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POSGRADO EN BIOCIENCIAS

OCTENYL SUCCINATE STARCH FILMS WITH NUT BY-PRODUCTS EXTRACTS: ANTIMICROBIAL PROPERTIES FOR MEDICAL APPLICATIONS.

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presenta:

MARCOS LEON BEJARANO

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DERECHOS DE AUTOR

El presente trabajo de tesis se presenta como uno de los requisitos parciales para la obtención del grado de **Maestro en Biociencias** de la Universidad de Sonora.

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THESIS

To obtain the Degree of:

MAESTRO EN BIOCIENCIAS

By:

MARCOS LEON BEJARANO

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APPROVAL FORM

The Thesis Committee members designed to review the thesis entitled "Octenyl Succinate Starch Films with Nut By-Products Extracts: Antimicrobial Properties for Medical Applications" presented by Marcos Leon Bejarano, have found it satisfactory and recommend that it is accepted as a partial requirement to obtain the Degree of Maestro en Biociencias (Biotecnología de Recursos Naturales).

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ABSTRACT

The use of starch-based films with rich phenolics extracts for medical purposes has been increasing due to the biocompatible characteristics of starch and the antimicrobial properties of phenolic extracts. Therefore, the aim of this work was to evaluate the antibacterial properties of octenyl succinated starch (OSS) based films with nut by-product extracts: pecan nutshell extract (PSE) and hazelnut skin extract (HSE). The OSS (0.013 degree of substitution) showed a greater swelling, pasting and gelatinization properties than native starch (NS), indicating that the film forming property was improved after the modification. Pecan nutshell and hazelnut skin were a great source of phenolic compounds (PC) (656.46±4.91 and 693.00 ± 5.65 mgEAG per-g of extract, respectively). Protocatehuic acid, epicatechin gallate, gallic acid and rutin were majority identified compounds. The PSE and HSE showed minimum inhbitory concentrations (MIC) against *Staphylococcus aureus* ATCC 6538P, *Staphylococcus epidermidis* ATCC 12228 (MIC= 250 µg/mL) and *Klebsiella pneumoniae* ATCC 13883 (MIC= 450 and 650 µg/mL, PSE and HSE, respectively). Besides, biofilm formation for all bacteria was reduced at MIC of both extracts. The PC of the extracts were dispersed trough the polymeric matrix of the OSS films. Resulting in homogeneous films, confirmed by scanning electron microscopy (SEM) and atomic force microscopy (AFM). Additionally, both extracts improved the water resistance, UV-Light barrier and mechanical properties (rigidity decrease). Films with 2500 and 5000 µg per-mL of extracts, did not show inhibition zone, however, there was not visual growth of *Staphylococcus* spp. below the films. In liquid medium, films with 5000 µg per-mL of extracts decrease the growth of *Staphylococcus* spp., *Pseudomonas aeruginosa* ATCC and *K. pneumonia* ATCC 13883. The OSS films with PSE or HSE presented suitable characteristics and properties that demonstrate its potential as a medical material, for the prevention of bacterial infections.

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GENERAL INTRODUCTION

Starch is one of the most used polysaccharides in the food and biomedical industries, mainly due to be easy to obtain, renewable, cheap, non-toxic, biodegradable and its highly versatile characteristics and properties (Chakraborty *et al*., 2018; Yazid *et al*., 2018). However, native starch (NS) properties are not enough for certain applications, for this reason structural modifications are made through chemical, physical and enzymatic processes, changing and improving the characteristics and properties of starch (Alcáraz-Alay & Meireles, 2015). Chemical modification, based on the aggregation or replacement of hydroxyl groups by other groups or molecules, is the most common modification method used in starch (Masina *et al*., 2016). Among the chemical modifications, the esterification with octenyl succinate anhydride (OSA) is mainly used as emulsifier agent in foods or as encapsulant agent for bioactive compounds (Agama-Acevedo & Bello-Perez, 2017; Zhu *et al*., 2017). On the other hand, recently few studies have shown improvement of the film forming properties of starch, and the water resistant and mechanical properties of these films (Li *et al*., 2015; Li *et al*., 2018; Naseri *et al*., 2019; Punia *et al*., 2019a). Overall, starch-based films have become a potential option to the replacement of plastic materials, food packaging and edible coatings (Gadhave *et al*., 2018). To further enhance the potential application of these films, bioactive compounds or plants extracts have been added, then providing new characteristics, such as UV light barrier, antioxidant and antimicrobial properties (Silva-Weiss *et al*., 2013b; Salgado *et al*., 2015).

Phenolic compounds (PC) are considered the largest family of bioactive compounds in plants and are characterized by their antioxidant potential (Cheynier, 2012). Nevertheless, the antimicrobial potential of PC is another characteristic with great impact. Due to this, PC are considered as antimicrobial agents (Barbieri *et al*., 2017; Rempe *et al*., 2017). Their wide distribution in the plant organisms, allow the obtention of PC from different vegetal sources. However, by-products generated by the agroindustry are considered as an important source of these compounds, due to have higher concentration of PC compared with the initial product (edible parts) (Kumar *et al*., 2017; Nguyen, 2017). In this context, the nut industry generates a large amount of by-products such as skin, shell, leaves as a result of the elaboration of processed nuts products (Chang *et al*., 2016). Among nuts, pecan nut [*Carya illinoinensis* (Wangenh) K. Koch] is an important commercial crop from northwest Mexico, from which its shell was

established as the main by-product. In addition, it has been reported that nutshell has the highest PC content than other by-products from pecan nut (Flores-Cordova *et al*., 2017; Alvarez-Parrila *et al*., 2018). On the other hand, hazelnut (*Corylus avellana*) is one of the most popular nuts worldwide and one of the main commercial crops from Turkey, especially for the Black Sea region. From this one, skin is generated as a by-product from de roasting process, which has a high PC content than other hazelnut by-products (Shahidi *et al*., 2007; Bottone *et al*., 2019).

With respect to the antibacterial potential of PC, some studies have demonstrated the antimicrobial activity of different phenolic extracts from pecan nut (*Carya illinoinensis*) and hazelnut (*Corylus avellana*) by-products against *Staphylococcus aureus*, *Staphylococcus epidermidis*, *Pseudomonas aeruginosa*, *Klebsiella pneumoniae,* among others (Oliveira *et al*., 2007; do Prado *et al*., 2014; Caxambú *et al*., 2016; Piccinelli *et al*., 2016). These pathogens are commonly related with the health care associated infections (HCAI) which are characterized by their high mortality index (Khan *et al*., 2017). Therefore, the antibacterial potential of PCs could be considered a solution to these infections, however the poor stability of PC (in environmental conditions) limits their application. In this manner, a protective matrix is required (Biasutto *et al*., 2014). In this way, starch-based films could act as a protective matrix for PC (Quirós-Sauceda *et al*., 2014). These films containing phenolic extracts could be used as wound dressings, coating materials or as a new material for the development of medical devices, to prevent the development of microbial infections (Torres *et al*., 2013). Recently, some evidences confirm that films or membranes based on starch and phenolic extracts or other bioactive compounds, are managed to prevent infection in wounds, in addition improved the wound healing (Salehi *et al*., 2017; Hadisi *et al*., 2018; Hassan *et al*., 2018; Eskandarinia *et al*., 2019).

According to the above and limited information about the combination of OSS and nut by-product extracts in films, the objective of this work was to elaborate, characterize and evaluate the barrier, mechanical and antimicrobial properties, of OSS based films with pecan nutshell [*Carya illinoinensis* (Wangenh) K. Koch] and hazelnut skin (*Corylus avellana*) phenolic extracts at different concentrations, in order to know its medical potential.

I. LITERATURE REVIEW

1.1 Starch

Starch is the main reserve carbohydrate in plants and a product of the photosynthetic process. This carbohydrate is stored in form of granules which consist in two glucose polymers, amylose and amylopectin. Amylose is a linear chain formed by glucose units linked through α-(1-4) bonds with few branches at α-(1-6) linkages. For its part, amylopectin is a highly branched polymer formed by glucose units linked through α-(1-4) and α-(1-6) bonds (**Figure 1)** (Pfister & Zeeman, 2016; Bertoft, 2017)**.** Besides being the main energy source in the human diet, this polysaccharide is one of the most used in the food, biomedical and pharmaceutical industries. Especially because it is easy to obtain, renewable, cheap, biocompatible, biodegradable and have highly versatile properties (Chakraborty *et al*., 2018). In the food industry, starch and its derivatives are commonly used as additives for several foods, mainly used to improve texture, quality and stability of bakery foods, sauces, pasta or mayonnaise (Yazid *et al*., 2018; Egharevba, 2019). Additionality, its use has been expanded towards the maintenance of food quality and safety, through the development of edible coatings or starch-based packaging materials (Jabeen *et al*., 2015; Pelissari *et al*., 2019). On the other hand, in the pharmaceutical and medical industry, starch is usually used as excipient, drug carrier, and recently as a basic material in the tissue engineering, mainly due to its excellent biocompatibility (Builders & Arhewoh, 2016; Hemamalini & Dev, 2018).

1.1.1 Octenyl succinate starch

Starch has become a great raw material for the industry, due to its low cost and easy isolation, which in addition to expand its application can easily be subjected to modification processes (Alcáraz-Alay & Meireles, 2015). Starch modification can be carried out by different physical, chemical or enzymatic methods, depending on the properties that need to be improved or modified, for a specific application (Bemiller, 1997; Kaur *et al*., 2012). Within these modification processes, chemical modification is considered the most used in the industry level and practically consist in the aggregation or substitution of the hydroxyl groups by others functional groups or molecules (Chen *et al*., 2015; Masina *et al*., 2016).

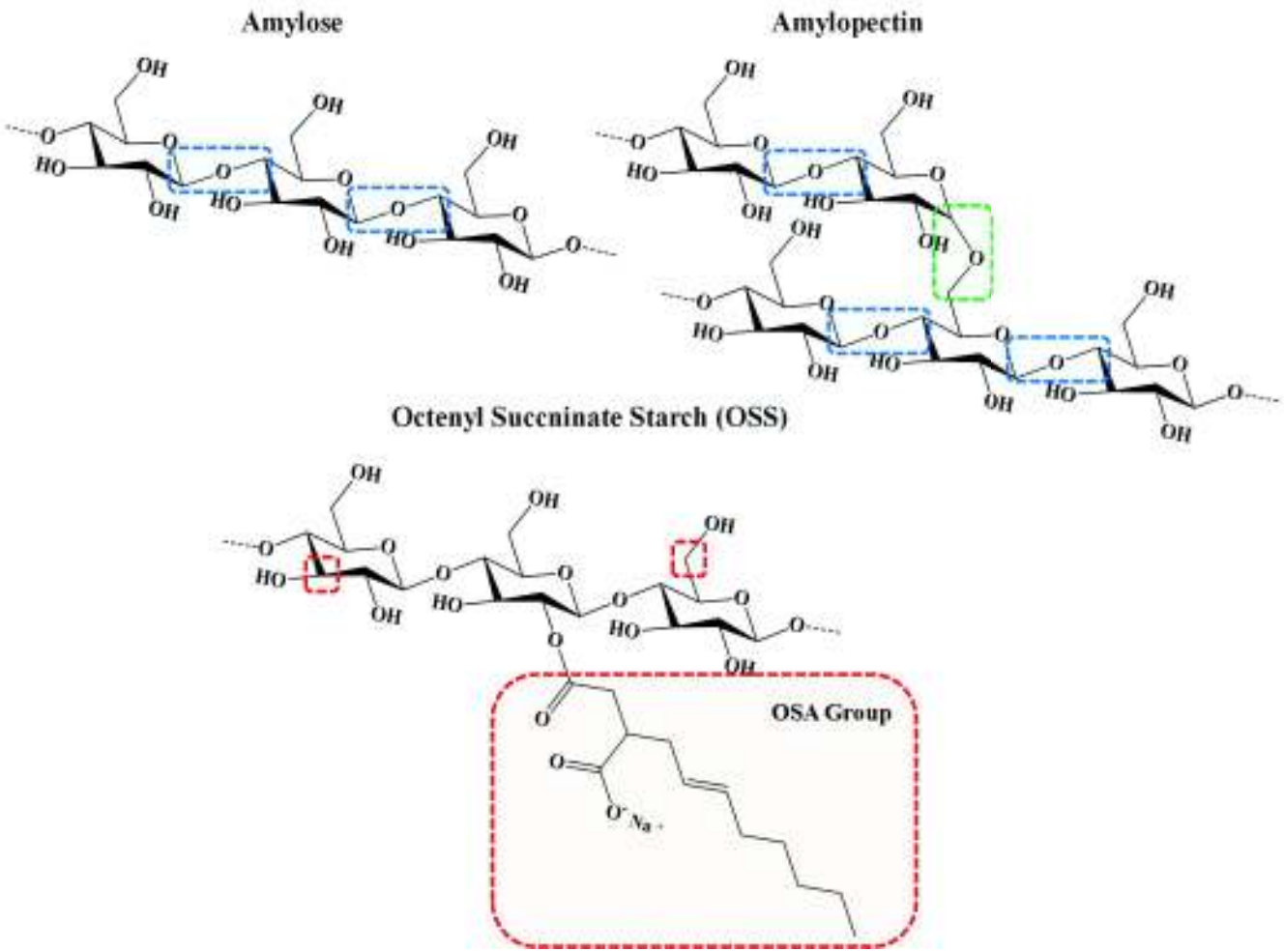

Figure 1. Amylose, amylopectin and octenyl succinate starch. Blue squares indicate the α-(1,4) glycosidic bond, green squares indicates the α-(1,6) and red squares indicate the modification sites.

Starch esterification with OSA is one of the modification processes of greater use, mainly in the food industry. This process consists in the aggregation of OSA groups within the glucose units of the starch, by substitution of the hydroxyl groups, specifically those found in the C2, C3 and C6 **(Figure 1)** (Tizzotti *et al*., 2011; Sweedman *et al*., 2013). The inclusion of these hydrophobic groups causes significant changes in the starch properties, such as swelling, pasting, thermal, textural, digestibility and amphiphilic character or emulsifier properties (Wang *et al*., 2016; Ovando-Martínez *et al*., 2017; Zhang *et al*., 2017). Due to these improved properties, octenyl succinate starch (OSS) is used as emulsions stabilizer, food additive and as encapsulating agent for bioactive compounds (Agama-Acevedo & Bello-Perez, 2017; Zhu *et al*., 2017). Additionally, OSS use has been extended to the starch-based films production, where the use of OSS improves certain mechanical properties and the water resistance of films (*Li et al*., 2015; Li *et al*., 2018; Naseri *et al*., 2019; Punia *et al*., 2019a).

1.1.2 Starch-based films

Starch-based films emerged as a solution for petroleum-based plastics pollution, mainly due to be a renewable source and its biodegradable characteristics, being used as food packing material or as edible coatings (Versino *et al*., 2016; Gadhave *et al*., 2018). Despite this, the different modification processes manage to improve certain characteristics and properties of the films, which extend its application to new areas (Jiménez *et al*., 2012; Shah *et al*., 2016).

The use of modified starch has shown to cause changes in different film properties, compared to NS based films. da Rosa Zavareze *et al*. (2012) in oxidized starch-based films reported a decrease in the solubility, elongation at break (EB), water vapor permeability (WVP). Also, an increase in the tensile strength (TS) was observed. In addition, same authors found that heat treated starch-based films only increased the TS and WVP, in comparison with the NS based film. The same trend was reported in crosslinked starch-based films, which presented a high TS and WVP than NS based films (Gútierrez *et al*., 2015). Li *et al*. (2015) reported that the addition of OSS in the starch films formulation enhanced the moisture proof and optical properties, as well as increase the EB and decreases the TS.

On the other hand, the characteristics and properties of the starch-based films could be improved or modified with the addition of bioactive compounds or with plant extracts rich in PC (Silva-Weiss *et al*., 2013b, Salgado *et al*., 2015; Benbettaïeb *et al*., 2019). Pyla *et al*. (2010) reported that the addition of tannic acid in corn starch-based films provides antibacterial and antioxidant properties, reducing the lipid oxidation. On the other hand, Romero-Bastida *et al*. (2011) reported that cinnamon essential oil affects the solubility, mechanical and barrier properties of oxidized banana starch-based films. Besides, essential oils provided antibacterial activity to the films. In the case of corn starch-based films added with *Zataria multiflora* boiss and *Mentha pulegium* essentials oils an improvement of mechanical, barrier and antibacterial properties was reported (Ghasemlou *et al*., 2013). More studies about the effect of bioactive compounds or plants extracts on the starch-based films properties are shown in **Table 1**.

1.2 Nuts and their by-products as a source of phenolic compounds

The PC are considered the major group of secondary metabolites in plants, especially due to that they have a great diversity of chemical structures and wide distribution in plants. The PC are characterized by presenting aromatic rings with hydroxyl groups as substituents in its chemical structure. The hydroxyl groups have been related with the antioxidant potential of these compounds (Harborne, 1984; Bravo, 1998; Cheynier, 2012).

In this context, it has been reported that nuts such as almonds, peanuts, cashews, hazelnut, pecan and others owe their great popularity to the large number of bioactive compounds (including PC), which are responsible for the close relationship between their consumption and health benefits. Among these benefits can be mentioned the prevention of cardiovascular, neurodegenerative and inflammatory diseases, cancer, diabetes, weight control, and others. For this reason, nuts are considered as an important group of food in the human diet (Alasalvar & Bolling, 2015; de Souza *et al*., 2017; Zhang *et al*., 2017). This last, has caused that nut production increases every year. According to the International Nut & Dried Fruit Council (ICN) during the season 2018-2019, the production reached closely to 4.5 million metric tons, an increase of 62% in 10 years (ICN, 2019). However, the high demand and consumption of nuts, mainly in a processed way, has caused that the nut industry generates a large amount of

Table 1. Starch and modified starch-based films with bioactive compounds.

Film Composition	Bioactive Compounds Effect	Reference
Cassava starch, glycerol and ethanolic propolis extract	- Plasticizing effect - Hydrophobic characteristic - Antioxidant activity - Antibacterial activity	de Araujo *et al*. (2015)
Cassava starch, glycerol and yerba matte extract	- Plasticizing effect - Improve soil biodegradation	Medina-Jaramillo *et al*. (2016)
Cassava starch, glycerol and Rosemary extract	- Antioxidant properties - UV-Light barrier properties - Provide hydrophobic characteristic	Piñeros-Hernández *et al*. (2017)
Hydroxypropyl starch, glycerol and tea PC	- Antioxidant properties - Antibacterial properties	Feng *et al*. (2018)
OSA sweet potato starch, glycerol and oregano essential oil	- Antibacterial Properties - Water resistance properties - Reduction of film rigidity	Li *et al*. (2018)
Hydroxypropyl high amylose starch, glycerol and pomegranate peel extract	- Antibacterial properties - Mechanical reinforcement	Ali *et al*. (2019)
Kamut starch, sorbitol and moringa leaf extract	- Plasticizing effect - Antioxidant properties - UV-Light properties - Improve biodegradation in vegetable compost	Ju *et al*. (2019)
Modified cassava starch, sorbitol, and hibiscus flowers extracts	- pH changes indicator - UV-Light barrier properties	Peralta *et al*. (2019)
Cassava starch, glycerol and *Lycium ruthenicum* anthocyanins	- Mechanical reinforcement - Barrier properties - Antioxidant properties - pH changes indicator	Qin *et al*. (2019)

by-products such as leaves, shells, husks, skins, among others, which are still an important PC source (Chang *et al*., 2016; Alasalvar *et al*., 2019). As well as other by-products, nut by-products could be considered an excellent option for obtaining bioactive compounds (such as PC), which can be used in various industries such as food and pharmaceutical, providing added value to the initial product (Kumar *et al*., 2017; Nguyen, 2017).

1.2.1 Pecan Nut [*Carya illinoinensis* (Wangenh) K. Koch]

Pecan [*Carya illinoinensis* (Wangenh) K. Koch] is a large deciduous nut tree (20 to 40 meters) belongs to the Juglandaceae family, native from the south of the United States and extended to the northern of Mexico (Fronza *et al*., 2018). During the season 2018-2019, the pecan nut worldwide production exceeds 140,200 metric tons (kernels), being Mexico the main producer (52%) and exporter (62% of shelled nuts) (INC, 2019). Chihuahua, Sonora and Coahuila states were the mainly Mexican states producers of these nuts, becoming this product in one of the most important economic crops for them (Zaragoza-Lira *et al.*, 2011; Orona-Castillo *et al*., 2013).

Pecan nut (**Figure 2**) consumption has reached high popularity as a result of their health-related benefits. These benefits are attributed to the high content of multiple bioactive compounds including fatty acids, vitamins, minerals and antioxidants such as tocopherols and PC (Azadmard-Damirchi *et al*., 2011; Atasanov *et al*., 2018). This popularity has led to an increment of the demand for pecans, with an average annual production increase of 6,753 metric tons (INC, 2019). However, the high demand of pecan nut has leading to the generation of large quantities of by-products (shells, cakes and leaves), which are important sources to obtain bioactive compounds, such PC (Alvarez-Parrilla *et al*., 2018). Among these pecan nut by-products, shell goes over than the other by-products by their higher PC content, mainly phenolic acids (gallic, ellagic, chlorogenic and hydroxybenzoic) and flavonoids (catechins, rutin and kaempferol) (de la Rosa *et al*., 2014; do Prado *et al*., 2014; El Hawary *et al*., 2016; Flores-Cordova *et al*., 2017; Hilbig *et al*., 2018a; Flores-Estrada *et al*., 2019). Due to this, some studies have focused on the use of this source to obtain PC extracts for antifungal (Osorio *et al*., 2010),

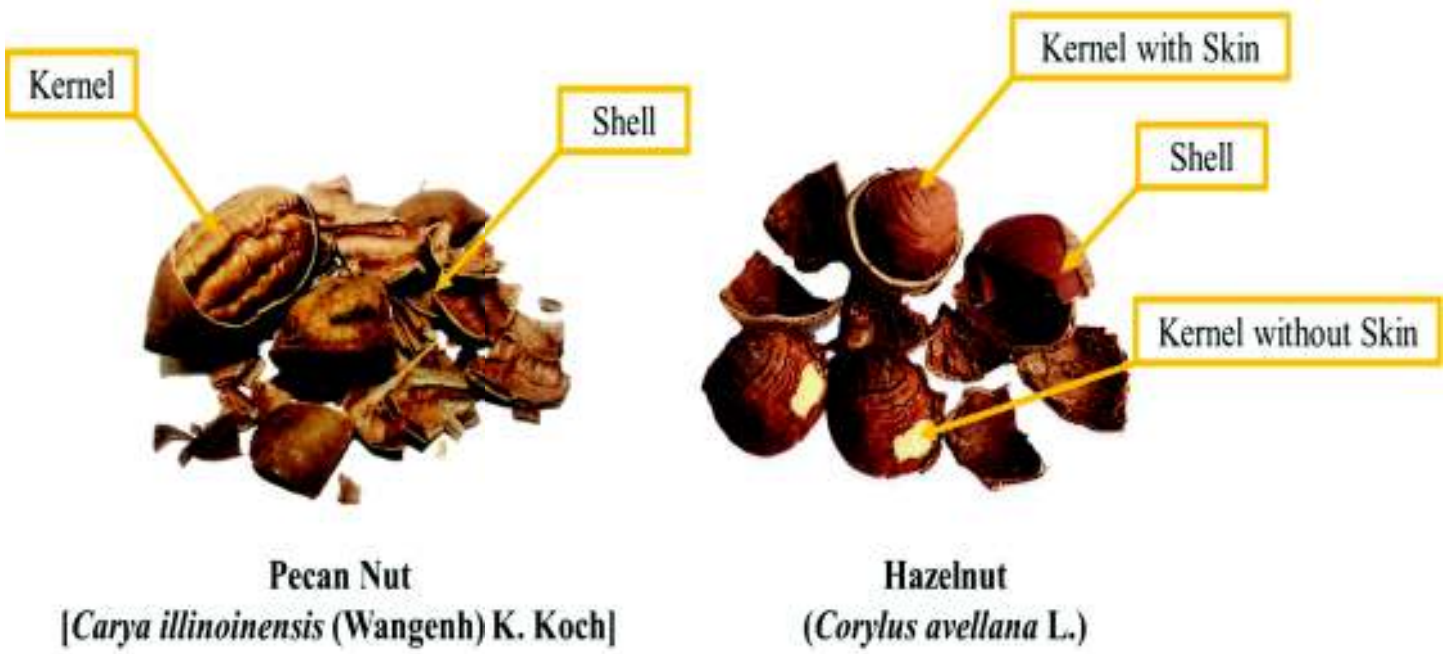

Figure 2. Pecan nut [*Carya illinoinensis* (Wangenh) K. Koch] and hazelnut (*Corylus avellana* L.)

hepatoprotective (Müller *et al*., 2013), antibacterial (do Prado *et al*., 2014), anti-hyperglycemic (El Hawary *et al*., 2016), anti-hypercholesterolemic (Porto *et al*., 2015), antiproliferative (Hilbig *et al*., 2018b), and antioxidant agent in biodiesel (Amaral *et al*., 2018) applications.

1.2.2 Hazelnut (*Corylus avellana* L.)

Hazel (*Corylus avellana* L.) belongs to the Betulaceae family, is a large nut scrub (2 to 5 meters) mainly distributed along of the coasts in the Black Sea region (Contini *et al*., 2011; Ramalhosa *et al*., 2011). Hazelnuts are an important commercial crop for Turkey, being the largest hazelnut producer. In the season 2018-2019, Turkey produced the 63% of the worldwide production (460, 000 metric tons, kernel basis) (INC, 2019). Such production was distributed by 14 provinces in the Black Sea region, standing out Ordu, Giresum and Samsun as the main national producers (Baojun *et al*., 2017).

Hazelnuts (**Figure 2**) are one of the most popular nuts due to its good organoleptic characteristics. Besides, hazelnuts are characterized by the high content of bioactive compounds related to health benefits (Contini *et al*., 2011; Amaral & Oliveira, 2016). Usually, this nut is consumed roasted, which has the skin as its main by-product. In addition, its presence in a wide variety of processed foods, increases the generation of other by-products such as shells, green leafy covers and leaves (Özdemir *et al*., 2014; Bottone *et al*., 2019). Among these by-products, the skin has the highest PC content (Shahidi *et al*., 2007). The mainly PC includes phenolic acids (protocatechuic, gallic, hydroxybenzoic and vanillic) and flavonoids (catechins, procyanidins, quercetin) (Del Rio *et al*., 2011; Montella *et al*., 2013; Özdemir *et al*., 2014; Pelvan *et al*., 2018). According to some studies, hazelnut skin and its extracts has an potential application as antioxidant (Contini *et al*., 2009), antiproliferative (Li & Parry, 2011), functional ingredient in beverages (Contini *et al*., 2012) and foods (Bertolino *et al*., 2015; Zeppa *et al*., 2015; Longato *et al*., 2019), prebiotic (Montella et al., 2013), anti-*Candida albicans* agent (Piccinelli *et al*., 2016) and others.

