res. 2014, 3, 100.
- [26] Alqahtani, W.S. Effect of Saudi and EgyptianPomegranate Polyphenolsin Regulatingthe Activity of Pon1,Pon2 and Lipid Profile for Preventing Coronary Heart Disease. J. Regen. Biol. Med. 2019, 1, 1–12.
- [27] Zhao, C.; Sakaguchi, T.; Fujita, K.; Ito, H.; Nishida, N.; Nagatomo, A.; Tanaka-Azuma, Y.; Katakura, Y. Pomegranate-Derived Polyphenols Reduce Reactive Oxygen Species Production via SIRT3-Mediated SOD2 Activation. Oxidative Med. Cell. Longev. 2016, 2016, 2927131.
- [28] Gullon, B.; Pintado, M.E.; Fernández-López, J.; Pérez-Álvarez, J.A.; Viuda-Martos, M. In vitro gastrointestinal digestion of pomegranate peel (Punica granatum) flour obtained from coproducts: Changes in the antioxidant potential and bioactive compounds stability. J. Funct. Foods 2015, 19, 617–628.
- [29] Scichilone, N. Asthma Control: The Right Inhaler for the Right Patient. Adv. Ther. 2015, 32, 285–292.
- [30] Heffler, E.; Madeira, L.N.G.; Ferrando, M.; Puggioni, F.; Racca, F.; Malvezzi, L.; Passalacqua, G.; Canonica, G.W. Inhaled Corticosteroids Safety and Adverse Effects in Patients with Asthma. J. Allergy Clin. Immunol. Pract. 2018, 6, 776–781.

- [31] Sarica S, Urkmez D. 2016. The use of grape seed olive leaf and pomegranate peel extracts as alternative natural antimicrobial feed additive in broiler diets. Europ Poult Sci. 80:1–13.
- [32] Selim NA, Nada SA, Abdel-Sala AF, Youssef SF. 2013b. Evaluations of some natural antioxidant sources in broiler diets: 1-effect on growth, physiological and immunological performance in broiler chicks. Int J Poult Sci. 12(10):572–571.
- [33] Sharifian M, Hosseini-Vashan SJ, Fathi Nasri MH, Perai AH. 2019. Pomegranate peel extract for broiler chickens under heat stress: Its influence on growth performance, carcass traits, blood metabolites, immunity, jejunal morphology, and meat quality. Livest Sci. 227:22–28.
- [34] Singleton VL, Orthofer R, Lamuela-Raventos RM. 1998. Analysis of total phenols and other oxidation substrates and antioxidants by means of Folin-Ciocalteu reagent. Methods Enzymol. 299:152–178.
- [35] Statistical Analysis System Institute Inc. 2010. Users Guide. Carry (NC): SAS. Tavarez MA, Boler DD, Bess KN, Zhao J, Yan F, Dilger AC, McKeith FK, Killefer J. 2011. Effect of antioxidant inclusion and oil quality on broiler performance, meat quality and lipid oxidation. Poult. Sci. 90(4):922–930.
- [36] Thema K, Mlambo V, Snyman N, Mnisi CM. 2019. Evaluating alternatives to zinc-bacitracin antibiotic growth promoter in broilers: Physiology and meat quality responses. Anim. 9(12):1160.
- [37] Oloruntola OD, Agbede JO, Ayodele SO, Oloruntola DA. 2018d. Neem, pawpaw and bamboo leaf meal dietary supplementation in broiler chickens: effect on performance and health status. J Food Biochem. :12723.
- [38] Ou B, Hampsch-Woodill M, Prior RL. 2001. Development and validation of an improved oxygen radical absorbance capacity assay using fluorescein as the fluorescent probe. J Agric Food Chem. 49(10):4619–4626.
- [39] Rajani J, Karimi Torshizi MA, Rahimi SH. 2011. Control of ascites mortality and improved performance and meat shelflife in broilers using feed adjuncts with presumed antioxidant activity. Anim. Feed Sci. Technol. 170(3-4):239–245.
- [40] Rajput R, Sagar VS, Shalini AR. 2011. Effect of Punica granatum peel extract on burn wound healing in Albino Wistar Rats. Int. J. of Applied Biol. Pharm. Technol. 2:353–357.