1.2.3 Phenolic compounds from nut by-products as antimicrobials

In addition to the antioxidant activity, PC have antimicrobial activity against a wide variety of pathogens and consequently are being considered as antimicrobial agents (Daglia, 2012; Albuquerque *et al*., 2013). Several studies demonstrated that PC or rich phenolic extracts have different mechanisms of action against bacteria and yeasts. Among these mechanisms are the membrane disruption, protein synthesis inhibition, metabolic activity inhibition, and pathogenic mechanisms inhibition such as biofilm (Lee & Lee, 2015; Slobodníková *et al*., 2016; Barbieri *et al*., 2017; Rempe *et al*., 2017). Previously reported mechanisms against bacteria are shown in **Figure 3.**

In this context, phenolic extracts obtained from nut by-products showed antimicrobial activity against pathogen microorganisms. Oliveira *et al*. (2008) and Fernández-Agulló *et al*. (2013) reported antibacterial activity of walnut green husks extracts against Gram-positive bacteria such as *Bacillus* spp. and *Staphylococcus* spp. On the other hand, Mandalari *et al*. (2010) and Smeriglio *et al*. (2016) reported that almond skins extracts had antibacterial activity against Gram-positive bacteria (*Streptococcus mutans*, *Listeria* spp., *Staphylococcus* spp. and *Enterococcus* spp.), and Gram-negative (*Escherichia coli*, *P. aeruginosa*, *Salmonella* Typhimurium and *Serratia marcenses*). Similarly, Arekemase *et al*. (2011) and da Silva *et al*. (2016) reported antimicrobial potential of extracts from different parts of cashew nuts against Gram-positive and Gram-negative bacteria, also against *Candida* spp. Recently, antibacterial potential of peanut by-products against nine food-borne pathogens was reported (de Camargo *et al*., 2017). In the case of pecan nut and hazelnut by-products extracts, the antimicrobial activity has also been reported (**Table 2)**.

1.3 Health care associated infections

One of the most serious health problems for developed and developing countries are the HCAI or nosocomial infections, due to the increase in their incidence and high mortality rate, directly related to the presence of resistant microorganisms (Burnham *et al*., 2017; Ferri *et al*., 2017; Khan *et al*., 2017). The HCAI include all those infections acquired during the stay in a health care unit, without symptoms prior to admission such as pneumonia (ventilator associated),

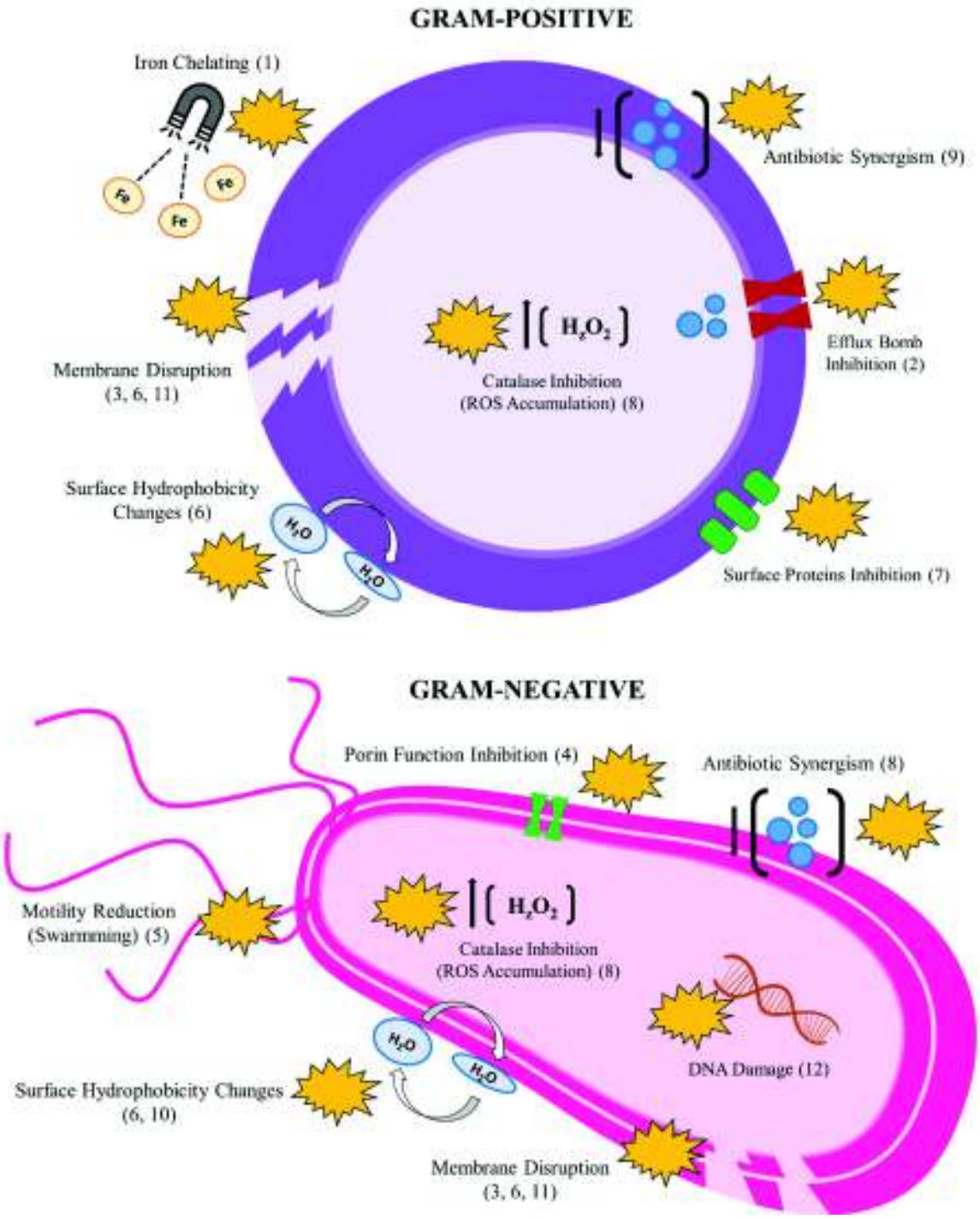

Figure 3. Antibacterial mode of action of phenolic compounds and phenolic extracts. Reported mode of action of phenolic compounds and phenolic extracts against Gram-positive and Gram-negative bacteria. (1) Engels *et al*. (2011), (2) Fiamengos *et al*. (2011), (3) Lou *et al*. 2011, (4) Nakayama *et al*. (2013), (5) Salaheen *et al*. (2014), (6) Lopez-Romero *et al*. (2015), (7) Nakayama *et al*. (2015), (8) Carlvaho *et al*. (2016), (9) Lima *et al*. (2016), (10) Rodríguez-Pérez *et al*. (2016) (11) Gonelimali *et al*. (2018), (12) Singh *et al*. (2018).

Table 2. Antimicrobial activity of pecan nut and hazelnut phenolics extracts.

Extract	Phenolic Compounds Profile	Microorganism	Reference
Hazelnut Leaves (Aqueos Extract)	(3,4 and 5)- caffeoylquinic acid, caffeoyltartaric acid, *p*-coumaroyltartaric acid, myricetin 3-rhamnoside, quercetin 3-rhamnoside and kaempferol 3-rhamnoside.	*Bacillus* spp, *Staphylococcus aureus*, *E. coli*, *Klebsiella pneumoniae* and *Cryptococcus neoformans*	Oliveira *et al*. (2007)
Pecan Nutshell (Aqueos and Ethanolic Extract)	Gallic acid, chlorogenic acid, p-hydroxibenzoic acid, epigallocatechin, epicatechin gallate	*S. aureus*, *Listeria monocytogenes*, *Vibrio parahemolyticus, Bacillus cereus*	do Prado *et al*. (2014)
Pecan Nutshell (Aqueous Extract)	-	*Staphylococcus aureus*, *B. cereus*, *Listeria* spp., *Salmonella* Enteritidis, *P. aeruginosa Aeromonas hydrophilla*	Caxambú *et al*. (2016)
Hazelnut Skin (Methanolic Extract)	Proanthocyanidins	*C. albicans*	Piccinelli *et al*. (2016)
Pecan Leaves (Aqueous and Ethanolic Extract)	Gallic acid, ellagic acid, catechin, epigallocatechin, rutin	*Citrobacter freudii, Salmonella* spp., *S. aureus*, *Streptococcus* spp., *Shigella sonei*, *Acinetobacter baumannii*, *Stenotrophomonas maltophilia, Penibacillus* spp., *Candida* spp., *Cryptococcus grubii*	Bottari *et al*. (2017)

bloodstream (intravascular catheters), urinary tract infections (urinary catheters) and wounds or surgical site infections, all these closely related to the ability to form biofilm by pathogenic microorganisms (Percival *et al*., 2015; Stoica *et al*., 2017).

Frequently, the HCAI are caused by microorganisms that belong to normal microbiota. However, the hospital environment also plays an important role in these infections, by providing an environment for development and dissemination of microorganisms and resistance genes (Suleyman *et al*., 2018; Wohrley & Bartlett, 2019). The main pathogens involved in these infections are Gram-positive bacteria (*Streptococcus* spp, *Staphylococcus* spp, *Enterococcus* spp. and *Clostridium difficile*) and Gram-negative bacteria such as the Enterobacteriaceae family (*Proteus* mirabilis, *K. pneumoniae*, *E. coli* and *S. marcenses*), *P. aeruginosa* and *Acinetobacter* spp. (Khan *et al*., 2015). Additionally, yeasts such as *Candida* spp. and others with less incidence (*Cryptococcus* spp., and *Malassezia* spp.) are considered the main fungal pathogens in HCAI (Suleyman & Alangaden, 2016; Enoch *et al*., 2017). It is important to mention, that the distribution and incidence of pathogens varies for each country. For instance, the main pathogen associated to pneumonia were *S. aureus* and *P. aeruginosa* in US and Spain, respectively (Magill *et al*., 2014; Zaragoza *et al*., 2014). By type of infection, *E. coli* is the most common pathogen isolated from urinary tract infections, whereas *Staphylococcus* spp. leads the catheter-related bloodstream infections (Salazar-Holguín & Cisneros-Robledo, 2016; Chen *et al*., 2017; Sticchi *et al*., 2018). **Figure 4**., shows the most common pathogens isolated from the mainly HCAI in different countries.

1.3.1 *Staphylococcus* spp.

Around 49 species and 27 subspecies of Gram-positive cocci grouped in clusters, in pairs or short chains are part of the genus *Staphylococcus* (Murray *et al*., 2015). Only few species, are pathogenic for humans, being *S. aureus* and *S. epidermidis* the most common species related to HCAI (Barberán *et al*., 2014).

Possibly, *S. aureus* is considered the major pathogen for humans due to the large number of virulence factors that it possesses, and for being part of the normal human microbiota in different parts of the body. This allows it to cause a wide variety of infections such as bacteremia

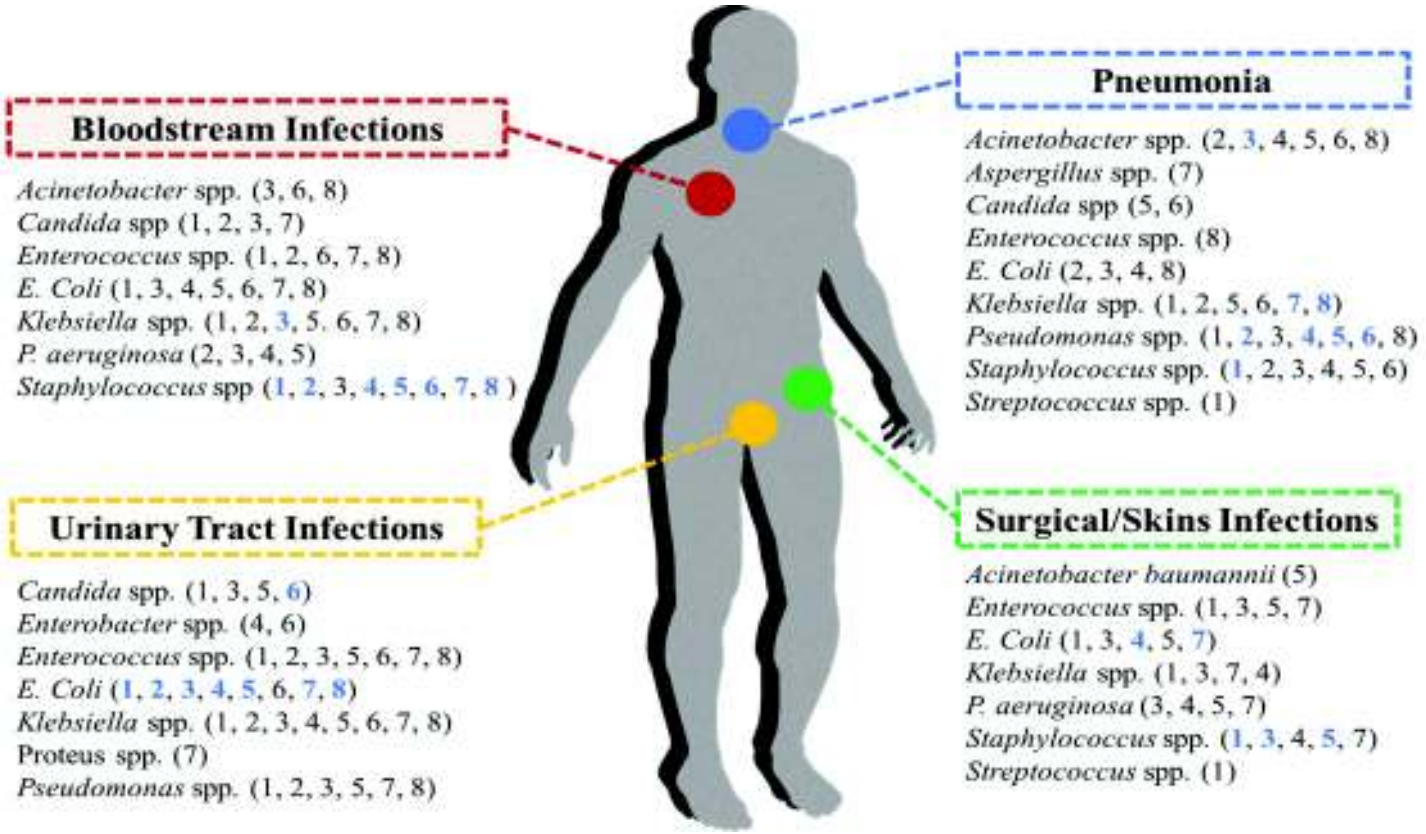

Figure 4. Common pathogens isolated from health care associated infections. (1) Magill *et al*., 2014 (US), (2) Zaragoza *et al*., 2014 (Spain), (3) Ghanshani *et al*., 2015 (India), (4) Salazar-Holguín & Cisneros-Robledo, 2016 (Mexico), (5) Chen *et al*., 2017(China), (6) Braga *et al*., 2018 (Brazil), (7) Sticchi *et al*., 2018 (Italy) (8) Hassan *et al*., 2019 (Egypt).

* Blue bold number indicates the mainly pathogen isoleted by study.

* The main species includes: *Acinetobacter* spp. (*A. baumannii*), *Candida* spp. (*C. albicans*), *Enterobacter* spp. (*E. cloacae*) *Enteroccocus* spp. (*E. faecium* and *E. faecalis*), *Klebsiella* spp. (*K. peneumoniae* and *K. oxytoca*), *Proteus* spp. (*P. mirabilis*), *Pseudomonas* spp. (*P.aeruginosa*) (*Staphyococcus* spp. (*S. aureus* and *S. epidermidis*) and *Streptococcus* spp. (*S. pneumoniae*).

skin and soft tissue infections, device-related infections, among others (Tong *et al*., 2015; Balasubramanian *et al*., 2017). Recently, the severity of infections produced by this pathogen is increasing, due to the wide repertoire of antibiotic resistance mechanisms that its possess against the majority of antibiotics commonly used in medicine (Foster, 2017; McGuinness *et al*., 2017).

On the other hand, *S. epidermidis* is a normal resident of the human skin microbiota, maintaining a commensal relationship with the host. However due to its proximity it is capable of producing infections in susceptible people, becoming in an opportunistic pathogen, whose main pathogenicity mechanism is the formation of biofilm (Sabaté Brescó *et al*., 2017; Le *et al*., 2018). Due to the biofilm formation capacity, this opportunistic pathogen has been considered as the main cause of infections associated with medical devices, mainly intravascular catheters, causing bacteremia and sepsis, being both of them of great concern for health institutions **(**Büttner *et al*., 2015; Nguyen *et al*., 2017).

1.3.2 *Klebsiella pneumoniae*

K. pneumoniae belongs to the Enterobacteriaceae family, it is a Gram-negative bacillus characterized by its prominent capsule, which is considered as its main pathogenicity factor (Li *et al*., 2014). This opportunistic pathogen is mainly associated with pneumonia, urinary tract infections, bacteremia, and medical devices related infections in immunocompromised patients (Clegg & Murphy, 2016; Paczosa & Mecsas, 2016). Currently, *K. pneumonia* is recognized as one of the most important pathogenic microorganisms, due to the wide range of virulence factors, resistance mechanisms and genes, and the appearance of hypervirulent strains. Nowadays, the infections caused by *K. pneumoniae* are not only limited to health care environments, also they are expanding towards the community (Follador *et al*., 2016; Wyres & Holt, 2016; Navon-Venezia *et al*., 2017; Martin & Bachman, 2018; Russo & Marr, 2019).

1.3.3 *Pseudomonas aeruginosa*

The genus *Pseudomonas* comprises approximately 200 species of Gram-negative mobile bacilli. Nowadays, *P. aeruginosa* is the most clinically relevant specie (Murray *et al*., 2015). This is

one of the main pathogens in HCAI, because is responsible of ventilator-associated pneumonia, meningitis, urinary infections, bacteremia, wound and soft tissue infections, among others (Gellatly & Hancock, 2013; Chatterjee *et al*., 2016). The wide variety of infections is mainly due to the vast pathogenic arsenal that it possesses, which in turn provides some protection against the immune system as well as the action of antibiotics, being the ability to form biofilm a specific situation (Streeter & Katouli, 2016). Besides, *P. aeruginosa* infections have a high mortality incidence, related to its great adaptability and high tolerance to antibiotics. In addition, it has the ability to obtain resistance genes, generating multiresistant strains (Stefani *et al*., 2017; Pang *et al*., 2018; Ciofu & Tolker-Nielsen, 2019).

1.4 Medical potential of starch-phenolic extracts films

Due to the high incidence of HCAI associated with invasive medical devices and surgical site or wounds, the development of new medical devices materials, coatings and wound dressings with antimicrobial properties, has become the possible solution for the prevention of these infections (Ren *et al*., 2017; Vowden & Vowden, 2017; Ding *et al*., 2018; Simões *et al*., 2018). **Figure 5** shown the mode of action of these new antimicrobial materials and coatings.

On this context, polymers of natural origin also called biopolymers such as cellulose, chitosan, alginate, dextran, and starch, deserve a special attention because they have biocompatible characteristics and present some resistance to microbial adhesion (Arora *et al*., 2016; Junter *et al*., 2016; Rebelo *et al*., 2017). Besides, the antimicrobial potential of PC could be the solution to antibiotics resistance problem (Slobodníková *et al*., 2016; Chandra *et al*., 2017; Yang *et al*., 2018). However, their potential is limited by their poor stability, which could be solved, by adding in a polymer matrix that provides protection and stability (Biasutto *et al*., 2014; Conte *et al*., 2016). At this point, combination of biopolymers and PC could be representing a solution to reduce the incidence of HCAI. Promising results of the medical application of starch in combination with PC rich extracts are described in **Table 3.** Nowadays, there is not information about octenyl succinate starch-based films with nut by-products extracts for medical applications. In this way, the obtained results could extend the study of both materials and establish their potential in medical applications.

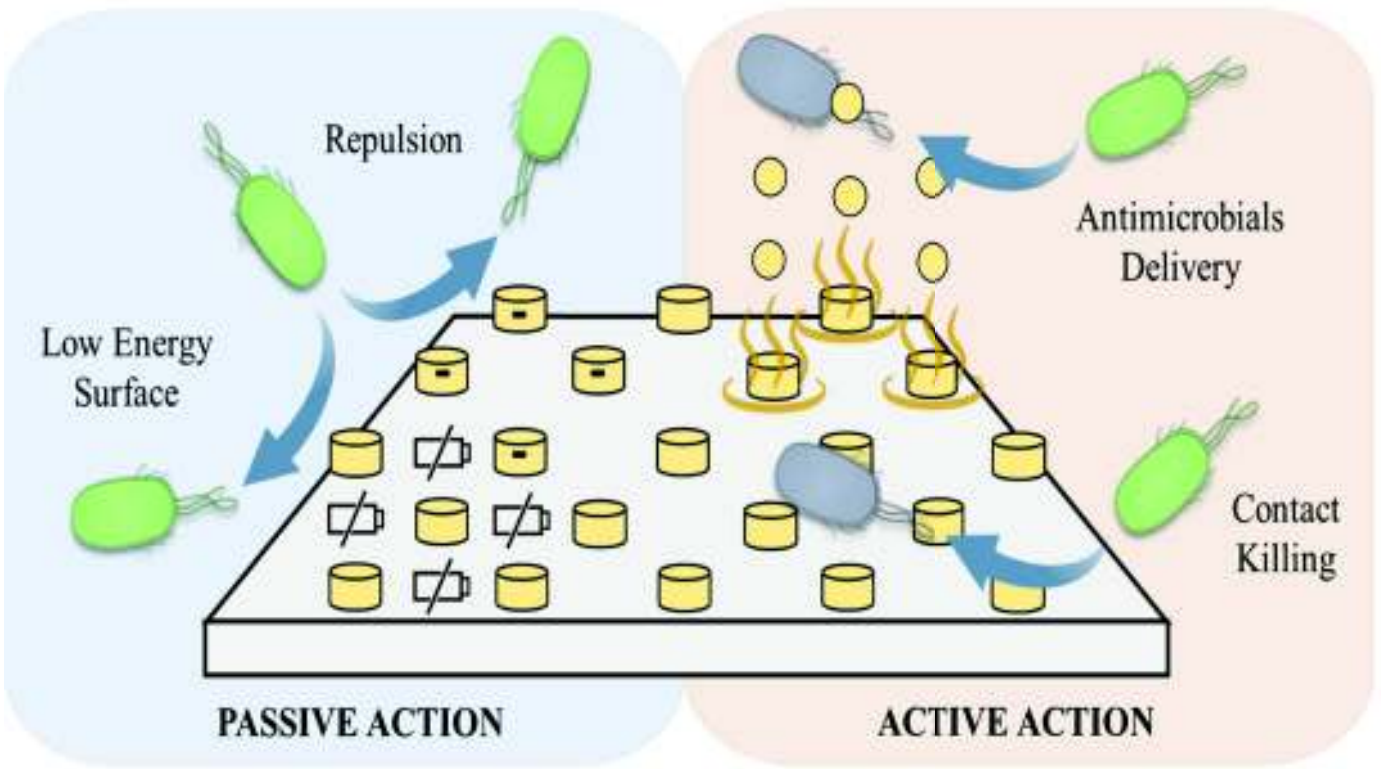

Figure 5. Mode of action of antimicrobial materials and coatings. Passive action prevents microbial adhesion and active action eliminate microorganisms. *Repulsion, includes electrostatic and hydrophilic/hydrophobic

Table 3. Medical applications of starch and phenolic compounds extracts combination.

Components	Founding's	Reference
Chitosan-collagen-starch and *Punica granatum* pericarp extract	The membrane showed antibacterial activity against *P. aeruginosa* with the disc diffusion method (18.1 ± 0.32 mm). The *in* vivo study showed that the membrane achieved 98.3 ± 1.2 % of re-epithelialization of 2 cm^2 wound in guinea pigs at the 25th day.	Amal *et al*. (2015)
Starch-zeolite nanoparticles and chamomile extract	The hydrogel showed a cytocompatibility with fibroblasts cells, promoting the proliferation and maturation of these cells after 4 and 7 days. The *in vivo* study in rats showed that the hydrogel improved the burn wound healing, promoting the epithelialization, collagen formation and angiogenesis. Finally, the clinical study showed the wounds healing in 6 patients, with a mean healing time of 31 days.	Salehi *et al*. (2017)
Poly vinyl alcohol-starch and turmeric	The hydrogel membranes showed antimicrobial activity against *E. coli* (DH5-alpha) and *S. aureus* (MRSA) having 9.9 mm and 11.3 mm of inhibition zone, respectively. The hydrogel membrane presented adequate mechanical, swelling and water retention properties.	Hassan *et al*. (2018)
Gelatin-oxidized starch and henna extract	The *in vitro* studies showed that nanofibrous mats improved the fibroblasts proliferation and the collagen secretion. In addition, presented antibacterial properties against *E. coli* and *S. aureus*. The *in vivo* studies showed the accelerated closure of burns wounds in mouse.	Hadisi *et al*. (2018)
Starch, hyaluronic acid and propolis extract	Films showed antibacterial activity against *E. coli*, *S. aureus* and *S. epidermidis* and cytocompatibility with fibroblast cells *in vitro*. The *in vivo* studies in Wistar rats, showed at reduction of the open wound area at the 7 day, while at the 14 the wounds were practically healed.	Eskandarinia *et al*. (2018) Eskandarinia *et al*. (2019)

II. HYPOTHESIS

Octenyl succinate starch-based films with nut by-products extracts present suitable characteristics and properties with potential for medical use as antimicrobial material.

III. OBJECTIVES

3.1 General Objective

To evaluate the antimicrobial properties of octenyl succinate starch-based films with nut by-products extracts for their potential medical application.

3.2 Specifics Objectives

1. To determine the physicochemical properties of native starch and octenyl succinate starch.

2. To determine the antibacterial activity of pecan nutshell and hazelnut skin ethanolic extracts, against Gram-positive and Gram-negative bacteria.

3. To determine the characteristics, physicochemical and antibacterial properties of octenyl succinate starch-based films with nut by-products extracts.

IV. MATERIALS AND METHODS

4.1 Starch modification

The commercial potato starch (Sigma-Aldrich, USA) modification consisted in an esterification with the OSA reagent (Dixie Chemical Company) according with the procedure described by Ovando-Martínez *et al*. (2017). Firstly, 100 g of starch were dissolved in 225 mL of deionized water with constant stirring (400 rpm). Consequently, 3 mL of OSA reagent were added at 0.1 mL/min flow speed. The solution was maintained with constant stirring and the pH was keep at 8.5-9.0 with 1 M NaOH. After 6 h of reaction, the pH was adjusted to 7.0 and centrifugated (Allegra X-12 Centrifuge, Beckman Coulter, Indianapolis, IN, U.S.A) during 15 min at 2500 g. The supernatant was discarded, and the pellet was first washed with deionized water (x3) and later washed with acetone (x3). The modified starch (OSS) was dried 24 h at 40 °C. Finally, the degree of substitution was determined with ^{1}H nuclear magnetic resonance (NMR), using a 400 MHz Bruker Avance III HD (Billerica, U.S.A) according to Whitney *et al*. (2016).

4.1.1 Proximate composition

4.1.1.1 Total and damage starch content. Total and damage starch content were determined using the Megazyme Kit (International Ireland), according to the American Association of Cereal Chemists 76-13.01 (AACC, 1999a) and 76-31.01 methods (AACC, 2014), respectively.

4.1.1.2 Amylose and amylopectin content. High-performance size exclusion chromatography (HPSEC) was used to obtain the amylose and amylopectin content according to Simsek *et al*. (2013). Starch samples (30 mg) were dissolved with a 1:10 (v/v) solution of 6 M Urea and 1 M KOH, respectively. Solutions were heated at 100 °C for 90 min and neutralized with 1 M HCl. Solutions were filtered through 0.45 μm nylon filters and injected (20 μL) in Agilent 1200 series high-performance liquid chromatography (HPLC) system (Agilent Technologies, Santa Clara, CA, U.S.A.) with a refractive index detector. Ultra hydrogel guard and linear size exclusion column (Milford, MA) at 40 °C were the stationary phase. The movil phase was HPLC water grade at a flow rate of 0.4 mL/min.

4.1.1.3 Ash, moisture and protein content. Ash and moisture content were determined gravimetrically, according to the methods approved by the American Association of Cereal Chemists, 08-01.01 (AACC, 1999b) and 44-15.02 (AACC, 1999c), respectively. Ash and moisture percentage were calculated according to the follow equation (1).

$$(1)\ \%\ Ash\ or\ Moisture = \frac{Initial\ Weight - Final\ Weight}{Initial\ Weight}\ x\ 100$$

Protein content was determined by the Dumas combustion method following the American Association of Cereal Chemists, 46-30.01 method (AACC 1999d).

4.1.2 Swelling property

Swelling volume was determined with a Rapid Viscosity Analyzer, RVA 4500 (RVA 4500, Perten Instruments, Springfield, IL, U.S.A) according to Ovando-Martínez *et al*. (2017). The sample (200 mg dry basis) was weighed in aluminum pans and mixed with 10 mL of distilled water. The pans were placed in the Rapid Viscosity Analyzer and maintained at 25 °C for 30 min. Subsequently, the samples were heated at 50, 60, 70, 80 and 90 ˚C during 30 min. Finally, the samples were transferred to 15 mL tubes, centrifuged (1000 g for 15 min), and the supernatant was measured. The swelling factor was calculated whit the following equations (2) and (3).

$$(2)\ Gel\ Volume = (10\ mL - Supernatant\ Volume)$$

$$(3)\ \ Swelling\ Factor = \frac{Gel\ Volume}{Sample\ Weight\ (Dry\ Basis)}$$

4.1.3 Pasting property

Rapid Viscosity Analyzer RVA 4500 was using to measure the pasting properties according to the method 76-21.02 of the American Association of Cereal Chemists (AACC, 2017). Starch samples (3g) were mixed with 25 mL of deionized water in aluminum pans. The pans were placed in the RVA instrument and held at 50 °C for 1 min. Later, the pans were heated from 50°C to 95°C in a rate of 12 °C/min, and held 2 min at 95°C. Finally, the pans were cooled down in a rate of 12 °C/min and held 2 min at 50°C. The pasting temperature, time peak, peak viscosity, breakdown, setback, and final viscosity were obtained using the software supplied with the RVA instrument.

4.1.4 Gelatinization property

Gelatinization properties were determined by Differential Scanning Calorimetry (DSC), using a Perkin-Elmer Differential Scanning Calorimeter DSC-6000 according to Ovando-*Martínez et al*. (2017). Starch (3.5 mg) and 8 µL of deionized water were placed in aluminum pans. The pans were hermetically sealed and stored in a room temperature overnight. Next day, the pans were placed in the DSC and heated 10°C per-min., from 20°C to 120 °C. Enthalpy of gelatinization (ΔH), onset, peak and end temperature were obtained using the software supplied with the DSC instrument.

4.1.5 Starch granule morphology

The starch morphology was obtained by scanning electron microscopy (SEM) using a JEOL JSM-6490LV scanning electron microscope (JEOL USA, Peabody MA, U.S.A) with accelerating voltage of 15 kV. The starch samples were placed in cylindrical aluminum mounts with XYZ conductive tape (Electron Microscopy Sciences, Hatfield, NJ, U.S.A) and coated with gold using a Cressington 108auto sputter coater (Ted Pella Inc., Redding CA, U.S.A).

4.1.6 Amylopectin chain length distribution

To analyze the chain length distribution of OSS, it firstly was fractionated in amylose and amylopectin. For this, a gel permeation chromatography (GPC) system was used. Modified starch was dissolved in 2 M NaOH with constant stirring at 80 °C. The dissolved starch was filtered and loaded in the GPC column (1.6 x 100 cm) packed with Sephadex CL-2B gel. The mobile phase was 10 mM NaOH with a 0.4 mL/min flow rate. The collected fractions were used to identify the amylose and amylopectin with the phenol sulfuric acid and blue value assay. Once detected the amylopectin fraction, it was combined, subjected to dialysis, and finally freeze-dried for further analysis of chain length distribution of amylopectin (Whitney *et al*., 2016).

High performance anion exchange chromatography (HPAEC) was used to determine the chain length distribution of amylopectin according to Whitney *et al*. (2016). Amylopectin sample was dissolved in deionized water by heating at 80 °C for 15 min with constant stirring. Samples were diluted with sodium acetate buffer (4 mL, 10 mM, pH 3.5) and the α-(1-6) linkages were hydrolyzed with isoamylase (48 h, 40 °C). After it, samples were freeze-dried, resuspended in deionized water, and filtered thought a 0.45 µm syringe. Finally, the sample (25 µL) was injected into the HPAEC system (Dionex, CA, U.S.A) equipped with a Carbopac PA-100 column. The gradient system was as follow: (A) 150 mM NaOH and (B) 600 mM sodium acetate with 150 mM NaOH. The gradient started from 100% A to 100% B, for 100 min, increasing 1% eluent B per-min. The samples were monitored with the ED-40 detector in pulsed amperometric mode. The chain length distribution was calculated with a Dionex software.

4.2 Nut by-products phenolic extraction

Nut by-products used as a source to obtain the phenolic compounds were pecan nutshell (*Carya illinoinensis*) and hazelnut skin (*Corylus avellana*). Pecan nuts Wichita (variety) were donated by Grupo Alta S.A de C.V., a processing plant located in Hermosillo Coast of Sonora State, Mexico. Nutshell was milled in a hammer mill (Tomas Model 4 Willey-Mill) and sifter to a particle size less than 1 mm. On the other hand, hazelnut skin was obtained from commercial

markets in Ordu, Turkey. The hazelnut skin was milled in a coffee grinder and sifted to a particle size between 0.85–0.50 mm. Both by-products were stored at 4°C until further analysis.

Ethanolic extraction was used to obtain the phenolic extracts according to the method described by Liu *et al*. (2013), with slight modifications. The sample was mixed with 60% ethanol (ratio1:30, w/v) and sonicated during 15 min (Branson 1510, Danbury, CT, U.S.A). Later, the solution was centrifuged for 15 min at 5000 g and 4 ˚C. The supernatant was filtered using a vacuum system with Whatman paper #4. The solvent was removed using a rotavapor system at 45°C. The resulting extracts of pecan nutshell (PSE) and hazelnut skin (HSE) was freeze-dried (Labconco FreeZone 6-liter, Kansas City, MO, U.S.A) and finally stored at 4°C until further analysis.

4.2.1 Total phenol and flavonoid content

Total phenol and flavonoid content were measured in serial dilutions of extracts resuspended in 60% ethanol (1 mg per-mL). The assays are described below.

The total phenolic content (TPC) was determined by the Folin-Ciocalteu assay (Singleton & Rossi, 1965), with modifications. The sample (30 µL, PSE or HSE) was placed in flat-bottom 96-well microplate. Briefly 150 µL of Folin-Ciocalteu reagent (1:10 v/v) and 120 µL of 7.5% Na_2CO_3 were added. Then the microplate was incubated for 30 min in dark conditions. Finally, the absorbance was measured at 750 nm using a microplate reader (Multiskan Ascent, Thermo Electron Corporation). The results were expressed as mg of gallic acid equivalents per-gram of extract (mg GAE/g), using gallic acid as external standard (R^2= *0.9992*). Total flavonoids content (TFC) was determined using the aluminum chloride assay previously described by Zhishen *et al*. (1999), with slight modifications. In a test tube 250 µL of sample (PSE or HSE), 1000 µL of deionized water and 75 µL of 5% $NaNO_2$ were mixed with vortex and incubated for 5 min. After the incubation, 75 µL of 10 % $AlCl_3$ was added and mixed. After 1 min, 500 µL of 1M NaOH and 600 µL of deionized water were added and mixed. Finally, 300 µL of the reaction solution were placed in a flat-bottom 96-well microplate. The absorbance was measured at 492 nm using a microplate reader. The results were expressed as mg of catechin equivalents per-gram of extract (mg CE/g), using catechin as external standard (R^2= *0.9999*).

4.2.2 Antioxidant activity

The antioxidant activity was measured in serial dilutions of extracts resuspended in 60% ethanol (1 mg per-mL). The assays are described below.

4.2.2.1 ABTS radical inhibition assay. The ABTS•+ radical cation (2,2′-azino-bis(3-ethylbenzothiazoline-6-sulfonic acid)) inhibition assay was realized according to Re *et al*. (1999) whit modifications. In a test tube 20 µL of sample (PSE or HSE) were mixed with 2 mL of ABTS•+ radical cation (previously adjusted to an absorbance of 0.7 ± 0.02 at 750 nm). After 5 min of incubation in darks conditions, 250 µL of the reaction solution were placed in a flat-bottom 96-well microplate and the absorbance was measured at 750 nm using a microplate reader. The results were expressed as µmol of TROLOX equivalents per-g of extract. (µmol TE/g), using TROLOX as external standard curve ($R^2 = 0.9988$).

4.2.2.2 DPPH radical inhibition assay. The DPPH• radical (2,2′-diphenyl-1-picrylhydrazyl) inhibition assay was realized according to Brand-Williams *et al*. (1995) with slight modifications. In a flat-bottom 96-well microplate were placed 20 µL of sample (PSE and HSE) and 280 µL of DPPH• radical, previously adjusted to an absorbance of 0.7 ± 0.02 at 516 nm. The microplate was incubated 30 min in darkness conditions. The absorbance was measured at 516 nm using a microplate reader. The results were expressed as µmol of TROLOX equivalent per-g of extract (µmolTE/g), using TROLOX calibration curve ($R^2 = 0.9981$).

4.2.2.3 Ferric reducing antioxidant power (FRAP) assay. The FRAP assay was realized according to Benzie & Strain (1996), with slight, modifications. Firstly, the FRAP reagent was prepared by mixing sodium acetate buffer (0.03M, pH 3.6), 10 mM TPTZ (2,4,6-Tris(2-pyridyl)-s-triazine) in 40 mM hydrochloric acid solution, and 20 mM $FeCl_3$ aqueous solution, (10:1:1 ratio). Afterwards, in a flat-bottom 96-well microplate 20 µL of sample (PSE or HSE) and 280 µL of FRAP reagent were combined and incubated for 30 min in dark conditions. The

absorbance was measured at 595 nm using a microplate reader. The results were expressed as µmol TE/g, using TROLOX as external standard ($R^2 = 0.9988$).

4.2.3 Phenolic profile

Prior to the identification and quantification of PC present in the extracts by high performance liquid chromatography with diode array (HPLC-DAD), an acid hydrolysis was performed according to Hilbig *et al*. (2018b), with modifications. The freeze-dried extract (150 mg, PSE or HSE) was mixed 2 M HCl (12 mL) with constant stirring at 175 rpm during 2 h, in a water bath at 80 °C. Later, the solution was cool down with sonication for 10 min and then adjusted to pH 2, with NaOH. Later, ethyl ether (18 mL) was added, mixed and the organic phase was collected. This process was done three times, collecting and mixing all the organic phases. The ethyl ether was removed with a rotavapor system at 28°C. The resulting hydrolyzed extracts were freeze-dried and stored at -4 °C until their analysis.

A modified method of Nour *et al*. (2012) was used to identify and quantify the PC. Firstly, the hydrolyzed extracts were resuspended in methanol and filtered through a nylon filter (0.20 µL). The sample (50 µL) was injected in an Agilent 1200 series high-performance liquid chromatography (HPLC) equipped with Supelcosil C18 (25 cm x 4 mm x 5 µm) column used as stationary phase. The elution phase consisted in acidified water (1% acetic acid) (A) and methanol (B) with 1 mL/min of flow rate following the gradient: 90% of A from 0 to 27 min, from 90 to 60 % of A in 28 min, 60% of A for 5 min, from 60 to 56% of A in 2 min, 56% of A for 8 min, from 56 to 90% in 1 min, and 90% for 4 min. Identification and quantification of PC were done at 254, 278, 300 and 360 nm. A calibration curve of different standards was used to obtain the concentration of PC in the extracts, which was reported as mg per-gram of extract (mg/g).

4.2.4 Antibacterial activity

The antibacterial activity of the PSE and HSE was evaluated against *Staphylococcus aureus* ATCC 6538P, *Staphylococcus epidermidis* ATCC 12228, *Pseudomonas aeruginosa* ATCC

27853 and *Klebsiella pneumoniae* ATCC 13883. The strains were provided by the Laboratorio de Microbiología Polifásica y Bioactividades, CIAD Hermosillo, Sonora. The antimicrobial activity consisted in the determination of the minimum inhibitory (MIC) and bactericidal (MBC) concentrations and biofilm formation inhibition.

4.2.4.1 Inoculum preparation. Inoculum was prepared according to the approved methods of the Clinical Laboratory Standards Institute (CLSI): M07-A10 (2015). From 18-24 h previously inoculated Müeller-Hinton broth, approximately 1 mL was transfer to 0.85% sterile saline solution (SS), mixed and adjusted at 0.08-0.12 absorbance at 625 nm (0.5 McFarland scale, 1 x 10^8 UFC). From the adjusted solution, a 1:150 dilution ratio in Müeller-Hinton was prepared to obtain 1-2 x 10^6 UFC. The inoculum was used within 15 min, to maintain the bacteria concentration.

4.2.4.2 Extracts preparation. First, the lyophilized extracts (PSE or HSE) were dissolved with dimethyl sulfoxide (DMSO) (100 mg/mL, ratio) according to do Prado *et al*. (2014). The dissolved extracts were added to the corresponding culture media approved by CLSI, Müeller-Hinton for bacteria and RPMI 1640 for yeast. A stock solution of 2 mg of extract per-mL of broth medium was prepared and used, to obtain dilutions in a concentration a range from 0 to 2 mg/mL (each 0.100 mg/mL).

4.2.4.3 Minimum inhibitory and bactericidal concentrations determination. The microdilution broth assay was adapted from the M07-A10 (CLSI, 2015). In a sterile flat-bottom COSTAR 96-well microplate 100 µL of the prepared inoculum and 100 µL of medium with extract (PSE or HSE) at different concentrations were added, and the microplate was incubated 24 h at 37 ˚C. The final concentration of the extract in the microplate was half of the prepared concentration, while the final inoculum was 0.5-1 x 10^6 and 0.5-2.5 x 10^3 UFC for bacteria and yeast, respectively. After the incubation time, 20 µL of 0.5% TTZ (2,3,5-triphenyltetrazolium chloride) solution were added in each well and the microplate was incubated again for 1 h at 37

˚C (do Prado *et al.,* 2014). The concentration with absence of red color was established as the minimum inhibitory concentration (MIC). To obtain the minimum bactericide concentration (MBC), 20 µL from each well of the MIC microplate was inoculated in Petri dishes with Müeller-Hinton agar, and incubated 24 h at 37 ˚C. The concentration that did not show any growth (colonies) was established as the MBC.

4.2.4.4 Biofilm formation inhibition. Following the crystal violet assay described by Stepanović *et al.* (2004) whit some modifications, 125 µL of the prepared inoculum and 125 µL of the MIC of the corresponding extract, were placed in a sterile flat-bottom COSTAR 96-well microplate. After 24 h of incubation at 37˚C, the broth was removed, and the wells were washed whit sterile water three times. Later, 250 µL of methanol were added to each well to fix the attached bacteria. After 15 min, methanol was removed, and the microplate was air-dried. The dried wells were stained with 250 µL of 0.1% crystal violet solution and 5 min later the solution was removed, washed with distilled water and air dried. Finally, the stained cells were resuspended with 250 µL of 33% glacial acetic acid solution and the absorbance was measured using a Varioskan Lux, Thermo Scientific, microplate reader at 570 nm. The inhibition percentage was calculated according to Shao et al. (2015) using the following equation (4)

$$(4)\ \%\ Inhibition = \frac{Abs\ Ctl - AbsMIC}{Abs\ Ctl}\ x\ 100$$

Where: Abs Ctl was the inoculum without extract at MIC

4.3 Films preparation

Films were prepared with the casting method according to Zamudio-Flores *et al*. (2015) and Li *et al*. (2018), with modifications. The films components are shown in **Table 4.** The film forming solution was placed in a flask and was mixed at constant stirring (1000 rpm) in a heating plate

Table 4. Films formulation with octenyl succinate starch and pecan nutshell extract or hazelnut skin extract.

Film	Film Forming Solution			Extract Solution	
	OSS (g)	Glycerol (g)	Water (mL)	60% Ethanol Solution (mL)	PSE or HSE (mg/100 mL)
OSS (Control)	4	2	90	10	0
OSS-PSE or HSE					
250	4	2	90	10	25
500	4	2	90	10	50
750	4	2	90	10	75
1000	4	2	90	10	100

OSS: Octenyl succinate starch, PSE: Pecan nutshell extract, HSE: Hazelnut skin extract.

at 95 °C for 10 min. Later, the film forming solution was cooling down to 50 °C, and 10 mL of the extract solution were added. Both solutions were mixed during 15 min with constant stirring at 1000 rpm. The final solution was casting in square plastic plates (12x12 cm) and dried at 60 °C during 4-5 h. The dried films were removed from the plates and the thickness was measured in five aleatory points using a Mitutoyo 2416F micrometer. The films were stored in a 50% of relative humidity (RH) chamber and ambient temperature, for 5 days before the analysis.

4.3.1 Surface morphology

4.3.1.1 Micrographs by Scanning Electron Microscopy (SEM). Surface micrographs were obtained using a scanning electron microscope (JEOL JSM-6490LV, JEOL USA, Peabody MA, USA) with accelerating voltage of 15 kV. Films were placed in cylindrical aluminum mounts

with XYZ conductive tape (Electron Microscopy Sciences, Hatfield, NJ, USA) and coated with gold using a Cressington 108auto sputter coater (Ted Pella Inc., Redding CA, USA).

4.3.1.2 Topography by Atomic Force Microscopy (AFM). Surface topography was analyzed using a Veeco Dimension 3100 Atomic Force Microscope according to the modified version of the American Society of Testing and Materials method E2382-04 (ASTM, 2012). Films were attached in 12 mm diameter disk Ted Pella, Incorporated (Product No. 16208). The cantilever used was Golden Silicon Probe NSG01 (reflective side: Au; tip height: 14–16 μm; tip curvature radius: 10 nm; chip size: 3.4 × 1.6 × 0.3 mm, cantilever length: 125 ± 5 μm; cantilever width: 30 ± 5 μm; cantilever thickness: 1.5–2.5 μm).

4.3.2 Fourier-Transform Infrared Spectroscopy (FTIR).

The interactions between the phenolics extracts (PSE or HSE) and OSS were identified by FTIR analysis using a Thermo Scientific Nicolet 8700 FTIR instrument. Smart iTR Accessory with a diamond crystal was used for the reflectance mode. The FT-IR spectra of PSE, HSE, OSS, OSS-PSE and OSS-HSE were measured with 128 scans at 4000 to 650 cm^{-1} wave number range and resolution of 4 cm^{-1}.

4.3.3 Optical properties

4.3.3.1 Color measurement. Using a MacBeth Color Eye 7000 spectrophotometer with Pro Palette 5.0 software, the CIELab scale color values were obtained with the standard light source D65 at 10° (Luchese *et al*. 2018). The color values obtained were **L* (0 to 100, black to white), **a* (-*a* to +*a,* greenness to redness) and **b* (-*b* to +*b*, blueness to yellowness). To obtain the color values, the films were placed in a standard white calibration surface (**L*= 95.69, **a*= -0.90 and **b*= 1.94) and measured in different aleatory points (Khanmani & Rhim, 2014).

4.3.3.2 Transparency and UV-vis light absorption. Using a Hach DR/4000 UV-Vis spectrophotometer (Hach, Loveland, CO, U.S.A.) the transparency and UV-Vis absorption were analyzed according to Khanmani & Rhim (2014) with modifications. The films were cut in rectangular pieces (1x4 cm) and placed into a quartz cell. Transmittance (T%) was measured at 280 and 660 nm. On the other hand, to obtain the UV-Vis spectra the absorbance was measured in a wavelength range of 200 to 800 nm. Air was used as a blank.

4.3.4 Water barrier properties

4.3.4.1 Water content and water solubility. These assays were realized according to the method described by Nouri & Nafchi (2014) with slight modifications. Films pieces (2 x 3 cm) were weighed before and after drying in an oven at 105 °C for 24 h. The dried film pieces were placed in a flask with 80 mL of distilled water with constant stirring at 125 rpm for 1 h. After that, the solution of the flasks was filtered through a Steel mesh (45 microns) and the solids were placed in the oven at 65 °C overnight. The dried films solids were weighed. The water content and solubility percentage were calculated with the following equation (5)

$$(5)\ \%\ Water\ Content\ or\ Solubility = \frac{Initial\ Weight - Final\ Weight}{Initial\ Weight}\ x\ 100$$

4.3.4.2 Hydrophobicity. Films hydrophobicity was determined by measurement of the contact angle according to the American Society for Testing and Materials method D7334-08 (ASTM, 2013a). Whit a syringe a drop of deionized water was placed in random points of the films. The contact angle values were obtained with a Contact Angle Analyzer (First Ten Angstroms 125) with a CCD camera, and a First Ten Angstroms 32 Video 2.0 Software.

4.3.4.3 Water vapor transmission rate (WVTR). The water dish method was used to obtain the water vapor transmission rate (WVTR) according to the American Society for Testing and Materials method E96/E96M-15 (ASTM, 2015). Films between two metal plates with inner diameters of 5.4 cm were placed over Petri dishes with 20 mL of water. Separation between the water and the films was 13 mm. Using parafilm the metal plates and the Petri dishes were held and sealed. The whole assembly was weighed with a Mettler Toledo New Classic MF analytical balance (Model No. ML203E/03). Mass was recorded at 0, 1, 3, 6, 12 and 24 h and plotted. The WVTR was calculated with the follow equation (6).

$$(6)\ WVTR = \frac{GT}{A}$$

Where:

GT: Slope of the weight variation versus time plot (g/h)

A: area in m^2

4.3.5 Mechanical Properties

Evaluation of the tensile properties, tensile strength (TS), elongation at break (EB) and Young´s modulus (YM) were carried out according to the American Society for Testing and Materials method D882-18 (ASTM, 2018). An Instron 5545 tensile test machine with a 100 N load cell was used for the test. The testing conditions were 51 mm/min strain rate with initial grip separation of 25.4 mm. Results were obtained with the Instron Bluehill 2.1 software.

4.3.6 Antimicrobial Properties

To evaluate the antimicrobial properties against the strains mentioned in section **4.2.4**, the films were sterilized with UV-Light during 25 min, each side. Inoculums were prepared as described in the section **4.2.4.1**.

4.3.6.1 Antimicrobial Activity in Solid Media. The inhibition zone or agar disc diffusion method was carried out. In trypticase soy agar (TSA) plates, 100 µL of inoculum were spread using a sterile swab. Circular films with a diameter of 2.5 cm, were placed in the center of the plates. The plates were incubated for 24 h at 37°C. After incubation the inhibition zone was measured (mm).

4.3.6.2 Antimicrobial Activity in Liquid Media. The growth inhibition in liquid media was determined according to Kart *et al*. (2017), with modifications. The film (1 cm^2) and 2 mL of inoculum were placed in a sterile flat-bottom COSTAR 12-well microplate and incubated 24 h at 37°C. After incubation, the supernatant was collected and absorbance was measured at 600 nm using (Volova *et al*., 2018).

4.4 Statistic Analysis

For the determination of significant differences with a significant level of $p \leq 0.05$, student T-test for the starch and extracts characterization, whereas one-way analysis of variance (ANOVA) with post-hoc Tuckey HSD were used with the IBM SPSS 23 version statistic software.

V. RESULTS AND DISCUSIONS

5.1 Octenyl succinate starch composition

Starch was successfully modified showing a degree of substitution of 0.013, which is indicating the number (average) of hydroxyl groups that were substituted by OSA group for each unit of glucose in the starch structure (Tizzotti *et al.*, 2011). The changes in the proximate composition are shown in **Table 5** and are discussed below.

Total starch decreased around 8%, maybe because of the OSA groups, which could interfere during the total starch determination. On the other hand, amylose content increased after the modification. This result is different to that reported by Simsek *et al*. (2015), Abiddin *et al*. (2018), Lopez-Silva *et al*. (2019) and Punia *et al*. (2019b). These authors reported that amylose decrease in different starches, because the inclusion of OSA groups occurs preferentially in the amylose chains of the amorphous region of the starch granule (Whitney *et al*., 2016; Won *et al*., 2017). However, the increase of amylose content has been reported by Bajaj *et al*. (2019) in different starches, including potato starch. This could be due to the hydrolysis of the amylopectin chains during the modification process, which led to the formation of new amylose chains, then explaining the decrease of the amylopectin content during the starch modification. Bai *et al*. (2014) and Wang *et al*. (2016) reported that the distribution of OSA groups occurs close the branching points of the amylopectin chains. The differences and similarities with these studies, could be related to the nature of the starch (botanical source) and the conditions of the modification process (Huber & BeMiller, 2001). Starch damage decrease significantly ($p \leq 0.05$). This trend was reported previously by Ovando-Martínez *et al*. (2017) in potato starch. According with this author, damage starch is more susceptible to be affected by the OSA reagent, because this provides a greater area of interaction between OSA groups and starch chains. Besides, during the modification process the damage granules could be solubilized. Moisture and ash content showed significant changes ($p \leq 0.05$), whereas protein content was similar both starches. The low moisture content in OSS could be related with the reduction of hydroxyl groups by the substitution with OSA groups. On the other hand, the ash content increase could be a result of the presence of sodium in the OSA molecules added to the starch (**Figure 1**).

Table 5. Proximate composition of native and octenyl succinate starch.

	NS	OSS
Total starch (%)	99.31 ± 0.51^{a}	91.51 ± 0.64^{b}
Amylose (%)	10.28 ± 0.13^{b}	12.19 ± 0.07^{a}
Amylopectin (%)	89.72 ± 0.13^{a}	87.81 ± 0.07^{b}
Starch damage (%)	1.56 ± 0.03^{a}	1.43 ± 0.07^{b}
Moisture (%)	17.26 ± 0.04^{a}	11.56 ± 0.26^{b}
Ash (%)	0.16 ± 0.05^{a}	0.48 ± 0.07^{a}
Protein (%)	0.10 ± 0.05^{a}	0.04 ± 0.04^{a}

Data represent mean ± standard deviation, n=3. Different literals between columns indicate significant differences ($p \leq 0.05$). NS: Native starch, OSS: Octenyl succinate starch.

5.2 Octenyl Succinate starch properties

An improvement in the swelling property was observed after the starch esterification with the OSA reagent (**Figure 6**). The OSS showed a greater capacity to water absorption, and it was significative different than the NS ($p \leq 0.05$). Results were consistent with those reported by Bello-Flores *et al*., (2014), Ovando-Martínez *et al*., (2017), Remya *et al*. (2018) and Punia *et al*. (2019b). According with these authors, the increase of water absorption occurs due to the weakening of intermolecular hydrogen bond in the starch structure and the consequent damage in the starch granule surface by the inclusion of OSA groups. This facilitates the entry of water molecules into the granule, then allowing greater interaction between these molecules with the hydroxyl groups of the internal starch chains. The increase in the swelling factor observed in the OSS, specifically at 50, 60 and 70 °C temperatures, could facilitate the entry of the PCs of the extracts into the starch granules, favoring the distribution throughout the complete structure of the starch, during the film formation.

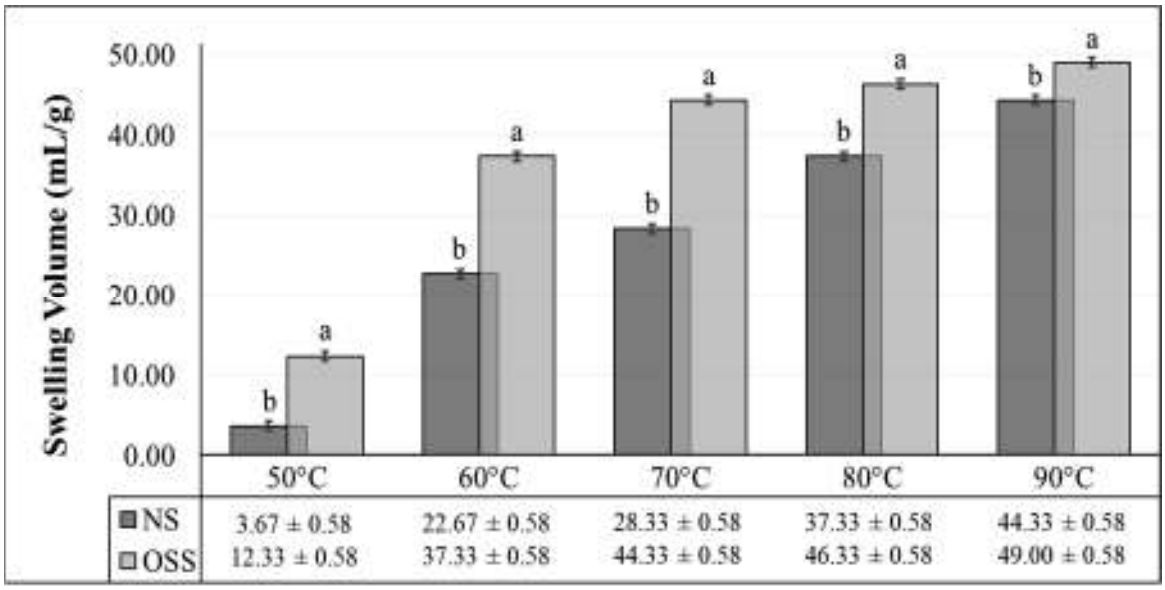

Figure 6. Swelling volume of native and octenyl succinate starch at different temperatures. Error bars indicate standard deviation (n=3). Different letters between bars at same temperature indicates significant differences ($p \leq 0.05$). NS= Native starch, OSS= Octenyl succinate starch.

Pasting properties were improved in OSS (**Table 6**). Firstly, the pasting temperature decreased significantly ($p \leq 0.05$) from 68.65 ± 0.05 to 62.72 ± 0.03. This behavior was reported in previous studies, indicating that the structural changes caused by the inclusion of OSA groups, allow to the starch granules swell at a lower temperature compared to the unmodified starch (Bello-Flores *et al*., 2014; No *et al*., 2019; No & Shin, 2019; Punia *et al*., 2019b; Velásquez-Barreto *et al*., 2019). The increase in the peak time could be related to the increase in swelling property (**Figure 6**). It means that by having a greater capacity to absorb water, the starch granule would take longer time to fully swell. Commonly, viscosity peak, breakdown and setback decrease after the OSA groups inclusion into the starch structure (Sweedman *et al*., 2013). In this work, these parameters decreased, similar to that reported by Ovando-Martínez *et al*. (2017). Additionally, Won *et al*. (2017) reported a lower peak and setback viscosity, while Velásquez-Barreto *et al*. (2019) reported a lower setback viscosity compared to unmodified starch. Finally, the final viscosity showed a significant increase ($p \leq 0.05$), which agrees with

Table 6. Pasting and gelatinization properties of native and octenyl succinate starch.

	NS	OSS
Pasting properties		
Pasting temp (˚C)	68.65 ± 0.05[a]	62.72 ± 0.03[b]
Peak time (min)	3.07 ± 0.00[b]	4.67 ± 0.00[a]
Viscosity peak*	924.64 ± 12.20[a]	615.00 ± 8.95[b]
Breakdown*	779.83 ± 10.73[a]	275.58 ± 6.42[b]
Setback *	169.19 ± 9.75[a]	94.17 ± 10.07[b]
Final viscosity*	314.00 ± 9.46[b]	433.58 ± 6.91[a]
Gelatinization properties		
Enthalpy (J/g)	15.08 ± 0.14	16.42 ± 0.25
Onset temperature (˚C)	62.78 ± 0.20	59.41 ± 0.82
Peak temperature (˚C)	66.69 ± 0.24	64.75± 0.30
End temperature (˚C)	73.25 ± 0.09	73.15 ± 0.82

Data represent mean ± standard deviation, n=3. Different literals between columns indicate significant differences ($p \leq 0.05$). NS: Native starch, OSS: Octenyl succinate starch. *RVU= Rapid viscosity units.

starch. Finally, the final viscosity showed a significant increase ($p \leq 0.05$), which agrees with several studies (Bello-Flores *et al*., 2014; Ovando-Martínez *et al*., 2017; Bajaj *et al*., 2018; No & Shin, 2019; No *et al*., 2019).

Gelatinization values obtained by DSC are shown in **Table 6.** The low onset and peak temperature in OSS indicate that the starch granule requires lower temperature to gelatinize. This occurs due to the structural weakening of the modified starch as mentioned above (Swedeeman *et al*., 2013). This is consistent with the swelling and pasting properties observed in **Figure 6** and **Table 6**, respectively. Similar behavior was reported in different starches including potato starch (Bello-Flores *et al*., 2014; Wang *et al*., 2016; Ovando-Martínez *et al*., 2017; Zhang *et al*., 2017; Abiddin *et al*., 2018; Velásquez-Barreto *et al*., 2018; No & Shin, 2019). Regarding to the end temperature, parameter related to the temperature where starch is completely gelatinized (Sweedman *et al*., 2013), no significant changes ($p < 0.05$) were found between NS and OSS. This result was similar to that reported by Won *et al*. (2017) and No *et al*. (2019). On the other hand, commonly the decrease in temperature associated with structural weakness due to the inclusion of OSA groups is confirmed by the decrease in the enthalpy of gelatinization (Sweedman *et al*., 2013). However, in this work and previous work carried out by Ovando-Martínez *et al*. (2017) and Bajaj *et al*. (2018) reported an increase in the gelatinization enthalpy in potato starches after the OSA modification. This could be related to the formation of amylose-OSA inclusion complexes and hydrophobic interactions between the OSA chains with neighbor amylopectin branch chains, factors which take more energy to break down the crystallinity of the modified starch granule (Ortega-Ojeda *et al*., 2005, Thirathumthavorn & Charoenrein, 2006).

All of these pasting and thermal properties suggest that the OSS has better properties than native starch for the film formation. So, it was for this reason, OSS was used in the present work to elaborate the films, and also to protect the phenolic compounds presented in the nut by-products extracts.

5.3 Octenyl succinate starch morphology and structure

To corroborate the results described above, the morphological and structural properties of both starches was carried out. Starch granule micrographs obtained by SEM showed that the inclusion of OSA groups affected the surface morphology of the granule, showing the presence of small fissures and desquamation. Also, it was observed the generation of some cumulus and non-morphology changes (size and shape) (**Figure 7**). Same characteristics were reported previously by other authors (Wang *et al*., 2010; Ovando-Martínez *et al*., 2017; Zhang *et al*., 2017; Lopez-Silva *et al*., 2019. This damage in the starch granule surface could be related with the increase of the swelling, (**Figure 6**), pasting and gelatinization properties (**Table 6**).

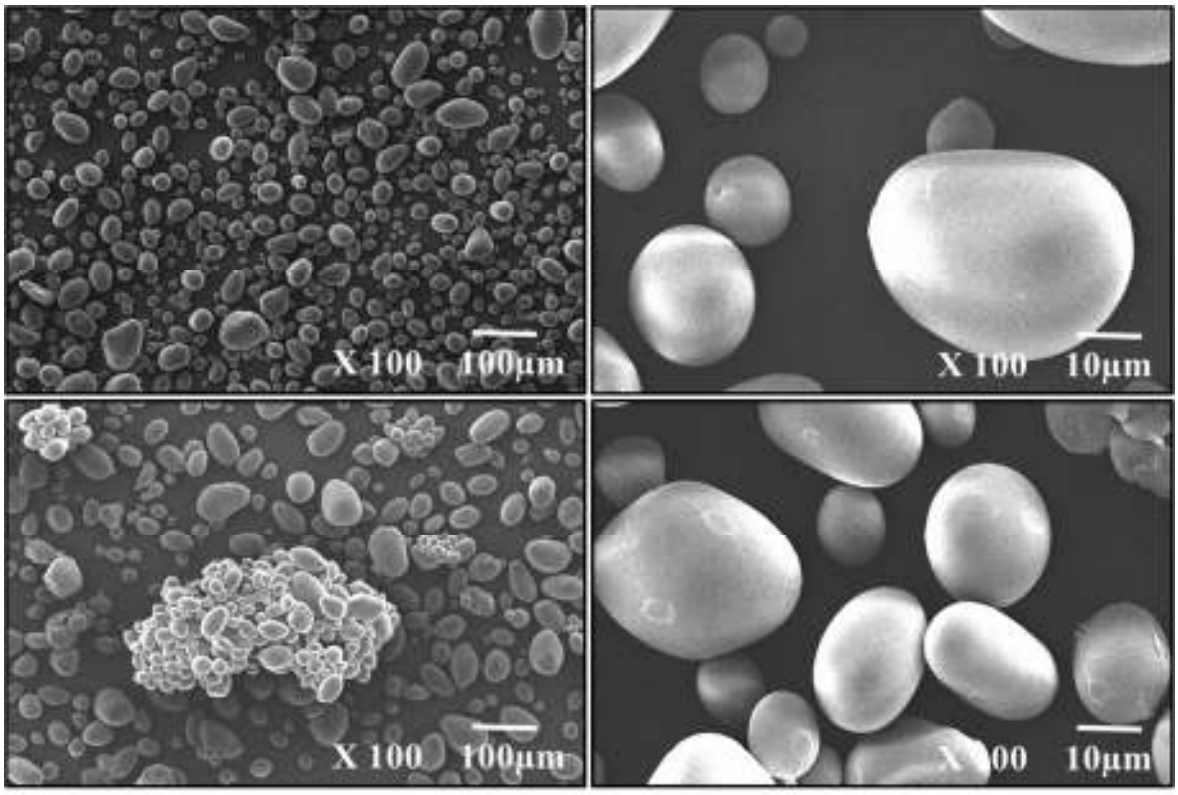

Figure 7. Native and octenyl succinate starch granule micrographs. Native starch (up) and octenyl succinate starch (down).

In the case of the amylopectin chain length distribution no significant differences were observed ($p > 0.05$) between NS and OSS (**Table 7**). However, a tendency to increase short A chains (6-12) and a decrease in long B chains (≥13) was observed. This could indicate the hydrolysis of long chains, which could explain the increase in amylose content and the decrease in amylopectin content (**Table 5**). On the other hand, the change in the outer chains could explain the desquamation observed on the granule surface (**Figure 7**).

According to the morphological and structural analysis, it can be inferred that the inclusion of OSA groups occurred mainly in the amorphous regions of the granule, along of amylose chains and branching points of the B chains of amylopectin.

Table 7. Native and octenyl succinate starch amylopectin chain length distribution.

	NS	OSS
Degree of polymerization (%)		
A (6-12)	16.89 ± 0.31^{a}	17.47 ± 1.14^{a}
B (13-24)	66.58 ± 0.30^{a}	65.50 ± 0.98^{a}
B 2 (25-36)	15.82 ± 0.13^{a}	16.21 ± 0.56^{a}
B 3 (>37)	0.71 ± 0.09^{a}	0.81 ± 0.07^{a}
DPW	18.31 ± 0.06^{a}	18.34 ± 0.14^{a}
DPn	15.87 ± 0.06^{a}	15.91 ± 0.19^{a}

Data represent mean ± standard deviation, n=3. Different literals in same files indicate significant differences ($p \leq 0.05$). NS: Native starch, OSS: Octenyl succinate starch. DPW= Degree of polymerization weight average, DPn= Degree of polymerization number average.

5.4 Phenolic composition of nut by-products extracts

Initial phenolic characterization (TPC, TFC and antioxidant activity) of PSE and HSE extracts are shown in **Table 8**. The TPC obtained in PSE was higher than that reported by Kureck *et al*. (2018) in aqueous (186.02 ± 2.31 mg GAE/g) and 80% ethanolic extracts (275.24 ± 41.88 mg GAE/g) in Barton variety. This could be related to the nut variety, as well as the growing area and the extraction method, being both important factors involved in the PC content (de la Rosa *et al*., 2010; El Hawary *et al*., 2016). In the case of HSE, the TPC was higher compared to those results reported by Contini *et al*. (2008) using a different solvent systems (426.7 to 502.3 mg GAE/g); and were similar to the results obtained by Contini *et al*. (2012), whom used an ethanolic maceration (680.3 ± 11.6 mg GAE/g). In another study, it was reported that the TPC in hazelnut skins from Italy, varied from 166.80 to 869.72 mg GAE/g, and these results were related to the solvent type and extraction method (Piccinelli *et al*., 2016). These results could be explained by the extraction method, the hazelnut variety and the previous process to which the skin was subjected before the PC extraction (Locatelli *et al*., 2010; Taş & Gökmen, 2015).

In the case of TFC, it is not possible to compare the obtained results with other studies, because these studies report the TFC in the initial samples and not in the final extracts. However, the results obtained are consistent with previous reports in pecan nutshell and hazelnut skin samples. In this work, the TFC obtained in PSE represents around 35% of the TPC, which is similar to that reported by de la Rosa *et al*. (2010) in pecan nutshells with values between 30-40% of the TPC. Contrary to this, lower values of TFC (29%) were reported by El Hawary *et al*. (2016). Respect to hazelnut skin, Taş & Gökmen (2015) reported that the TFC corresponds around 60% of the TPC, this agrees with the results obtained in the HSE (61.72 %). In the same way as TPC, factors such as variety, the growing area and the extraction method are determinants in the TFC values. The significant differences ($p \leq 0.05$) found in the TPC and TFC values between both extracts (**Table 8**), could be related mainly to the nature or composition of the sample, considering that PCs are interacting with the main components of the food matrix (carbohydrates, lipids and proteins) (Jakobek, 2015). In pecan nutshell, close of 90% of the food matrix corresponds to carbohydrates and crude fiber (lignin) (do Prado *et al*., 2013), whereas in in skin close of 50% corresponds to lipids and proteins (Locatelli *et al*., 2010). In this context, the extraction from highly polymeric carbohydrate matrix is the most difficult

Table 8. Total phenol content, total flavonoid content and antioxidant activity of pecan nutshell and hazelnut skin extracts.

	PSE	HSE
TPC (mgGAE)	656.46 ± 4.91	693.00 ± 5.65
TFC (mgCE/g)	235.35 ± 1.50	427.77 ± 1.97
Antioxidant Activity (µmolTE)		
ABTS	3564.47 ± 11.42[b]	3674.78± 12.03[a]
DPPH	3098.61 ± 23.97[b]	3621.44 ± 13.54[a]
FRAP	3001 ± 17.20[b]	3767.8 ± 9.46[a]

Data are expressed as mg per-g of extract and represent mean ± standard deviation, n=3. Different literals between columns indicate significant differences, $p \leq 0.05$. PSE= Pecan nutshell extract, HSE= Hazelnut skin extract, TPC= Total phenolic content, TFC= Total flavonoid content, mgGAE= mg of gallic acid equivalents, mgCE= mg of catechin equivalents, µmolTE= micromol of TROLOX equivalents.

process, due to the large number of intramolecular and intermolecular interactions maintained among them, highlighting hydrogen bonds, hydrophobic interactions, covalent bonds and complex formation within the structure of carbohydrates (Jakobek, 2015).

One of the most important properties of the PC and PC extracts is their antioxidant activity (Bravo *et al*., 1998). This property occurs through three main mechanisms, directly related to the structure of the PC, (a) single electron transfer (SET), (b) hydrogen atom transfer (HAT), and (c) transition metal chelation (Leopoldini *et al*., 2011). For this reason, it is important to evaluate the antioxidant activity of phenolic extracts at least with two of these mechanisms. The ABTS and DPPH assays could be used to quantify the antioxidant activity by de HAT and SET mechanisms, depending of the reaction conditions (Apak *et al*., 2017). In this work, the conditions in both assays were favorable for HAT mechanism. Having as main

difference that the ABTS assay is more easily interacting with lipophilic and hydrophilic compounds (Re *et al*., 1999). In the case of the SET mechanism, FRAP assay has frequently used (Apak *et al*., 2017). Results indicate that the PC of PSE preferably perform their antioxidant activity by HAT mechanism. On the contrary, the PC of HSE act by both mechanisms in a similar way (**Table 8)**. With respect to previous studies, Kureck *et al*. (2018) reported antioxidant activity values of 1108.50 ± 27.77 and 1207.62 ± 7.68 μmolTE/g for ABTS; and for DPPH values of 1130.79 ± 6.04 and 1191.69 ± 10.18 μmolTE/g, in aqueous and hydroalcoholic extracts, respectively. These values were lower than the obtained in this work. Such results could be related to the TPC, which was also lower than the ones obtained in this work. Contini *et al*. (2012) reported higher antioxidant activity (1549.9 ± 54.7 mgTE/g) for DPPH assay in comparison whit this work, in this case TPC was similar, however the difference in the DPPH values could be explained to the phenolic profile of the extracts.

Phenolic profile of the nut by-products extracts used in this work are shown in **Table 9.** The PSE showed a total of 14 PC, from which gallic acid (68.51 ± 3.52 mg per-g) and epicatechin gallate (52.30 ± 1.88 mg per-g) were the major compounds. Previous studies have reported gallic acid as a majority phenolic acid in PSE (do Prado *et al*., 2014; Engler Ribeiro *et al*., 2017). Also, it has been reported pyrogallic acid as the most abundant phenolic acid in pecan nutshells extracts (El Hawary *et al*., 2016). However, Hilbig *et al*. (2018b) and Kureck *et al*. (2018) reported that ellagic acid was the main phenolic acid, followed by gallic acid. According with Porto *et al*. (2013), pecan nuthsell is a matrix rich in hydrolysable tannins (polymer units mainly formed by gallic and ellagic acid). This may explain why gallic acid is the major phenolic acid after the hydrolysis process prior to the identification and quantification of the PC in the PSE. The other phenolic acids identified in this work also has been reported previously (El Hawary *et al*., 2016; Engler Ribeiro *et al*., 2017; Hilbig *et al*., 2018a; Kureck *et al*., 2018). In the case of flavonoids, rutin was reported as a majority flavonoid in pecan nutshells by El Hawaray *et al*. (2016). However, in this work rutin was the second main flavonoid, behind of epicatechin gallate. According with some authors, pecan nutshell represents a great source of the catechins, among them, catechin, epicatechin, epigallocatechin epicatechin gallate and others) (Engler Ribeiro *et al*., 2017; Hilbig 2018a; Hilbig *et al.*, 2018b; Kureck *et al*., 2018). Also, quercetin in PSE has been reported by El Hawary *et al*. (2016) and Hilbig *et al*. (2018a).

Table 9. Phenolic profile of pecan nutshell and hazelnut skin extracts.

	PSE	HSE
Gallic acid	68.51 ± 3.52^{Aa}	20.98 ± 0.42^{Cb}
Protocatechuic acid	26.93 ± 3.77^{Db}	180.67 ± 0.60^{Aa}
P-Hydroxybenzoic Acid	10.35 ± 0.30^{Ga}	10.25 ± 1.25^{Fa}
Vanillic acid	4.73 ± 0.01^{Jb}	5.10 ± 0.01^{Ia}
Chlorogenic acid	5.42 ± 0.05^{Hb}	17.59 ± 3.37^{DCa}
Caffeic acid	10.20 ± 0.20^{Gb}	13.17 ± 0.21^{Ea}
P-Coumaric Acid	5.22 ± 0.02^{IHb}	5.29 ± 0.01^{Ha}
Ferulic acid	5.36 ± 0.19^{Hb}	6.90 ± 0.22^{Ga}
Sinapic acid	4.18 ± 0.18^{Kb}	5.11 ± 0.13^{Ia}
Total phenolic acids	140.9 ± 8.24	265.06 ± 6.22
Catechin	15.74 ± 0.68^{Fb}	23.49 ± 2.24^{Ca}
Epicatechin	21.54 ± 0.56^{Ea}	13.23 ± 1.21^{Eb}
Epicatechin gallate	52.30 ± 1.88^{Bb}	128.84 ± 0.51^{Ba}
Vitexin	-	0.94 ± 0.29^{Ka}
Rutin	34.73 ± 0.98^{Ca}	1.74 ± 0.27^{Jb}
Quercetin	1.28 ± 0.36^{Lb}	1.97 ± 0.06^{Ja}
Total flavonoids	125.59 ± 4.46	170.21 ± 4.58

Data are expressed as mg per-g of extract and represent the mean ± standard deviation, n=3. Different capital letters in same column and different lower case letter between files indicate significant differences, $p \leq 0.05$. PSE= Pecan nutshell extract, HSE= Hazelnut skin extract.

Fifteen PC were identified and quantified in the HSE (**Table 9**), being protocatechuic acid (180.67 ± 0.60 mg g) and epicatechin gallate (128.84 ± 0.51 mg-per g) the main compounds. According to Gültekin-Özgüven *et al*., (2015), protocatechuic acid was the predominant phenolic acid, and presented in higher amount than gallic acid (2.4 and 1.9 mg/100 g, respectively) in Giresum hazelnut skin, indicating similar behavior in this work. However, this behavior was contrary for other varieties. Montella *et al*., (2013) reported that hydroxybenzoic acid was the major phenolic acid in Tonda Gentile Trilobata hazelnut skin, whereas Pelvan *et al*., (2018) reported that gallic acid was the main phenolic acid in Tombul hazelnut skin. This indicates that the variety and the growing area, as well as the extraction method has an impact on the hazelnut compounds profile. The presence of other phenolic acids in this work has been reported in hazelnut skin by other authors (Shahidi *et al*., 2007; Del Rio *et al*., 2011; Montella *et al*., 2013; Özdemir *et al*., 2014; Gültekin-Özgüven *et al*., 2015; Pelvan *et al*., 2018). It was reported that hazelnut skin is a rich source of catechins, and condensed tannins named procyanidins (Taş & Gökmen 2017). This would explain the large amount of epicatechin gallate identified in this work. According to Del Rio *et al*. (2011), catechin concentration in aqueous extracts was higher than epicatechin gallate, indicating that water favors the extraction of catechin, while the mixture of ethanol and water favors the extraction of epicatechin gallate as obtained in this work. Respect to the other identified flavonoids in this work, various authors reported a similar profile in hazelnut skins (Del Rio *et al*., 2011; Montella *et al*., 2013; Özdemir *et al*., 2014; Gültekin-Özgüven *et al*., 2015).

Results showed significant differences ($p \leq 0.05$) in the PC profile between both extracts (**Table 9**). The most obvious differences were, a) the major compounds present in each extract, b) the concentrations of some PC and c) the presence of vitexin in HSE. Finally, the obtained results indicate that both nut by-products were an excellent source to obtain phenolic compounds, being HSE the one that showed the highest concentration of TPC, TFC and antioxidant activity. However, both extracts were considered candidates to assess their antimicrobial potential, since the structure of the PC is decisive in the activity and antimicrobial mode of action of these compounds (Xie *et al*., 2015).

5.5 Antimicrobial activity of nut by-product extracts

Both extracts showed antimicrobial activity against all tested strains (*Staphylococcus aureus* ATCC 6538P, *Staphylococcus epidermidis* ATCC 12228, *Pseudomonas aeruginosa* ATCC 27853 and *Klebsiella pneumoniae* ATCC 13883).

5.5.1 Minimum inhibitory and bactericide concentration

Antibacterial activity of both extracts was higher in the Gram-positive than the Gram-negative bacteria (**Table 10**). This agrees with previous studies about the antimicrobial potential of nut by-product extracts (Oliveira *et al*., 2007; Oliveira *et al*., 2008; Mandalari *et al*., 2010; Caxambú *et al*., 2016; Smeriglio *et al*., 2016). This is directly related to the outer layer that Gram-negatives have compared to Gram-positive ones, which provides greater protection against antibacterial compounds (Livermore, 2012). In this work the extracts only showed inhibitory effect against *K. pneumoniae*, whereas *P. aeruginosa* showed resistance to the concentrations tested.

Results were comparable with previous studies of antimicrobial activity of nut and their by-products extracts. According to do Prado *et al*. (2014), *S. aureus* showed a MIC in a range of 230 to 620 µg/mL. Bottari *et al*. (2017) reported a MIC of 6.25 mg/mL for the same microorganism. Besides, MICs values obtained in this study for *S. aureus* and *P. aeruginosa* were similar to those previously reported by Mandalari *et al*. (2010) with a rich flavonoid extract from almond skins. Non inhibitory effect of *Juglans regia* bark extracts against *P. aeruginosa* was reported by Chaieb *et al*. (2013). For its part, Smeriglio *et al*. (2016) reported MICs values lower than 125 µg/mL for *S. aureus* from natural almond skin, blanched skin and blanched water extracts. Also, same authors reported MICs values for *S. epidermidis* of 125, 1000 and 250 µg/mL, being the last one similar to the obtained in this work. Finally, these authors reported 500 and 1000 µg/mL as MIC values for *P. aeruginosa*. Recently, MICs of 312.5 and 156.25 µg/mL for *Juglans regia* leaves extracts against *S. aureus* and *S. epidermidis*, respectively, has been reported by Nicu *et al*. (2018). It is important to mention that these results were obtained with the same strains tested in this work. With respect to other strains, Santos *et al*. (2013) reported a MIC of 512 µg/mL against *S. aureus* and *P. aeruginosa* and MIC higher than 1024 µg/mL against *K. pneumoniae* for *Anacardium occidentale* steam peel ethanolic extracts. Range

Table 10. Minimum inhibitory and bactericide concentrations of pecan shell and hazelnut skin extracts against nosocomial impact pathogens.

	PSE		HSE	
	MIC (µg/mL)	**MBC (µg/mL)**	**MIC (µg/mL)**	**MBC (µg/mL)**
***Staphylococcus aureus* ATCC 6538P**	250	850	250	650
***Staphylococcus epidermidis* ATCC 12228**	250	800	250	600
***Pseudomonas aeruginosa* ATCC 27853**	>1000	>1000	>1000	>1000
***Klebsiella pneumoniae* ATCC 13883**	450	900	650	650

Data was obtained in three different inoculums (1 x 10^6). PSE= Pecan nutshell extract, HSE= Hazelnut skin extract, ATCC= American Type Culture Collection, MIC= Minimum inhibitory concentration, MCB= Minimum bactericidal concentration.

of MIC from 32 to 1024 µg/mL against some *K. pneumoniae* strains were reported by Dzotam & Kuete (2017) using *Coula edulis* (African walnut) extract. Aditionally, this extract showed no effect against *P. aeruginosa* strains. For its part, de Camargo *et al*. (2017) reported a MIC of 301 µg/mL against *S. aureus* and *P. aeruginosa.* Dolatabadi *et al*. (2018) reported a MIC average of 4 ± 3.56 mg/mL for 50 isolates of *P. aeruginosa* using a *Juglans regia* L. leaves aqueous extract.

In the case of *Staphylococcus* spp., both extracts showed the same MIC (250 µg/mL), indicating that TPC of the extracts (**Table 8**) are not directly related to the antimicrobial activity. Despite this, the HSE showed a lower MBC (600 and 650 µg/mL for *S. aureus* and *S. epidermidis*, respectively). Similar behavior was observed in *K. peneumoniae*. Although the PSE has a lower MIC (450 µg/mL) than the HSE (650 µg/mL), the MBC was higher. This could indicate that PC of PSE and HSE acts with different mechanisms. According to Salaheen *et al*. (2014), the MBC:MIC ratio values < 2 indicates that the extracts have bactericidal action. In *S.*

aureus the MBC:MIC ratio values were 3.4 and 2.6 for PSE and HSE, respectively. Both extracts are considered as bacteriostatic agents. Same was observed in *S. epidermidis,* where MBC:MIC ratio values were 3.2 and 2.4 for PSE and HSE, respectively, both showing bacteriostatic effect. Regarding to *K. pneumoniae*, 2 and 1 were the MBC:MIC ratio values for PSE and HSE, respectively. In this case, HSE was bactericidal while PSE was bacteriostatic. In all cases HSE had the greater antibacterial activity than PSE. The high MBC:MIC ratio values in PSE could be related to the high content of tannins. Hydrolysable and condensed tannins could be interacting with the proteins of the media, and form insoluble complexes (Hagerman *et al*., 1992). In this context bacteria lose these nutrients and limit their growth. However, when bacteria are transferred to a new medium without extracts, they could growth well. It is important to mention that during the assays the PSE generated a large insoluble complex in the media, while HSE generated a low insoluble complex. So, this complex formation related to the condensed tannins in both extracts could be related to the type of by-product and the complexity of its matrix components.

5.5.2 Biofilm formation inhbition

Biofilm formation capacity is considered one of the most important pathogenic and resistance mechanisms of pathogenic microorganisms (Del Pozo, 2018). For this reason, it was important to evaluate the potential of PSE and HSE to inhibit the biofilm formation. The highest biofilm formation capacity was observed in *P. aeruginosa*, followed by *Staphyloccocus* spp. and *K. penumoniae*. Using the corresponding MIC obtained for each of pathogen **(Table 10)**, almost 100% of biofilm formation inhibition was observed (**Figure 8**). The biofilm formation assay used in this work, consisted in the measurement of the attached bacteria to the microplate wells. According to the literature, PC have antibiofilm potential, it means, they can affect various steps of this formation, including adhesion, the initial step for biofilm formation (Villa & Cappitelli, 2013; Slobodníková *et al*., 2016). Cell membrane hydrophobicity is a determining factor for bacterial adhesion. Changes in this property has been reported in phenolics extracts (Rodríguez-Pérez *et al*. 2015). Also, cell-cell interactions are determinants during adhesion, aggregation and subsequent biofilm formation. These interactions are mediated by the cell membrane surface

molecules such as proteins. The binding of PC with these proteins could interrupt the cell-cell interactions and reduce the attachment and biofilm formation (Signoretto *et al*., 2014). These mechanisms may have occurred during the trial, in addition to the mechanisms that affect bacterial growth (**Figure 3**).

Biofilm formation of S. aureus was inhibited around 70% using the half of MIC from both extracts, whereas, MIC inhibited around 98%. Previously, 50% of biofilm formation inhibition in *S. aureus* and *S. epidermidis* was reported at 30 and 43 µg/mL, respectively, with ethanolic *Juglans regia* bark extract (Chaieb *et al*., 2013). In the same study, 202 and 138 µg/mL inhibited the 90% of biofilm formation of *S. aureus* and *S. epidermidis*, respectively. These results are similar to the obtained ones in this work, but the differences could be related to the *Staphylococcus spp.* strain used. Studies indicating the antibiofilm potential of nut by-product extracts against *K. pneumoniae* were not found. The lack of information gives greater value to the results obtained in this work since it could be considered the first report of the antibiofilm potential of nut by-product extracts against *K. pneumoniae*. Biofilm formation reduction was around 50% with the half of MIC of both extracts, whereas the MIC inhibits around 92%. For *P. aeruginosa*, HSE (1000 µg/mL) showed the highest biofilm formation inhibition (~70%), whereas the lowest concentration of both extracts (250 µg/mL) showed inhibition above of 25%. Previously, Chaieb *et al*. (2013) reported a biofilm formation inhibition around 30% at 512 µg/mL. In this work, the inhibition at 500 µg/mL obtained was between 32-50%, for both extracts. These results showed a major antibiofilm activity from PSE and HSE than *Juglans regia* extract. Recently, around 60% biofilm inhibition was reported for methanolic *Juglans regia* L. leaves extracts at 16 mg/mL on clinical isolates of *P. aeruginosa* (Dolatabadi *et al*., 2018).

Overall, results demonstrate the antimicrobial potential of both extracts (PSE and HSE), capable of inhibiting growth and reducing the formation of biofilm by microorganisms of great impact in the medical and food area. Therefore, both were used for the elaboration of the antimicrobial OSS-based films.

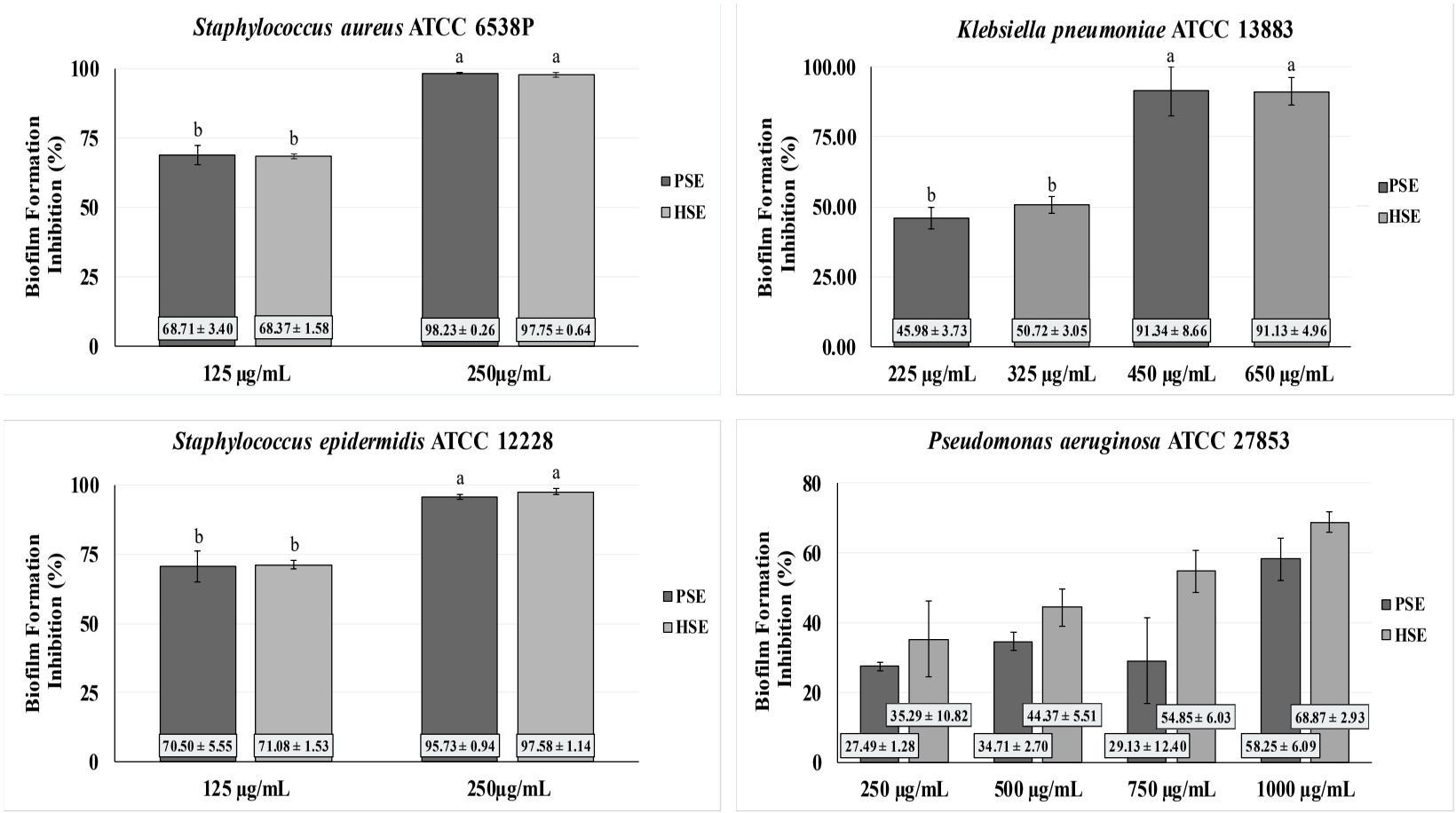

Figure 8. Biofilm formation inhibition of nut by-products extracts. Error bars indicates standard deviation, n=3. Different letter in bars indicates significant differences (p>0.05). ATCC= American Type Culture Collection, PSE= Pecan nutshell Extract, HSE= Hazelnut skin extract.

5.6 Octenyl succinate starch films with nut by-products extracts characterization

5.6.1 Surface morphology

Surface and cross-section micrographs of OSS, OSS-PSE and OSS-HSE are shown in the **Figure 9.** All films presented a homogenous surface, except for OSS-PSE films which presented few irregularities in the surface, but not cracks or holes were not observed. These results indicate a good coupling between PSE or HSE and OSA starch in the films. Feng *et al*. (2018) and Hamdi *et al*. (2019) considered that the homogeneity of the surface indicates the dispersion of the PC in the polymeric starch film structure. In another point, the small differences between OSS-PSE and OSS-HSE surfaces could be occurred by the different phenolic profile of PSE and HSE (**Table 9**). This behavior was observed by Prietto *et al*. (2017), where the cassava starch-based films with red cabbage anthocyanins showed a heterogeneous (rough) surface, while films with black bean anthocyanins showed a more homogeneous surface. In this way, red cabbage and black bean presented a different profile of anthocyanins.

The roughness values (RMS) of film surface obtained by AFM were very variable. For OSS the range of RMS was from 72.03 to 166.10 nm, for OSS-HSE films it was from 60.80 to 124.85 nm, and for OSS-PSE RMS was between 72.03 to 484.44 nm. The variation in RMS indicates that films have regions with greater roughness than others (**Figure 9**). According to Ghasemlou *et al*. (2013) and Medina-Jaramillo *et al*. (2015) the addition of bioactive compounds may increase or decrease the roughness of the films, indicating that the increase of the RMS is the result of a non-homogeneous dispersion of the compounds through the film. This could explain the slight differences between the surface micrographs obtained in OSS-PSE and OSS-HSE films. Surface homogeneity and roughness are factors with great impact on the antifouling properties of medical materials. Initial colonization of the microorganisms occurs mainly in the surfaces irregularities reason why it is preferred to generate materials with homogeneous surfaces. Low roughness was associated with the low fouling susceptibility of materials. However, there are studies that show the degree of roughness of the material does not have impact on microbial adhesion occurring on smooth and rough surfaces. This indicates than other properties of the material determine the susceptibility to the microbial adhesion (Gharechahi *et al*., 2012; Yeo *et al*., 2012; Desrousseaux *et al*., 2013; Song *et al*., 2015).

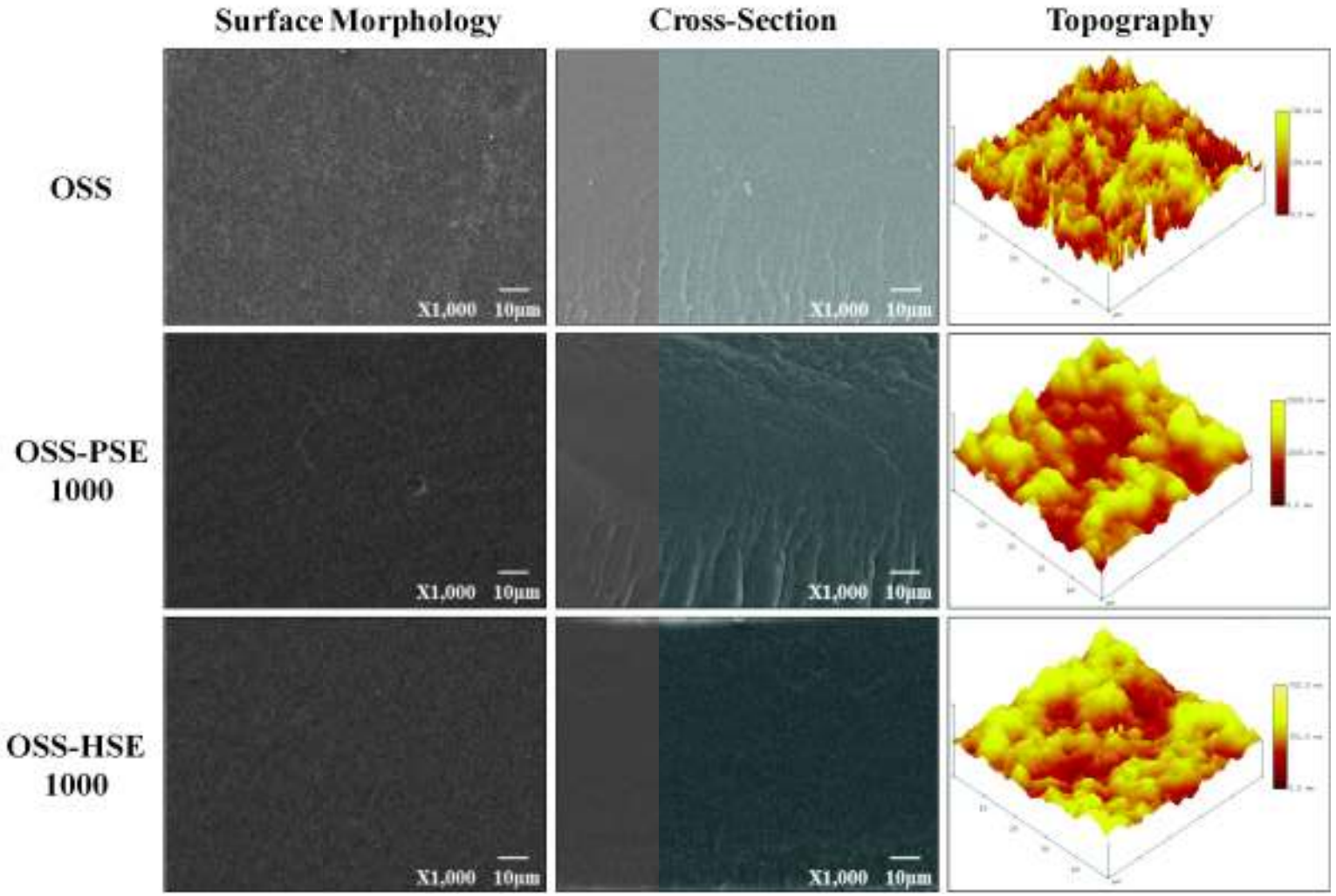

Figure 9. Octenyl succinate starch films with nut by-products extracts. OSS= Octenyl succinate starch film, OSS-PSE= Octenyl succinate starch film with pecan nutshell extract, OSS-HSE= Octenyl succinate starch film with hazelnut skin extract.

5.6.2 Transform Fourier Infrared Spectoscropy

Interactions between PC and OSS were identified, comparing the FIT-IR spectra of the extracts, OSS, OSS-PSE and OSS-HSE films (**Figure 10**).

The PSE and HSE presented bands associated to PC previously reported in these nuts (do Prado *et al.,* 2013; Battegazzore *et al.,* 2014). The broad band at 3300 cm^{-1} (OH- stretching), the bands at the 2800-3000 cm^{-1} region (CH stretching of the aliphatic compounds or aldehyde groups and CH_2 asymmetric stretching), the band at 1600 cm^{-1} (C=C aromatic rings stretching), the band at 1444 cm^{-1} (CH_2 bending), and the bands in the 1000-1400 region (CO and C-C bonds stretching). Other bands were observed, close to 1510 cm^{-1} (C=C aromatic ring) (Feng *et al*., 2018) and 900-700 cm^{-1} region (hydrogen atoms from aromatic rings) (Silva-Weiss *et al*., 2013a). Besides, the HSE presented higher intensity in some bands than PSE, also presented a new band close to 1715 cm^{-1} (C=O) (Kim *et al*., 2018) or a band at 1700 cm^{-1} corresponding to the carbonyl groups (Silva-Weiss *et al*., 2013a).

In the case of films, OSS film presented bands at 3300 cm^{-1} (OH stretching), 2936 cm^{-1} (CH stretching) 920-1160 cm^{-1} (C-O stretching) and 1150 cm^{-1} (glycosidic bond) typical of starch structure (Wang *et al*., 2010; Silva-Weiss *et al*., 2013a; Kim *et al*., 2018). Bands close to 1724 cm^{-1} and 1572 cm^{-1} corresponding to C=O for the ester carbonyl groups and asymmetric stretching for carboxylate group (RCOO-) respectively, were presented indicated the presence of the OSA groups in to the starch molecule (Wang *et al*., 2010; Naseri *et al*., 2019). The OSS-PSE and OSS-HSE films spectra did not presented variation with respect to OSS film. According to Eskandarinia *et al*., (2018) and Feng *et al.,* (2018), this indicates the dispersion of the PC into the starch-based film matrix. Some bands in the 1800 cm^{-1} to 800 cm^{-1} region showed a little intensity increase. According to Feng *et al*., (2018), Kim *et al*., (2018) and Qin *et al*., (2019), this indicates the intramolecular interactions between the PC and the starch trough hydrogen bonds.

It could be concluded that some PC dispersed along the polymer matrix, whereas others PC interacts directly with the starch structure.

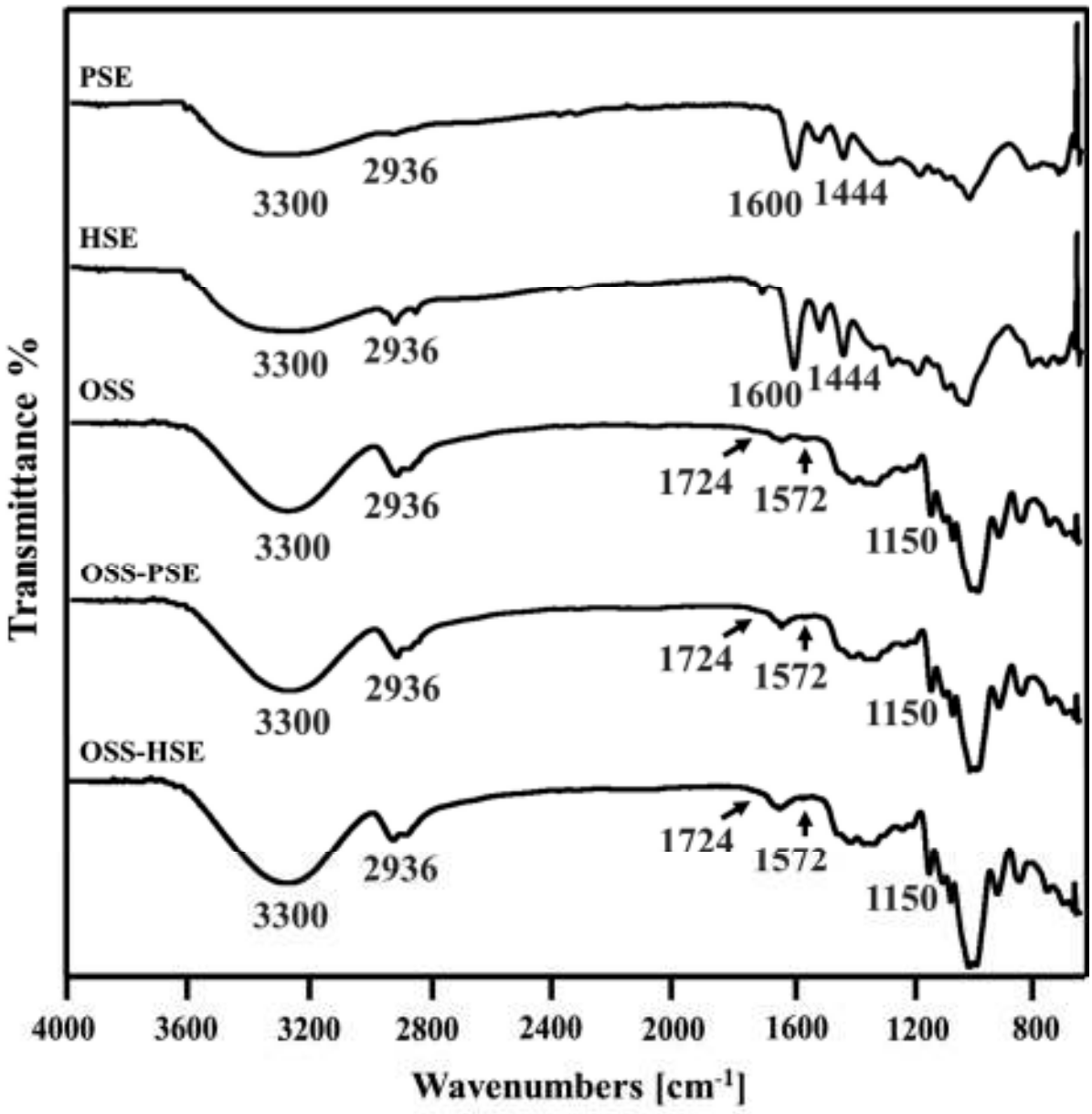

Figure 10. Nut by-products extracts and octenyl succinate starch with nut by-products extracts Fourier-Transform Infrared spectra. PSE= Pecan nutshell extract, HSE= Hazelnut skin extract, OSS= Octenyl succinate starch film, OSS-PSE= Octenyl succinate starch film with pecan nutshell extract at 1000 µg/mL, OSS-HSE= Octenyl succinate starch film with hazelnut skin extract at 1000 µg/mL.

5.6.3 Optical properties.

Results indicates that addition of PSE or HSE provide color to the OSS films (**Table 11**). The *L* values were decreased, indicating the reduction of the white color. While, the *a* and *b* values were increased which indicates a color trend towards yellow and red, respectively. This color change is a result of the presence of the PC, these compounds are the are responsible for sensory characteristics, such as the color of fruits, vegetables or plants in general (Cheynier *et al*, 2012). Likewise, this change in color gives us indications of the formation of the starch-PC complex.

On the other hand, OSS films transparency was decreased with the addition of both extracts. On the visible region (660 nm), a gradual decrease was observed as the concentration of the extract increased, from 86.17 ± 0.30 to 80.26 ± 0.21 and 80.22 ± 0.40 for OSS-PSE1000 and OSS-HSE1000, respectively. Similar behavior was previously reported in cassava starch-based films whit *yerba matte* extract (Knapp *et al*., 2019) and *Lycium ruthenicum* anthocyanins (Qin *et al*., 2019). Despite this transparency reduction, the visualization through films is not affected. In this context, this could be an interesting property because can be used as patches that allow the visualization of wounds or of some medical devices during their monitoring. On the other hand, in the UV region (280 nm), there was a more notorious decreased in transparency, from 71.24 ± 0.26 of OSS to 1.58 ± 0.11 and 0.22 ± 0.01 for OSS-PSE1000 and OSS-HSE1000, respectively. In this case, these results indicate that PSE and HSE provide UV-light blocking properties to the OSS films. This was proved with the absorption spectra obtained from the OSS, OSS-PSE and OSS-HSE films (**Figure 11**). In these absorption spectra, peaks close to 280 nm were observed for both extracts, which indicates the presence of PC. The UV-light blocking property was previously reported in several studies, concluding that this is beneficial for the elaboration of food packaging that prevents the damage caused by UV-light (Nouri & Nafchi, 2014; Piñeros-Hernandez *et al*., 2017; Kim *et al*., 2018; Knapp *et al*., 2019).

5.6.4 Water barrier properties

All films present a similar water content (≈30 %) without significant differences (p>0.05) (**Table 12**). This behavior has been reported in cassava starch-based films with rosemary extract (≈18 %) (Piñeros-Hernandez *et al*, 2017) and hydroxypropyl starch-based

Table 11. Optical properties of octenyl succinate starch films with nut by-products extracts.

Film	Color			Transparency %	
	a	*b*	*L*	T_{660nm}	T_{280nm}
OSS	95.09 ± 0.11^{a}	-0.96 ± 0.02^{f}	2.29 ± 0.04^{g}	-	71.24 ± 0.26^{a}
OSS-PSE 250	91.50 ± 0.35^{b}	2.07 ± 0.29^{e}	6.70 ± 0.52^{f}	6.50 ± 0.68^{e}	22.76 ± 0.16^{b}
OSS-PSE 500	88.66 ± 0.05^{c}	4.22 ± 0.10^{d}	9.51 ± 0.38^{de}	10.97 ± 0.30^{d}	11.08 ± 0.20^{d}
OSS-PSE 750	87.65 ± 0.52^{c}	4.95 ± 0.39^{d}	10.85 ± 0.37^{d}	12.79 ± 0.72^{d}	3.07 ± 0.14^{f}
OSS-PSE 1000	85.92 ± 0.52^{d}	6.09 ± 0.60^{c}	12.69 ± 0.74^{c}	15.56 ± 1.01^{c}	1.58 ± 0.11^{g}
OSS-HSE 250	88.38 ± 0.34^{c}	4.25 ± 0.29^{d}	9.21 ± 0.49^{e}	10.96 ± 0.66^{d}	14.39 ± 0.07^{c}
OSS-HSE 500	85.16 ± 0.61^{d}	6.55 ± 0.48^{c}	12.55 ± 0.69^{c}	16.15 ± 1.00^{c}	3.56 ± 0.25^{e}
OSS-HSE 750	81.45 ± 0.41^{e}	9.30 ± 0.31^{b}	15.79 ± 0.51^{b}	21.77 ± 0.65^{b}	0.61 ± 0.01^{h}
OSS-HSE 1000	78.11 ± 0.71^{f}	11.29 ± 0.55^{a}	18.70 ± 0.60^{a}	26.60 ± 0.96^{a}	0.22 ± 0.01^{h}

Data represent the mean ± standard deviation, n=3. Different literals in same column indicate significant differences, $p \leq 0.05$. T= Transmittance, OSS= Octenyl succinate starch film, OSS-PSE= Octenyl succinate starch film with pecan nutshell extract, OSS-HSE= Octenyl succinate starch film with hazelnut skin extract.

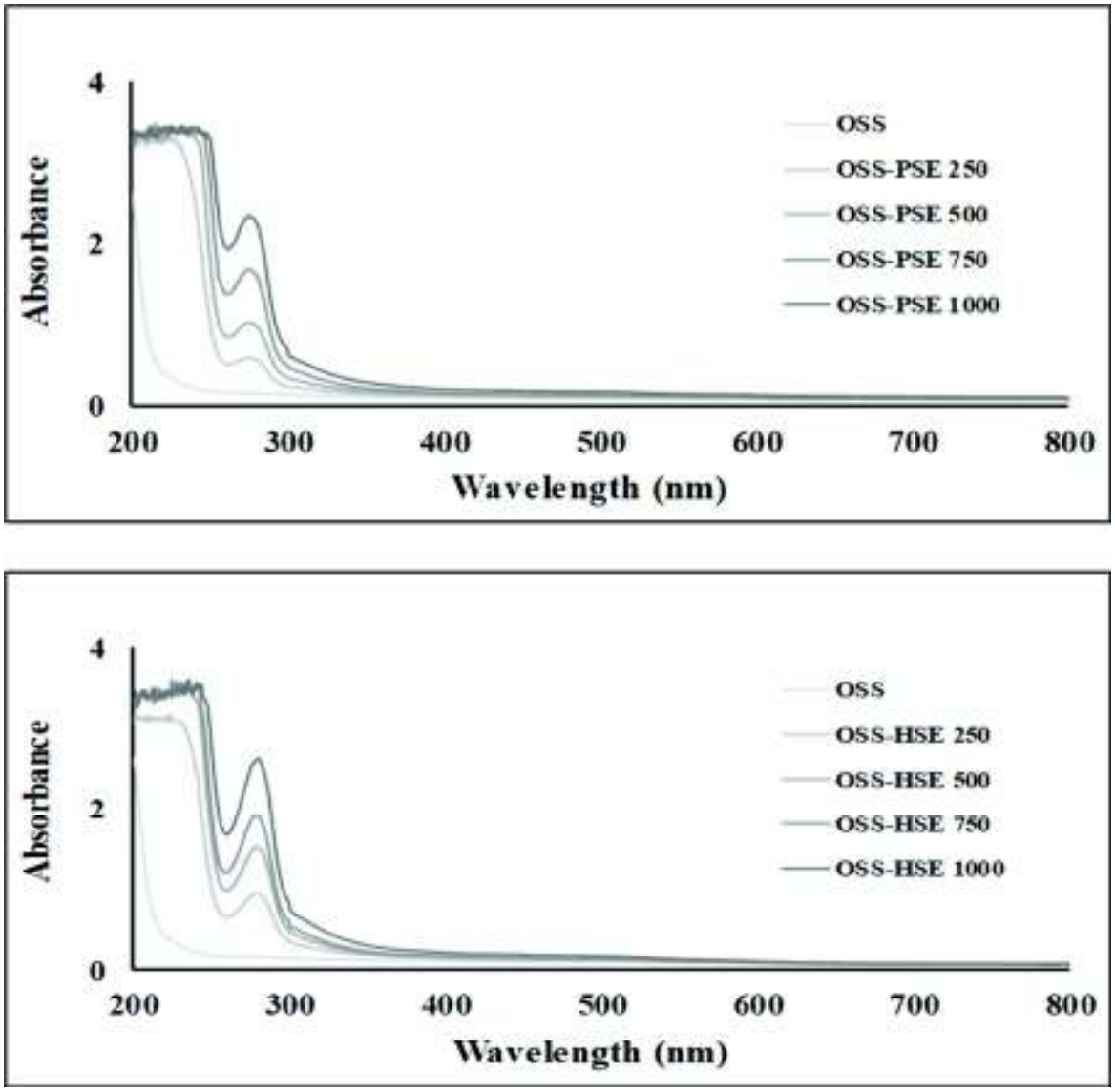

Figure 11. UV-light absorption spectra of octenyl succinate starch films with nut by-products extracts. Octenyl succinate starch film with pecan nutshell extract (up) and Octenyl succinate starch film with hazelnut skin extract (down). OSS= Octenyl succinate starch film, OSS-PSE= Octenyl succinate starch film with pecan nutshell extract, OSS-HSE= Octenyl succinate starch film with hazelnut skin extract.

Table 12. Water barrier properties of octenyl succinate starch films with nut by-products extracts.

Film	Water Content (%)	Water Solubility (%)	Contact Angle (°)	WVTR (g/m^2 h)
OSS	29.54 ± 0.28[a]	20.34 ± 0.44[a]	49.25 ± 0.27[g]	63.13 ± 2.53[ab]
OSS-PSE 250	29.22 ± 0.54[a]	20.23 ± 0.30[a]	55.80 ± 1.79f	59.46 ± 2.30[ab]
OSS-PSE 500	29.29 ± 0.34[a]	19.39 ± 0.55[ab]	72.35 ± 0.34e	59.34 ± 4.78[ab]
OSS-PSE 750	29.44 ± 0.78[a]	17.70 ± 0.56c	82.62 ± 0.88c	56.03 ± 1.45[b]
OSS-PSE 1000	29.62 ± 0.83[a]	17.14 ± 0.21c	96.80 ± 0.21a	61.46 ± 5.24[ab]
OSS-HSE 250	29.83 ± 0.35[a]	20.72 ± 0.77a	70.38 ± 0.89e	59.42 ± 2.24[ab]
OSS-HSE 500	29.74 ± 0.40[a]	18.05 ± 0.72bc	77.45 ± 2.91d	66.23 ± 4.59[a]
OSS-HSE 750	30.03 ± 0.41[a]	17.78 ± 0.49c	83.96 ± 1.26c	64.07 ± 2.64[ab]
OSS-HSE 1000	29.90 ± 0.56[a]	17.08 ± 0.68c	92.54 ± 1.28b	61.09 ± 0.68[ab]

Data represent the mean ± standard deviation, n=3. Different literals in same column indicate significant differences, $p \leq 0.05$. WVTR= Water vapor transmission rate, OSS= Octenyl succinate starch film, OSS-PSE= Octenyl succinate starch film with pecan nutshell extract, OSS-HSE= Octenyl succinate starch film with hazelnut skin extract.

films with tea polyphenols (≈13 %) (Feng *et al*, 2018). The high water content in the OSS, OSS-PSE and OSS-HSE films could be related to the great swelling property of the starch granule provide by the OSA groups (**Figure 7**). Films with high water content are considered a good option to use as wound dressings, due to water provides a moisture environment that favors the response of the immune and regeneration cells, accelerating the wound healing. This environment is also considered a factor that favors microbial growth (Hu *et al*., 2018).

However, materials with high water content are usually resistant to microbial adhesion, but, taking into account other factors of the material and the microorganism an opposite behavior could be produce (Dutta *et al*., 2012).

The water solubility was gradually decreasing when the extract concentration increased (**Table 12**). Similar behavior was reported by Li *et al*. (2018) in sweet potato OSS films with oregano essential oil. According to Ghasemlou *et al*. (2013), the hydrophobic compounds present in the essential oils reduce the solubility of corn starch films. In the specific case of PC, they are characterized by their low solubility directly related to its structural conformation (Kaur & Kaur, 2014). For its part, u Nisa *et al*. (2015) related the low solubility of potato starch films and green tea extract, with the strong interaction between the PC and the starch molecule. The PC could be interacting with the starch molecule forming simple inclusions (type V) into amylose helix or by hydrogen bonds between the hydroxyl groups (Zhu, 2015; Amoako & Awika, 2016). These interactions were observed in the FT-IR spectra shown in **Figure 11.** Therefore, the changes in the solubility properties are carried out by the hydrophilic/hydrophobic nature of the PC present in the extracts and the interactions between the PC and the starch structure. Results indicates that the PSE and HSE improve the films resistance in aqueous conditions, which suggests that the integrity of these films would be maintained in aqueous conditions, for example in contact with body fluids such as blood and urine, if used in catheter materials.

The contact angle is a value that provides information about the hydrophobicity or hydrophilicity characteristic of the material. According to Vogler (1998), the biomaterials (surface) with a contact angle lower than 65° are hydrophilic, while materials with a contact angle higher than 65° are hydrophobic. In this aspect, only the OSS and OSS-PSE (250 µg/mL) could be considerate hydrophilic (**Table 12**). This behavior is similar to that previously reported by other authors (Medina-Jaramillo *et al*., 2015; Piñeros-Hernandez *et al*., 2017; Eskandarinia *et al*., 2018; Naseri *et al*., (2019). These authors associate the increase of the contact angle with three factors. First, the hydrophobic nature of PC, they have a relative hydrophobicity, granted by the quantity and location of hydroxyl groups (hydrophilic area) (Selvaraj *et al*., 2015; Delmondes & Stefani, 2017), which leads to the second factor. The interaction between the hydroxyl groups of the PC and the starch, limited the free hydroxyl groups which could interact

with the water molecules, by consequence, the films hydrophobicity increase. The third factor is the increase in the roughness of the films, allowing the accumulation of air in the cavities and limiting the interaction between the water and the film. The contact angle values obtained in this work are comparable with commercial wound dressings. According to Braunwarth & Brill (2014) the contact angle of these dressings was between 71° to 120°. Surface hydrophobicity is a factor of great relevance for bacterial adhesion; however, it is not established whether hydrophobic or hydrophilic surfaces are more susceptible to adhesion. This is mainly due to the fact that other factors from the surface and from the bacteria determine their adhesion (Krasowska & Sigler, 2014; Song *et al*., 2015).

All films presented similar WVTR (**Table 12**) with average value of 61.14 (g/m^2 h). Low WVTR values in materials are suitable for their use as wound dressing. This is important because keeping a moisture environment is of great relevance during the healing process (Field & Kerstein, 1994). Similar values were reported by Hassan *et al*. (2018) in PVA/starch hydrogel membrane (60.99 ± 4.98 g/m^2 h) with turmeric (52.85 ± 2.85 g/m^2 h). Moghadas *et al*. (2016) reported a WVTR under 900 g/m^2 day in chitosan/montmorillonite nanohybrid films, whereas Adeli *et al*. (2019) reported WVTR values over 2300 g/m^2 day in PVA/chitosan/starch nanofibrous mats. Comparing the obtained results (1467.36 g/m^2 day) with the studies mentioned above, these are higher than those reported by Moghadas *et al*. (2016) and lower than those reported by Adeli *et al*. (2019). According to what was mentioned by the authors, the values obtained in this work indicate a potential use of these films (OSS-PSE and OSS-HSE) as wound dressings, since the retention or maintenance of the moisture environment would accelerate the wound healing process.

5.6.5 Mechanical properties

The OSS-based films were visually homogeneous (without cracks, bubbles and holes) and easy to manipulate. Films thickness are shown in **Table 12**. Results are similar with those reported before (Prietto *et al*., 2017; Knapp *et al*., 2019; Nogueira *et al*., 2019), where thickness increase is attributed to the increase of solids by the extract in the films composition.

Table 13. Tensile properties of octenyl succinate starch films with nut by-products extracts.

Film	Thickness (mm)	TS (MPa)	EB (%)	YM (MPa)
OSS	0.087 ± 0.002^{b}	9.60 ± 1.38^{ab}	32.41 ± 4.24^{a}	239.55 ± 15.39^{a}
OSS-PSE 250	0.090 ± 0.00^{ab}	7.94 ± 0.78^{ab}	30.98 ± 3.12^{a}	154.00 ± 7.23^{c}
OSS-PSE 500	0.090 ± 0.001^{ab}	7.87 ± 0.42^{ab}	25.90 ± 6.20^{a}	171.26 ± 21.00^{c}
OSS-PSE 750	0.091 ± 0.001^{a}	7.56 ± 1.16^{b}	23.99 ± 1.17^{a}	159.06 ± 17.61^{c}
OSS-PSE 1000	0.091 ± 0.001^{a}	8.62 ± 1.89^{ab}	27.28 ± 6.93^{a}	176.38 ± 19.83^{bc}
OSS-HSE 250	0.090 ± 0.001^{ab}	9.36 ± 0.99^{ab}	29.88 ± 1.89^{a}	215.00 ± 5.30^{ab}
OSS-HSE 500	0.090 ± 0.001^{ab}	10.58 ± 0.52^{a}	29.80 ± 3.15^{a}	224.85 ± 19.30^{a}
OSS-HSE 750	0.091 ± 0.001^{a}	8.35 ± 0.95^{ab}	31.65 ± 4.75^{a}	161.44 ± 11.58^{c}
OSS-HSE 1000	0.091 ± 0.001^{a}	7.91 ± 0.93^{ab}	29.58 ± 4.91^{a}	161.20 ± 13.43^{c}

Data represent the mean ± standard deviation, n=3. Different literals in same column indicate significant differences, $p \leq 0.05$. TS= Tensile strength, EB= Elongation at Break, YM= Young´s modulus, OSS= Octenyl succinate starch film, OSS-PSE= Octenyl succinate starch film with pecan nutshell extract, OSS-HSE= Octenyl succinate starch film with Hazelnut skin extract.

Evaluation of tensile properties in new materials is decisive, since their function and possible application will depend on them. In this study, the addition of both extracts reduced the TS of films, however, did not present significant differences ($p > 0.05$) (**Table 13**). The Same trend has been reported in cassava starch films with propolis extracts (de Araújo *et al*., 2015), and corn starch films with red cabbage anthocyanins (Prietto *et al*., 2017). According to these

authors, this occurs due to the structural weakening in the starch polymer matrix caused by the interactions between the PC of the extracts and the starch chains, which decreases the structural strength of the film. In comparison with other studies, the obtained TS values of OSS-PSE and OSS-HSE films were higher than those reported in wound dressings based on corn starch and propolis extracts (Eskandarinia *et al*., 2018; Eskandarinia *et al*., 2019) and PVA/chitosan/starch (Adeli *et al*., 2019); and lower than those in chitosan/montmorillonite nanohybrid films (Moghadas *et al*., 2016) and PVA/starch and turmeric hydrogel membrane (Hassan *et al*., 2018). The EB is a parameter that indicates the plastic behavior of the material. All films showed EB values around 30 % without significant differences ($p > 0.05$) (**Table 13**). Comparing these results with other wound dressings (previously mentioned), the EB values were higher than those reported by Moghadas *et al*. (2016) and lower than those reported by Eskandarinia *et al*. (2018) and Eskandarinia *et al*. (2019). Adeli *et al*. (2019) mentioned that the EB is influenced by the dry and wet state of the material, with EB average value of 160% in the wet state, and 40% for the dry state. On the other hand, it was observed that, except for OSS-HSE250 and OSS-HSE500, the addition of extracts significantly ($p \leq 0.05$) decreased the YM (**Table 13**). High values of YM indicates the rigidity of films, in this case, the YM decrease in the films indicate the plasticizing effect of HSE and PSE. This is due to the structural discontinuities in the polymer matrix caused by interactions between PC and starch (de Araújo *et al*., 2015). The obtained YM values were lower than those reported by Moghadas *et al*. (2016) and higher than the ones reported by Eskandarinia *et al*. (2018).

According to the literature, the tensile properties of the human skin have approximate values of TS from 10 to 35 MPa, EB values from 30 to 72 % and YM values from 10 to 210 MPa (Annaidh *et al*., 2012; Ottenio *et al*., 2015). In this aspect, the obtained results suggest that the OSS-PSE and OSS-HSE could be candidates for use as wounds dressing or tissue engineering material.

5.6.6 Antimicrobial Properties

Initial results (data not showed) indicated that OSS, OSS-PSE and OSS-HSE films apparently do not have antimicrobial properties (no inhibition zone) in all bacteria tested. For this reason,

it was decided to increase the concentration of the extracts in the OSS films to 250 and 500 mg per-100 mL of film forming solution to obtain the new films: OSS-PSE 2500, OSS-PSE 5000, OSS-HSE 2500 and OSS-HSE 5000. Despite the increase in the concentration, the OSS-PSE did not show inhibition zone (**Figure 12).** However, the *S. aureus* and *S. epidermidis* colonies observed below the films were lower in OSS-PSE 1000 than OSS films. Besides, in the OSS-PSE 2500 only few colonies were observed in the outline of the films, and in the OSS-PSE 5000 no colonies were observed in both strains. Similar behavior was observed in the OSS-HSE films (**Figure 13**). Although the number of visible growth colonies under the OSS-HSE films was lower, this could indicate that these films have a greater activity against *Staphylococcus* spp. than OSS-PSE films. This is consistent with the antimicrobial results previously obtained against *S. aureus* and *S. epidermidis* (**Table 11**). The absence of the inhibition zone could indicate that films tested in this work do not possess antimicrobial activity. However, Fang *et al*. (2019) mentioned that the antibacterial compounds were not released from the polymer matrix, and therefore did not exert their activity beyond the placement zone. In this point, the PC of the extracts were strongly complexed to the polymeric matrix of OSS and remained associated with it. The absence of growth under the films could indicate the possible antibacterial mechanism of the films (**Figure 5**). Firstly, bacteria were eliminated at the contact with the film surface. Zhu *et al*. (2019) observed a morphology damage in the cell membrane of *S. aureus* after their contact with antimicrobial chitosan-based hydrogel. On the other hand, bacteria were repelled to the periphery of the film surface. Trentin *et al*. (2015), proposed a repulsion mechanism for its proanthocyanidins coatings, where the negative nature of these compounds and the cell membrane of *S. epidermidis* prevents the adhesion of this pathogen to the surface.

Contrary, all OSS-PSE and OSS-HSE films presented *K. pneumoniae* growth below of the placement zone, even the presence of bubbles was observed. These could be result of the gas production (carbohydrate fermentation) by *K. pneumoniae*, which belongs to coliforms, a fermenting group of Gram-negative bacteria (Martin *et al*., 2016). What was observed could be similar to that expected in the Durham tube test for coliforms. In the case of *P. aeruginosa*, the plates turned slightly green, and it could be due to the presence of pyoverdine pigment produced by *P. aeruginosa* (Meyer, 2000). Besides, OSS-PSE and OSS-HSE (2500 and 5000) presented

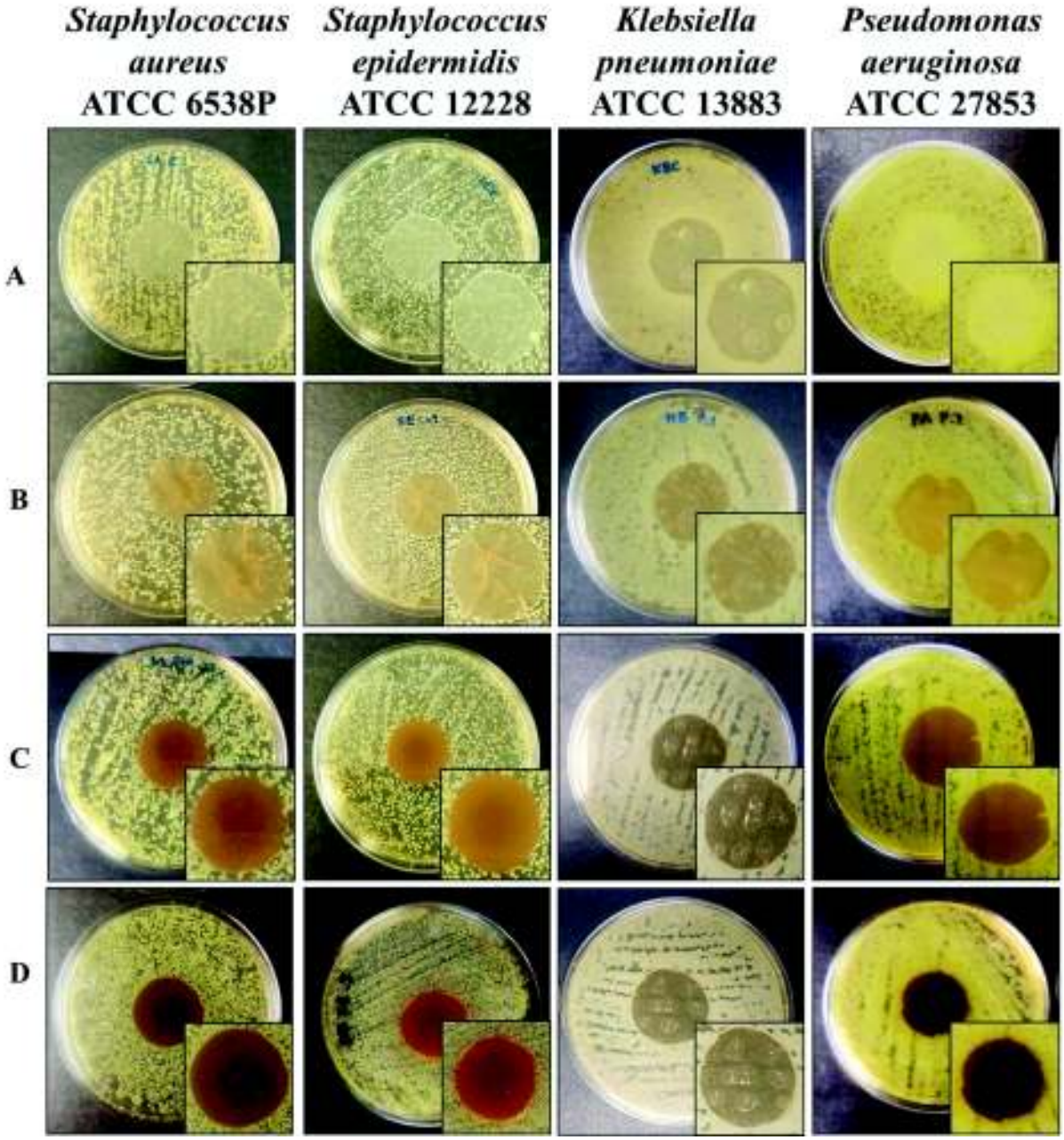

Figure 12. Disc diffusion assay of octenyl succinate starch films with pecan nutshell extract. (A) OSS, (B) OSS-PSE 1000, (C) OSS-PSE 2500 and (D) OSS-PSE 5000. ATCC= American Type Culture Collection, OSS= Octenyl succinate starch, OSS-PSE= Octenyl succinate starch with pecan nutshell extract.

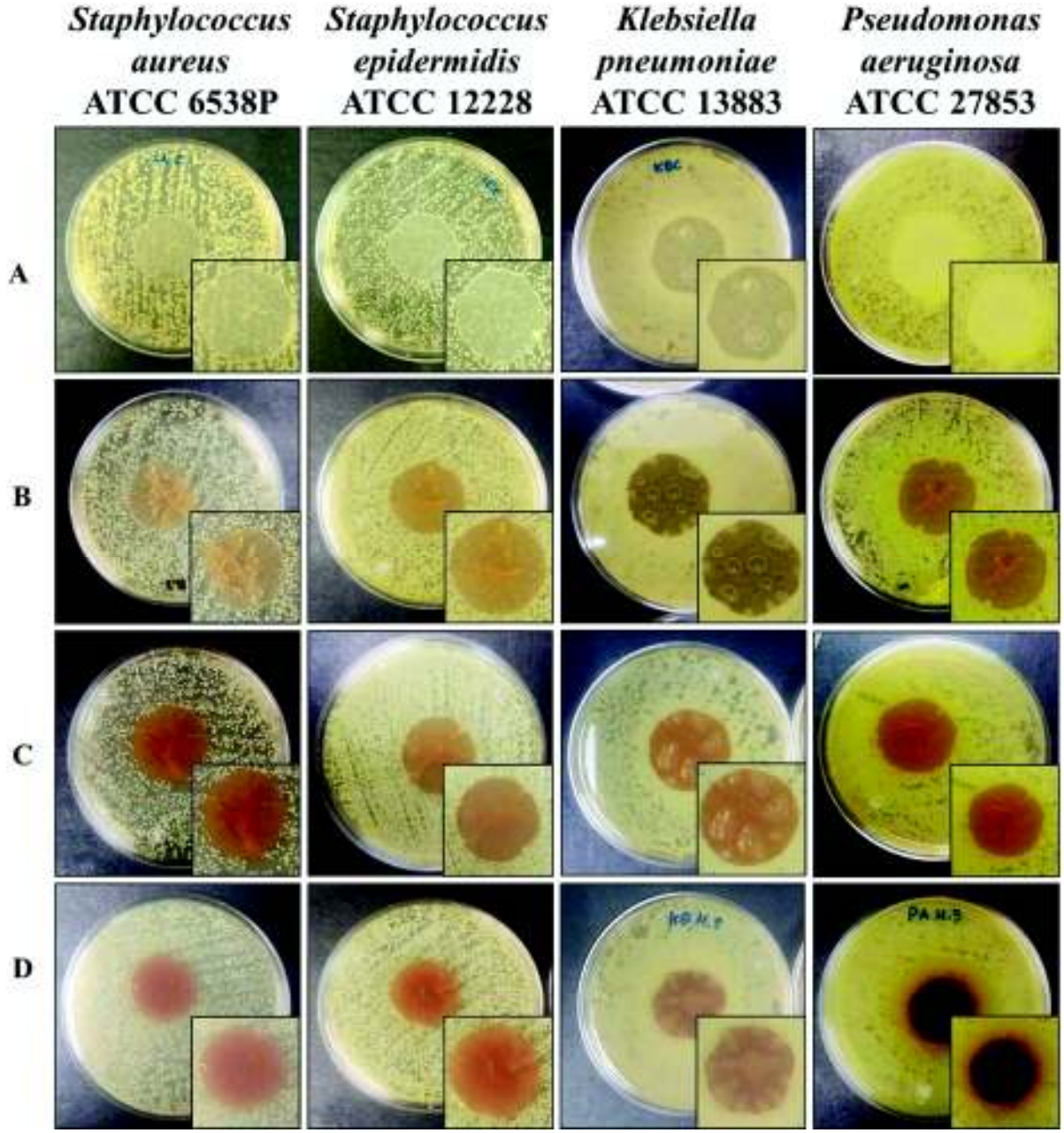

Figure 13. Disc diffusion assay of octenyl succinate starch films with pecan nutshell extract. (A) OSS, (B) OSS-HSE 1000, (C) OSS-HSE 2500 and (D) OSS-HSE 5000. ATCC= American Type Culture Collection, OSS= Octenyl succinate starch, OSS-PSE= Octenyl succinate starch with pecan nutshell extract.

changes in the color of films, and a halo of color that contrasted with the color of the medium. The color change of the films could be related with changes in the pH of the medium during the *P. aeruginosa* growth. According with some authors, films with phenolic extracts changed their coloration at different pH, due to the structural changes that the PC suffer (Prietto *et al*., 2017; Peralta *et al*., 2019). These results could be indicating that OSS-PSE and OSS-HSE films did not have the same repulsion or contact killing mechanism as observed in *Staphylococcus* spp.

Finally, antibacterial activity was evaluated in liquid medium, where favorable results were obtained (**Figure 14** and **Figure 15**). In the case of S. aureus, OSS-PSE 1000 and OSS-HSE 1000 reduces the OD around 40%, the OSS-PSE 2500 close to 70%, and the OSS-HSE-2500, OSS-PSE 5000 and OSS-HSE 5000 around 90%. Similarly, in *S. epidermidis*, OSS-PSE 1000 reduces the OD to 40%, OSS-HSE 1000 and OSS-PSE 2500 close to 60%, OSS-HSE 2500 around 90%, and OSS-PSE 5000 and OSS-HSE 5000 at 97% OD reduction. These results are similar to previous studies against *S. aureus*. Adeli *et al*. (2018) reported an antibacterial activity around 60-80% using PVA/chitosan/starch nanofibrous mats. For its part, Hadisi *et al*. (2018) reported bacterial inhibition of 20 - 40% after 24h and 20 - 100% after 48h using gelatin/oxidized-starch/henna extract mats. Finally, Fang *et al*. (2019) observed a similar trend in the OD reduction with ionic/PVA hydrogel. In the case of *S. epidermidis*, no comparable studies were found. mainly because S. aureus is considered as the Gram-positive reference bacterium for the antibacterial evaluation of any material or molecule. The observed antibacterial activity, could indicate that PC are released in liquid medium and thus affecting the growth of *Staphylococcus* spp.

In the case of the Gram-negative bacteria, only OSS-HSE 2500, OSS-PSE 5000 and OSS-HSE 5000 reduced the OD of *K. pneumoniae*, being the maximum observed reduction around 23% in OSS-HSE 5000 film. This indicates that *K. pneumoniae* is more resistance than *Staphylococcus* spp. It means that the PC released to the liquid medium do not have an efficient activity against *K. pneumoniae*. Perhaps the compounds that are still bound to the film are those that have the potential against *K. pneumoniae*. Regarding to *P. aeruginosa*, a distinctive behavior was observed: a) the culture medium took on a green coloration, possibly due to the production of pyoverdine (Mayer, 2000), and b) the presence of biofilm, in all films. However, the color intensity and the formed biofilm were lower as the concentration of the extracts

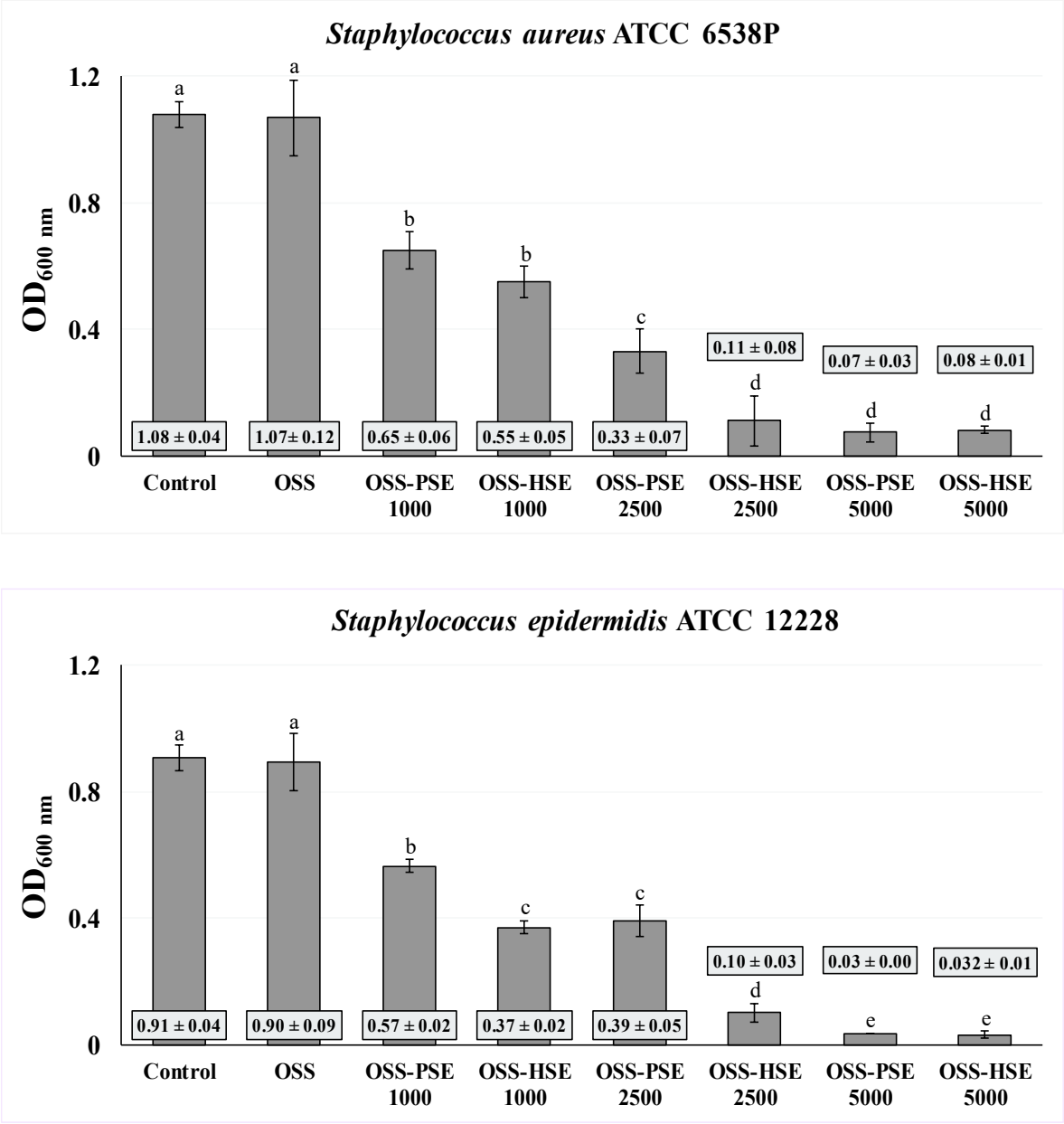

Figure 14. Gram-positive bacteria growth inhibition in liquid media of octenyl succinate starch films with nut by-products extracts. Error bar indicate standard deviation, n=3. Different letter in bars indicates significant differences (p>0.05). ATCC= American Type Culture Collection, OD= Optical density, OSS= Octenyl succinate starch, PSE= Pecan nutshell extract, HSE= Hazelnut skin extract. *Control was bacteria without film.

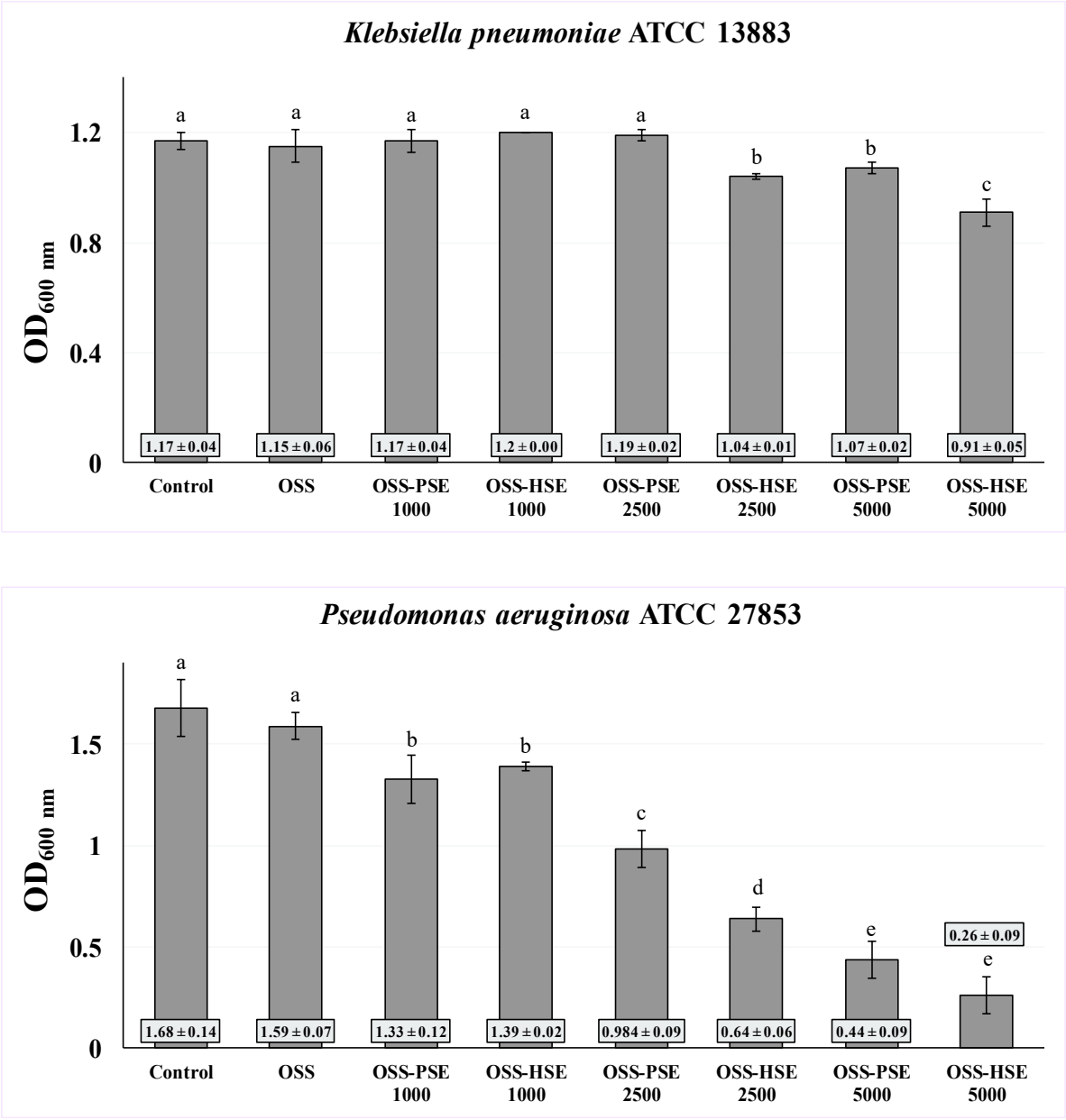

Figure 15. Gram-negative bacteria growth inhibition in liquid media of octenyl succinate starch films with nut by-products extracts. Error bar indicate standard deviation, n=3. Different letter in bars indicates significant differences (p>0.05). ATCC= American Type Culture Collection, OD= Optical density, OSS= Octenyl succinate starch, PSE= Pecan nutshell extract, HSE= Hazelnut skin extract. *Control was bacteria without film.

increased, and it was more evident in OSS-HSE films. This could indicate two things, a) released PC from the film decrease the production of pyoverdine, and b) the presence of the PC decreases the biomass of biofilms. Due to the formed biofilm and its contribution to the OD measurement, the biofilms were removed. An OD reduction was observed in all films, OSS-HSE 5000 presented the greatest OD reduction (approximately 85%). Similar to previous studies, the reduction of Gram-negative bacteria (*E. coli*) growth was lower compared to Gram-positive bacteria (Adeli *et al*, 2018, Hadisi *et al*., 2018, Fang *et al*., 2019). Which agrees with the MICs obtained previously (Table).

These results demonstrated the antibacterial potential of OSS-PSE and OSS-HSE films, against *S. epidermidis*, *S. aureus, P. aeruginosa* and *K. pneumoniae* (in order of effectiveness), especially in liquid medium.

VI. CONCLUSIONS

Interactions between antimicrobial nut by-product extracts and succinate starch resulted in films with suitable characteristics and properties for wound dressings materials. Also, showed antimicrobial properties: resistance to bacterial adhesion and inhibitory effect in liquid media. These results suggest their potential use in the medical area as a new antibacterial material.

Interactions between succinate starch and the antimicrobial nut by-product extracts resulted in films with suitable characteristics and properties for medical applications. Highlighting their antimicrobial properties, which are the resistance to bacterial adhesion and the inhibitory effect in liquid media. Therefore, these films could be used as antibacterial material to the development of wound dressings or antibacterial coating for medical devices, to prevent the health care associated infections caused by *S. aureus*, *S. epidermidis*, *K. pneumoniae* and *P. aeruginosa*.

VII. RECOMMENDATIONS

- Continue evaluating the antimicrobial potential of both extracts against other bacteria and yeasts, as well as multi-resistant or isolated strains.
- Elucidate the antimicrobial modes of action of the extracts.
- Perform cytotoxicity and biocompatibility tests of the extracts.
- Evaluate the physicochemical properties of films with high extracts concentrations, as well perform new tests related with medical applications.
- Perform cytotoxicity and biocompatibility tests of octenyl succinate starch films with nut by-products extracts.

VIII. REFERENCES

AACC International. (1999a). Approved Methods of Analysis. 11th Ed. Method 44-15.02. Total Starch Assay Procedure (Megazyme Amyloglucosidase/α-Amylase Method). Approved November 3, 1999. AACC International, St. Paul, MN, U.S.A. http://dx.doi.org/10.1094/AACCIntMethod-73-13.01.

AACC International. (1999b). Approved Methods of Analysis. 11th Ed. Method 44-15.02. Moisture-Air-Oven Methods. Approved November 3, 1999. AACC International, St. Paul, MN, U.S.A. http://dx.doi.org/10.1094/AACCIntMethod-44-15.02.

AACC International. (1999c). Approved Methods of Analysis. 11th Ed. Method 08-01.01. Ash-Basic Method. Approved November 3, 1999. AACC International, St. Paul, MN, U.S.A. http://dx.doi.org/10.1094/AACCIntMethod-08-01.01.

AACC International. (1999d). Approved Methods of Analysis. 11th Ed. Method 46-30.01. Crude Protein-Combustion Method. Approved November 3, 1999. AACC International, St. Paul, MN, U.S.A. http://dx.doi.org/10.1094/AACCInt Method-46-30.01

AACC International. (2014). Approved Methods of Analysis. 11th Ed. Method 76-31.01. Determination of Starch Damage-Spectrophotometric Method. Approved November 3, 1999, Edited Jaunary 10, 2014. AACC International, St. Paul, MN, U.S.A. http://dx.doi.org/10.1094/AACCIntMethod-76-31.01.

AACC International. (2017). Approved Methods of Analysis. 11th Ed. Method 76-21.02. General Pasting Method for Wheat or Rye Flour or Starch Using the Rapid Visco Analyser. Approved October 15, 1997, Revised November AACC International, St. Paul, MN, U.S.A. http://dx.doi.org/10.1094/AACCIntMethod-76-21.02.

Abiddin, N. Z., Yusoff, A., & Ahmad, N. (2018). Effect of octenylsuccinylation on physicochemical, thermal, morphological and stability of octenyl succinic anhydride (OSA) modified sago starch. *Food hydrocolloids*, *75*, 138-146.

Adeli, H., Khorasani, M. T., & Parvazinia, M. (2019). Wound dressing based on electrospun PVA/chitosan/starch nanofibrous mats: Fabrication, antibacterial and cytocompatibility evaluation and in vitro healing assay. *International journal of biological macromolecules*, *122*, 238-254.

Agama-Acevedo, E., & Bello-Perez, L. A. (2017). Starch as an emulsions stability: the case of octenyl succinic anhydride (OSA) starch. *Current Opinion in Food Science*, *13*, 78-83.

Alasalvar, C., & Bolling, B. W. (2015). Review of nut phytochemicals, fat-soluble bioactives, antioxidant components and health effects. *British Journal of Nutrition*, *113*(S2), S68-S78.

Alasalvar, C., Salas-Salvado, J., Ros, E., & Sabate, J. (2019). Health Benefits of Nuts and Dried Fruits.

Albuquerque AJR, Silva PMF, Cavalcante ALFA, Sampaio FC. (2013). Polyphenols as a Source of Antimicrobial Agents against Human Pathogens. *Plant Extracts,* 275-293.

Alcázar-Alay SC, Meireles MAA. (2015). Physicochemical Properties, Modifications and Applications of Starches from Different Botanical Sources. *Food Science and Technology (Campinas)*, *35*(2), 215-236.

Ali, A., Chen, Y., Liu, H., Yu, L., Baloch, Z., Khalid, S., ... & Chen, L. (2019). Starch-based antimicrobial films functionalized by pomegranate peel. *International journal of biological macromolecules*, *129*, 1120-1126.

Alvarez-Parrilla E, Urrea-López R, de la Rosa LA. (2018). Bioactive Components and Health Effects of Pecan Nuts and Their By-Products: A Review. *Journal of Food Bioactives, 1*, 56-92.

Amal, B., Veena, B., Jayachandran, V. P., & Shilpa, J. (2015). Preparation and characterisation of Punica granatum pericarp aqueous extract loaded chitosan-collagen-starch membrane: role in wound healing process. *Journal of Materials Science: Materials in Medicine*, *26*(5), 181.

Amaral, A. A. D., Schuster, G. C., Boschen, N. L., Benvegnú, D. M., Wyzykowski, J., Pinto Rodrigues, P. R., & Gallina, A. L. (2019). Antioxidant Evaluation of Extracts of Pecan NutShell (Carya illinoensis) in Soybean Biodiesel B100. *Global Challenges*, 1900001.

Amaral, J. S., & Oliveira, M. B. P. P. (2016). Bioactive compounds of hazelnuts as health promoters. *Natural Bioactive Compounds from Fruits and Vegetables*, *2*, 154-178.

Amoako D, Awika JM. (2016). Polyphenol Interaction with Food Carbohydrates and Consequences on Availability of Dietary Glucose. *Current Opinion in Food Science*, *8*, 14-18.

Anderson C, Simsek S. (2019). Mechanical Profiles and Topographical Properties of Films Made from Alkaline Extracted Arabinoxylans from Wheat Bran, Maize Bran, or Dried Distillers Grain. *Food Hydrocolloids*, 86, 78-86.

Annaidh, A. N., Bruyère, K., Destrade, M., Gilchrist, M. D., & Otténio, M. (2012). Characterization of the anisotropic mechanical properties of excised human skin. *Journal of the mechanical behavior of biomedical materials*, *5*(1), 139-148.

Apak, R., Capanoglu, E., & Shahidi, F. (2017). *Measurement of Antioxidant Activity and Capacity*. Wiley.

Arekemase, M. O., Oyeyiola, G. P., & Aliyu, M. B. (2011). Antibacterial activity of Anacaridum occidentale on some enterotoxin producing bacteria. *International Journal of Biology*, *3*(4), 92.

Arendrup, M. C., & Patterson, T. F. (2017). Multidrug-resistant Candida: epidemiology, molecular mechanisms, and treatment. *The Journal of infectious diseases*, *216*(suppl_3), S445-S451.

Arora, D., Sharma, N., Sharma, V., Abrol, V., Shankar, R., & Jaglan, S. (2016). An update on polysaccharide-based nanomaterials for antimicrobial applications. *Applied microbiology and biotechnology*, *100*(6), 2603-2615.

ASTM D7334-08 (2013a), Standard Practice for Surface Wettability of Coatings, Substrates and Pigments by Advancing Contact Angle Measurement, ASTM International, West Conshohocken, PA, 2013.

ASTM International (2012). ASTM E2382-04: Standard Guide to Scanner and Tip Related Artifacts in Scanning Tunneling Microscopy and Atomic Force Microscopy. ASTM International, West Conshohocken, PA (2012).

ASTM-D882-18. (2018). Standard Test Method for Tensile Properties of Thin Plastic Sheeting. (Vol. ASTM International). West Conshohocken, PA.

ASTM-E2382-04. (2012). Standard Guide to Scanner and Tip Related Artifacts in Scanning Tunneling Microscopy and Atomic Force Microscopy. West Conshohocken, PA: ASTM International.

Atanasov, A. G., Sabharanjak, S. M., Zengin, G., Mollica, A., Szostak, A., Simirgiotis, M., ... & Mocan, A. (2018). Pecan nuts: A review of reported bioactivities and health effects. *Trends in Food Science & Technology*, *71*, 246-257.

Azadmard-Damirchi S, Emami S, Hesari J, Peighambardoust SH, Nemati M. (2011). Nuts Composition and their Health Benefits. *World Academy of Science, Engineering and Technology, 5*, 544-548.

Bajaj, R., Singh, N., & Kaur, A. (2019). Properties of octenyl succinic anhydride (OSA) modified starches and their application in low fat mayonnaise. *International journal of biological macromolecules*, *131*, 147-157.

Balasubramanian, D., Harper, L., Shopsin, B., & Torres, V. J. (2017). Staphylococcus aureus pathogenesis in diverse host environments. *Pathogens and disease*, *75*(1), ftx005.

Baojun, Z. H. A. O., Xianzong, X. I. A., Akyazi, F., & Holubowicz, R. (2017). Common Hazelnut Production and Its Multiplication in Turkey. *Agricultural Science & Technology*, *18*(12).

Baranauskienė R, Rutkaitė R, Pečiulytė L, Kazernavičiūtė R, Venskutonis PR. (2016). Preparation and Characterization of Single and Dual Propylene Oxide and Octenyl Succinic Anhydride Modified Starch Carriers for the Microencapsulation of Essential Oils. *Food & Function*, *7*(8), 3555-3565.

Baranyi J, Roberts TA. (1994). A Dynamic Approach to Predicting Bacterial Growth in Food. *International Journal of Food Microbiology*, *23*(3-4), 277-294.

Barberán J, Varona JF, Tejeda MI. (2014). Infecciones por Estafilococos. *Medicine-Programa de Formación Médica Continuada Acreditado*, *11*(59), 3477-3484.

Barbieri R, Coppo E, Marchese A, Daglia M, Sobarzo-Sánchez E, Nabavi SF, Nabavi SM. (2017). Phytochemicals for Human Disease: An Update on Plant-Derived Compounds Antibacterial Activity. *Microbiological Research, 196*, 44-68.

Battegazzore, D., Bocchini, S., Alongi, J., & Frache, A. (2014). Plasticizers, antioxidants and reinforcement fillers from hazelnut skin and cocoa by-products: Extraction and use in PLA and PP. *Polymer degradation and stability, 108*, 297-306.

Bello-Flores, C. A., Nuñez-Santiago, M. C., San Martín-Gonzalez, M. F., BeMiller, J. N., & Bello-Pérez, L. A. (2014). Preparation and characterization of octenylsuccinylated plantain starch. *International journal of biological macromolecules*, *70*, 334-339.

Bemiller, J. N. (1997). Starch modification: challenges and prospects. *Starch-Stärke*, *49*(4), 127-131.

Benbettaïeb, N., Karbowiak, T., & Debeaufort, F. (2019). Bioactive edible films for food applications: Influence of the bioactive compounds on film structure and properties. *Critical reviews in food science and nutrition*, *59*(7), 1137-1153.

Bertoft E. (2017). Understanding Starch Structure: Recent Progress. *Agronomy, 7*(3), 56.

Bertolino, M., Belviso, S., Dal Bello, B., Ghirardello, D., Giordano, M., Rolle, L., ... & Zeppa, G. (2015). Influence of the addition of different hazelnut skins on the physicochemical, antioxidant, polyphenol and sensory properties of yogurt. *LWT-Food Science and Technology*, *63*(2), 1145-1154.

Biasutto L, Mattarei A, Sassi N, Azzolini M, Romio M, Paradisi C, Zoratti M. (2014). Improving the Efficacy of Plant Polyphenols. *Anti-Cancer Agents in Medicinal Chemistry (Formerly Current Medicinal Chemistry-Anti-Cancer Agents), 14*(10), 1332-1342.

Bolling, B. W., Chen, C. Y. O., McKay, D. L., & Blumberg, J. B. (2011). Tree nut phytochemicals: composition, antioxidant capacity, bioactivity, impact factors. A systematic review of almonds, Brazils, cashews, hazelnuts, macadamias, pecans, pine nuts, pistachios and walnuts. *Nutrition research reviews*, *24*(2), 244-275.

Bottari, N. B., Lopes, L. Q. S., Pizzuti, K., dos Santos Alves, C. F., Corrêa, M. S., Bolzan, L. P., ... & Baldissera, M. D. (2017). Antimicrobial activity and phytochemical characterization of Carya illinoensis. *Microbial pathogenesis*, *104*, 190-195.

Bottone, A., Cerulli, A., D'Urso, G., Masullo, M., Montoro, P., Napolitano, A., & Piacente, S. (2019). Plant Specialized Metabolites in Hazelnut (Corylus avellana) Kernel and Byproducts: An Update on Chemistry, Biological Activity, and Analytical Aspects. *Planta medica*.

Braga, I. A., Campos, P. A., Gontijo-Filho, P. P., & Ribas, R. M. (2018). Multi-hospital point prevalence study of healthcare-associated infections in 28 adult intensive care units in Brazil. *Journal of Hospital Infection*, *99*(3), 318-324.

Brand-Williams W, Cuvelier M, Berset C. (1995). Use of a Free Radical Method to Evaluate Antioxidant Activity. *LWT-Food Science and Technology, 28*(1), 25-30.

Bravo, L. (1998). Polyphenols: chemistry, dietary sources, metabolism, and nutritional significance. *Nutrition reviews*, *56*(11), 317-333.

Builders, P. F., & Arhewoh, M. I. (2016). Pharmaceutical applications of native starch in conventional drug delivery. *Starch-Stärke*, *68*(9-10), 864-873.

Burnham CAD, Leeds J, Nordmann P, O'Grady J, Patel J. (2017). Diagnosing Antimicrobial Resistance. *Nature Reviews Microbiology, 15*(11), 697.

Büttner H, Mack D, Rohde H. (2015). Structural Basis of *Staphylococcus epidermidis* Biofilm Formation: Mechanisms and Molecular Interactions. *Frontiers in Cellular and Infection Microbiology*, *5*, 14.

Câmara, C. R. S., Shi, Q., Pedersen, M., Zbasnik, R., Nickerson, K. W., & Schlegel, V. (2019). Histone acetylation increases in response to ferulic, gallic, and sinapic acids acting synergistically in vitro to inhibit Candida albicans yeast-to-hyphae transition. *Phytotherapy research*, *33*(2), 319-326.

Carvalho, R. S., Carollo, C. A., de Magalhães, J. C., Palumbo, J. M. C., Boaretto, A. G., e Sá, I. N., ... & Ferreira, J. M. S. (2018). Antibacterial and antifungal activities of phenolic compound-enriched ethyl acetate fraction from Cochlospermum regium (mart. Et. Schr.) Pilger roots: Mechanisms of action and synergism with tannin and gallic acid. *South African journal of botany*, *114*, 181-187.

Caxambú S, Biondo E, Kolchinski EM, Padilha RL, Brandelli A, Sant'anna V. (2016). Evaluation of the Antimicrobial Activity of Pecan Nut [*Carya illinoinensis* (Wangenh) C. Koch] Shell Aqueous Extract on Minimally Processed Lettuce Leaves. *Food Science and Technology (Campinas), 36*, 42-45.

Cetin-Karaca, H., & Newman, M. C. (2015). Antimicrobial efficacy of plant phenolic compounds against Salmonella and Escherichia Coli. *Food bioscience*, *11*, 8-16.

Chaieb, K., Kouidhi, B., Slama, R. B., Fdhila, K., Zmantar, T., & Bakhrouf, A. (2013). Cytotoxicity, antibacterial, antioxidant, and antibiofilm properties of tunisian Juglans regia bark extract. *Journal of herbs, spices & medicinal plants*, *19*(2), 168-179.

Chakraborty, R., Kalita, P., & Sen, S. (2018). Natural Starch in Biomedical and Food Industry: Perception and Overview. *Current drug discovery technologies*.

Chandra H, Bishnoi P, Yadav A, Patni B, Mishra AP, Nautiyal AR. (2017). Antimicrobial Resistance and the Alternative Resources with Special Emphasis on Plant-Based Antimicrobials—A Review. *Plants, 6*(2), 16.

Chang, S. K., Alasalvar, C., Bolling, B. W., & Shahidi, F. (2016). Nuts and their co-products: The impact of processing (roasting) on phenolics, bioavailability, and health benefits–A comprehensive review. *Journal of functional foods*, *26*, 88-122.

Chatterjee, M., Anju, C. P., Biswas, L., Kumar, V. A., Mohan, C. G., & Biswas, R. (2016). Antibiotic resistance in Pseudomonas aeruginosa and alternative therapeutic options. *International Journal of Medical Microbiology*, *306*(1), 48-58.

Chen Q, Yu H, Wang L, ul Abdin Z, Chen Y, Wang J, Zhou W, Yang X, Khan RU, Zhang H, Chen X. (2015). Recent Progress in Chemical Modification of Starch and its Applications. *RSC Advances*, *5*(83), 67459-67474.

Chen, Y., Zhao, J. Y., Shan, X., Han, X. L., Tian, S. G., Chen, F. Y., ... & Luo, A. (2017). A point-prevalence survey of healthcare-associated infection in fifty-two Chinese hospitals. *Journal of Hospital Infection*, *95*(1), 105-111.

Cheynier V. (2012). Phenolic Compounds: From Plants to Foods. *Phytochemistry Reviews, 11*(2-3), 153-177.

Choi I, Lee JY, Lacroix M, Han J. (2017). Intelligent pH Indicator Film Composed of Agar/Potato Starch and Anthocyanin Extracts from Purple Sweet Potato. *Food Chemistry*, *218*, 122-128.

Clegg, S., & Murphy, C. N. (2016). Epidemiology and Virulence of Klebsiella pneumoniae. *Microbiology spectrum*, *4*(1).

Clinical and Laboratory Standards Institute (CLSI). (2008). Reference Method for Broth Dilution Antifungal Susceptibility Testing of Yeast. Approved Standard. Third Edition. M27-A3.

Clinical and Laboratory Standards Institute (CLSI). (2015). Methods for Dilution Antimicrobial Susceptibility Tests for Bacteria That Grow Aerobically: Approved Standard. Tenth Edition. M07-A10.

Conte R, Calarco A, Napoletano A, Valentino A, Margarucci S, Di Cristo F, Di Salle A, Peluso G. (2016). Polyphenols Nanoencapsulation for Therapeutic Applications. *Biomolecular Research & Therapeutics, 5*(2).

Contini, M., Baccelloni, S., Frangipane, M. T., Merendino, N., & Massantini, R. (2012). Increasing espresso coffee brew antioxidant capacity using phenolic extract recovered from hazelnut skin waste. *Journal of Functional Foods*, *4*(1), 137-146.

Contini, M., Baccelloni, S., Massantini, R., & Anelli, G. (2008). Extraction of natural antioxidants from hazelnut (Corylus avellana L.) shell and skin wastes by long maceration at room temperature. *Food Chemistry*, *110*(3), 659-669.

Contini, M., Baccelloni, S., Massantini, R., Anelli, G., Manzi, L., & Merendino, N. (2009). In vitro and in vivo antioxidant potential of phenolic extracts obtained from hazelnut skin by-products. *Acta Horticulturae*, (845), 717-722.

Contini, M., Frangipane, M. T., & Massantini, R. (2011). Antioxidants in hazelnuts (Corylus avellana L.). In *Nuts and Seeds in Health and Disease Prevention* (pp. 611-625). Academic Press.

Coppo E, Marchese A. (2014). Antibacterial Activity of Polyphenols. *Current Pharmaceutical Biotechnology, 15*(4), 380-390.

da Rosa Zavareze, E., Pinto, V. Z., Klein, B., El Halal, S. L. M., Elias, M. C., Prentice-Hernández, C., & Dias, A. R. G. (2012). Development of oxidised and heat–moisture treated potato starch film. *Food chemistry*, *132*(1), 344-350.

da Silva, R. A., Liberio, S. A., do Amaral, F. M., do Nascimento, F. R. F., Torres, L. M. B., Neto, V. M., & Guerra, R. N. M. (2016). Antimicrobial and antioxidant activity of Anacardium occidentale L. flowers in comparison to bark and leaves extracts. *Journal of Biosciences and Medicines*, *4*(04), 87.

Daglia M. (2012). Polyphenols as Antimicrobial Agents. *Current Opinion in Biotechnology, 23*(2), 174-181.

de Araújo, G. K. P., de Souza, S. J., da Silva, M. V., Yamashita, F., Gonçalves, O. H., Leimann, F. V., & Shirai, M. A. (2015). Physical, antimicrobial and antioxidant properties of starch-based film containing ethanolic propolis extract. *International Journal of Food Science & Technology*, *50*(9), 2080-2087.

de Camargo, A. C., Regitano-d'Arce, M. A. B., Rasera, G. B., Canniatti-Brazaca, S. G., do Prado-Silva, L., Alvarenga, V. O., ... & Shahidi, F. (2017). Phenolic acids and flavonoids of peanut by-products: Antioxidant capacity and antimicrobial effects. *Food chemistry*, *237*, 538-544.

de la Rosa, L. A., Alvarez-Parrilla, E., & Shahidi, F. (2010). Phenolic compounds and antioxidant activity of kernels and shells of Mexican pecan (Carya illinoinensis). *Journal of Agricultural and Food Chemistry*, *59*(1), 152-162.

de la Rosa, L. A., Vazquez-Flores, A. A., Alvarez-Parrilla, E., Rodrigo-García, J., Medina-Campos, O. N., Ávila-Nava, A., ... & Pedraza-Chaverri, J. (2014). Content of major classes of polyphenolic compounds, antioxidant, antiproliferative, and cell protective activity of pecan crude extracts and their fractions. *Journal of functional foods*, *7*, 219-228.

de Souza, R., Schincaglia, R., Pimentel, G., & Mota, J. (2017). Nuts and human health outcomes: A systematic review. *Nutrients*, *9*(12), 1311.

Del Pozo, J. L. (2018). Biofilm-related disease. *Expert review of anti-infective therapy*, *16*(1), 51-65.

Del Rio, D., Calani, L., Dall'Asta, M., & Brighenti, F. (2011). Polyphenolic composition of hazelnut skin. Journal of agricultural and food chemistry, 59(18), 9935-9941.

Delmondes, P. H., & Stefani, R. (2017). Computational Study of Natural Phenolic Acid Solubility and Their Interactions with Chitosan.

Desrousseaux, C., Sautou, V., Descamps, S., & Traoré, O. (2013). Modification of the surfaces of medical devices to prevent microbial adhesion and biofilm formation. *Journal of hospital Infection*, *85*(2), 87-93.

Ding, X., Duan, S., Ding, X., Liu, R., & Xu, F. J. (2018). Versatile antibacterial materials: An emerging arsenal for combatting bacterial pathogens. *Advanced Functional Materials*, *28*(40), 1802140.

do Prado ACP, da Silva HS, da Silveira SM, Barreto PLM, Vieira CRW, Maraschin M, Ferreira SRS, Block JM. (2014). Effect of the Extraction Process on the Phenolic Compounds Profile and the Antioxidant and Antimicrobial Activity of Extracts of Pecan Nut [*Carya illinoinensis* (Wangenh) C. Koch] Shell. *Industrial Crops and Products, 52*, 552-561.

do Prado, A. C. P., Manion, B. A., Seetharaman, K., Deschamps, F. C., Arellano, D. B., & Block, J. M. (2013). Relationship between antioxidant properties and chemical composition of the oil and the shell of pecan nuts [Caryaillinoinensis (Wangenh) C. Koch]. *Industrial crops and products*, *45*, 64-73.

Dolatabadi, S., Moghadam, H. N., & Mahdavi-Ourtakand, M. (2018). Evaluating the anti-biofilm and antibacterial effects of Juglans regia L. extracts against clinical isolates of Pseudomonas aeruginosa. *Microbial pathogenesis*, *118*, 285-289.

Dutta, D., Cole, N., & Willcox, M. (2012). Factors influencing bacterial adhesion to contact lenses. *Molecular vision*, *18*, 14.

Dzotam, J. K., & Kuete, V. (2017). Antibacterial and antibiotic-modifying activity of methanol extracts from six Cameroonian food plants against multidrug-resistant enteric bacteria. *BioMed research international*, *2017*.

Egharevba, H. O. (2019). Chemical Properties of Starch and Its Application in the Food Industry. In *Chemical Properties of Starch*. IntechOpen.

El Hawary, S. S., Saad, S., El Halawany, A. M., Ali, Z. Y., & El Bishbishy, M. (2016). Phenolic content and anti-hyperglycemic activity of pecan cultivars from Egypt. *Pharmaceutical biology*, *54*(5), 788-798.

Engels, C., Schieber, A., & Gänzle, M. G. (2011). Inhibitory spectra and modes of antimicrobial action of gallotannins from mango kernels (Mangifera indica L.). *Appl. Environ. Microbiol.*, *77*(7), 2215-2223.

Engler Ribeiro, P. C., de Britto Policarpi, P., Dal Bo, A., Barbetta, P. A., & Block, J. M. (2017). Impact of pecan nut shell aqueous extract on the oxidative properties of margarines during storage. *Journal of the Science of Food and Agriculture*, *97*(9), 3005-3012.

Enoch, D. A., Yang, H., Aliyu, S. H., & Micallef, C. (2017). The changing epidemiology of invasive fungal infections. In *Human Fungal Pathogen Identification* (pp. 17-65). Humana Press, New York, NY.

Eskandarinia, A., Kefayat, A., Rafienia, M., Agheb, M., Navid, S., & Ebrahimpour, K. (2019). Cornstarch-based wound dressing incorporated with hyaluronic acid and propolis: In vitro and in vivo studies. *Carbohydrate polymers*, *216*, 25-35.

Eskandarinia, A., Rafienia, M., Navid, S., & Agheb, M. (2018). Physicochemical, Antimicrobial and Cytotoxic Characteristics of Corn Starch Film Containing Propolis for Wound Dressing. *Journal of Polymers and the Environment*, *26*(8), 3345-3351.

Fang, H., Wang, J., Li, L., Xu, L., Wu, Y., Wang, Y., ... & Li, Y. (2019). A novel high-strength poly (ionic liquid)/PVA hydrogel dressing for antibacterial applications. *Chemical Engineering Journal*, *365*, 153-164.

Feng, M., Yu, L., Zhu, P., Zhou, X., Liu, H., Yang, Y., ... & Chen, P. (2018). Development and preparation of active starch films carrying tea polyphenol. *Carbohydrate polymers*, *196*, 162-167.

Fernández-Agulló, A., Pereira, E., Freire, M. S., Valentao, P., Andrade, P. B., González-Álvarez, J., & Pereira, J. A. (2013). Influence of solvent on the antioxidant and antimicrobial properties of walnut (Juglans regia L.) green husk extracts. *Industrial crops and products*, *42*, 126-132.

Ferrer C, Almirante B. (2014). Infecciones Relacionadas con el Uso de los Catéteres Vasculares. *Enfermedades Infecciosas y Microbiología Clínica, 32*(2), 115-124.

Ferri M, Ranucci, E, Romagnoli P, Giaccone V. (2017). Antimicrobial Resistance: A Global Emerging Threat to Public Health Systems. *Critical Reviews in Food Science and Nutrition, 57*(13), 2857-2876.

Fiamegos, Y. C., Kastritis, P. L., Exarchou, V., Han, H., Bonvin, A. M., Vervoort, J., ... & Tegos, G. P. (2011). Antimicrobial and efflux pump inhibitory activity of caffeoylquinic acids from Artemisia absinthium against gram-positive pathogenic bacteria. *PLoS One*, *6*(4), e18127.

Field, C. K., & Kerstein, M. D. (1994). Overview of wound healing in a moist environment. *The American journal of surgery*, *167*(1), S2-S6.

Flores-Cordova, M., Muñoz-Márquez, E., Muñoz-Márquez, E., Ojeda-Barrios, D. L., Soto-Parra, J. M., & Preciado-Rangel, P. (2017). Phytochemical composition and antioxidant capacity in Mexican pecan nut. *Emirates Journal of Food and Agriculture*, 346-350.

Flores-Estrada, R. A., Gámez-Meza, N., Medina-Juárez, L. A., Castillón-Campaña, L. G., Molina-Domínguez, C. C., Rascón-Valenzuela, L. A., & García-Galaz, A. (2019). Chemical Composition, Antioxidant, Antimicrobial and Antiproliferative Activities of Wastes from Pecan Nut [Carya illinoinensis (Wagenh) K. Koch]. *Waste and Biomass Valorization*, 1-14.

Flórez, J. A. F., Mendoza, J. G. S., & Lora, M. C. R. (2016). ACETILACIÓN DE ALMIDÓN NATIVO DE BATATA (Ipomeas batata L)/ACETYLATION OF NATIVE SWEET POTATO STARCH.(Ipomeas batata L). *Vitae*, *23*, S174.

Follador, R., Heinz, E., Wyres, K. L., Ellington, M. J., Kowarik, M., Holt, K. E., & Thomson, N. R. (2016). The diversity of Klebsiella pneumoniae surface polysaccharides. *Microbial genomics*, *2*(8).

Foster, T. J. (2017). Antibiotic resistance in Staphylococcus aureus. Current status and future prospects. *FEMS microbiology reviews*, *41*(3), 430-449.

Gadhave, R. V., Das, A., Mahanwar, P. A., & Gadekar, P. T. (2018). Starch Based Bio-Plastics: The Future of Sustainable Packaging.

Gellatly, S. L., & Hancock, R. E. (2013). Pseudomonas aeruginosa: new insights into pathogenesis and host defenses. *Pathogens and disease*, *67*(3), 159-173.

Ghanshani, R., Gupta, R., Gupta, B. S., Kalra, S., Khedar, R. S., & Sood, S. (2015). Epidemiological study of prevalence, determinants, and outcomes of infections in medical ICU at a tertiary care hospital in India. *Lung India: official organ of Indian Chest Society*, *32*(5), 441.

Gharechahi, M., Moosavi, H., & Forghani, M. (2012). Effect of surface roughness and materials composition on biofilm formation. *Journal of Biomaterials and Nanobiotechnology*, *3*(4A), 541-6.

Ghasemlou M, Aliheidari N, Fahmi R, Shojaee-Aliabadi S, Keshavarz B, Cran MJ, Khaksar R. (2013). Physical, Mechanical and Barrier Properties of Corn Starch Films Incorporated with Plant Essential Oils. *Carbohydrate Polymers*, *98*(1), 1117-1126.

Gonelimali, F. D., Lin, J., Miao, W., Xuan, J., Charles, F., Chen, M., & Hatab, S. R. (2018). Antimicrobial properties and mechanism of action of some plant extracts against food pathogens and spoilage microorganisms. *Frontiers in microbiology*, *9*.

Gültekin-Özgüven, M., Davarcı, F., Paslı, A. A., Demir, N., & Özçelik, B. (2015). Determination of phenolic compounds by ultra high liquid chromatography-tandem mass spectrometry: Applications in nuts. LWT-Food Science and Technology, 64(1), 42-49.

Hadisi, Z., Nourmohammadi, J., & Nassiri, S. M. (2018). The antibacterial and anti-inflammatory investigation of Lawsonia Inermis-gelatin-starch nano-fibrous dressing in burn wound. *International journal of biological macromolecules*, *107*, 2008-2019.

Hagerman, A. E. (1992). Tannin—protein interactions.

Hamdi, M., Nasri, R., Li, S., & Nasri, M. (2019). Bioactive composite films with chitosan and carotenoproteins extract from blue crab shells: Biological potential and structural, thermal, and mechanical characterization. Food Hydrocolloids, 89, 802-812.

Harborne JB. (1984). Phenolic Compounds. In *Phytochemical Methods* (pp. 37-99). Springer, Dordrecht.

Hassan A, Niazi MBK, Hussain A, Farrukh S, Ahmad T. (2018). Development of Anti-Bacterial PVA/Starch Based Hydrogel Membrane for Wound Dressing. *Journal of Polymers and the Environment*, *26*(1), 235-243.

Hassan, R., El-Gilany, A. H., & El-Mashad, N. (2019). Device-associated infection rates in different intensive care units in a tertiary care hospital in Egypt. *AMERICAN JOURNAL OF PREVENTIVE MEDICINE*, *4*(1), 1-7.

Hemamalini, T., & Dev, V. R. G. (2018). Comprehensive review on electrospinning of starch polymer for biomedical applications. *International journal of biological macromolecules*, *106*, 712-718.

Hilbig, J., Alves, V. R., Müller, C. M. O., Micke, G. A., Vitali, L., Pedrosa, R. C., & Block, J. M. (2018a). Ultrasonic-assisted extraction combined with sample preparation and analysis using LC-ESI-MS/MS allowed the identification of 24 new phenolic compounds in pecan nut shell [Carya illinoinensis (Wangenh) C. Koch] extracts. Food research international, 106, 549-557.

Hilbig, J., de Britto Policarpi, P., de Souza Grinevicius, V. M. A., Mota, N. S. R. S., Toaldo, I. M., Luiz, M. T. B., ... & Block, J. M. (2018b). Aqueous extract from pecan nut [Carya illinoinensis (Wangenh) C. Koch] shell show activity against breast cancer cell line MCF-7 and Ehrlich ascites tumor in Balb-C mice. *Journal of ethnopharmacology*, *211*, 256-266.

Hu, B., Owh, C., Chee, P. L., Leow, W. R., Liu, X., Wu, Y. L., ... & Chen, X. (2018). Supramolecular hydrogels for antimicrobial therapy. *Chemical Society Reviews*, *47*(18), 6917-6929.

Huber, K. C., & BeMiller, J. N. (2001). Location of sites of reaction within starch granules. Cereal Chemistry, 78(2), 173-180.

Hui R, Qi-He C, Ming-liang F, Qiong X, Guo-qing, H. (2009). Preparation and Properties of Octenyl Succinic Anhydride Modified Potato Starch. *Food Chemistry*, *114*(1), 81-86.

INC (2019). International Nut & Dried Fruit Council. Nuts & Dried Fruits Statistical Yearbook 2017/2018.https://www.adm.gov.it/portale/documents/20182/4951387/dog-r-20190514-2D-statistiche.pdf/0b793ed5-2f03-4302-82eb-c1dd22f65c99.

Jabeen, N., Majid, I., & Nayik, G. A. (2015). Bioplastics and food packaging: A review. *Cogent Food & Agriculture*, *1*(1), 1117749.

Jakobek, L. (2015). Interactions of polyphenols with carbohydrates, lipids and proteins. *Food chemistry*, *175*, 556-567.

Jakopic, J., Petkovsek, M. M., Likozar, A., Solar, A., Stampar, F., & Veberic, R. (2011). HPLC–MS identification of phenols in hazelnut (Corylus avellana L.) kernels. Food chemistry, 124(3), 1100-1106.

Jiménez, A., Fabra, M. J., Talens, P., & Chiralt, A. (2012). Edible and biodegradable starch films: a review. *Food and Bioprocess Technology*, *5*(6), 2058-2076.

Ju, A., Baek, S. K., Kim, S., & Song, K. B. (2019). Development of an antioxidative packaging film based on khorasan wheat starch containing moringa leaf extract. *Food science and biotechnology*, *28*(4), 1057-1063.

Junter, G. A., Thébault, P., & Lebrun, L. (2016). Polysaccharide-based antibiofilm surfaces. *Acta biomaterialia*, *30*, 13-25.

Kanbur, G., Arslan, D., & Özcan, M. M. (2013). Some compositional and physical characteristics of some Turkish hazelnut (*Corylus avellana* L.) variety fruits and their corresponding oils. *International Food Research Journal*, *20*(5), 2161.

Kanmani P, Rhim JW. (2014). Antimicrobial and Physical-Mechanical Properties of Agar-Based Films Incorporated with Grapefruit Seed Extract. *Carbohydrate Polymers*, *102*, 708-716.

Kart, D., Kustimur, A. S., Sağıroğlu, M., & Kalkancı, A. (2017). Evaluation of antimicrobial durability and anti-biofilm effects in urinary catheters against *Enterococcus faecalis* clinical isolates and reference strains. *Balkan medical journal*, *34*(6), 546-552.

Kaur B, Ariffin F, Bhat R, Karim AA. (2012). Progress in Starch Modification in the Last Decade. *Food Hydrocolloids*, *26*(2), 398-404.

Kaur, H., & Kaur, G. (2014). A critical appraisal of solubility enhancement techniques of polyphenols. *Journal of pharmaceutics*, *2014*.

Kellett, M. E., Greenspan, P., Gong, Y., & Pegg, R. B. (2019). Cellular evaluation of the antioxidant activity of US Pecans [*Carya illinoinensis* (Wangenh.) K. Koch]. *Food chemistry*, *293*, 511-519.

Khan HA, Ahmad A, Mehboob R. (2015). Nosocomial Infections and their Control Strategies. *Asian Pacific Journal of Tropical Biomedicine, 5*(7), 509-514.

Khan HA, Baig FK, Mehboob R. (2017). Nosocomial Infections: Epidemiology, Prevention, Control and Surveillance. *Asian Pacific Journal of Tropical Biomedicine, 7*(5), 478-482.

Kim, S., Baek, S. K., Go, E., & Song, K. (2018). Application of Adzuki Bean Starch in Antioxidant Films Containing Cocoa Nibs Extract. *Polymers, 10*(11), 1210.

Knapp, M. A., dos Santos, D. F., Pilatti-Riccio, D., Deon, V. G., dos Santos, G. H. F., & Pinto, V. Z. (2019). Yerba mate extract in active starch films: Mechanical and antioxidant properties. *Journal of food processing and preservation*, *43*(3), e13897.

Krasowska, A., & Sigler, K. (2014). How microorganisms use hydrophobicity and what does this mean for human needs?. *Frontiers in cellular and infection microbiology*, *4*, 112.

Kumar, K., Yadav, A. N., Kumar, V., Vyas, P., & Dhaliwal, H. S. (2017). Food waste: a potential bioresource for extraction of nutraceuticals and bioactive compounds. *Bioresources and Bioprocessing*, *4*(1), 18.

Kureck, I., de Brito Policarpi, P., Toaldo, I. M., Maciel, M. V. D. O. B., Bordignon-Luiz, M. T., Barreto, P. L. M., & Block, J. M. (2018). Chemical Characterization and Release of Polyphenols from Pecan Nut Shell [Carya illinoinensis (Wangenh) C. Koch] in Zein Microparticles for Bioactive Applications. *Plant foods for human nutrition*, *73*(2), 137-145.

Le, K. Y., Park, M. D., & Otto, M. (2018). Immune evasion mechanisms of Staphylococcus epidermidis biofilm infection. *Frontiers in microbiology*, *9*, 359.

Lee H, Lee DG. (2015). Mode of Action of Bioactive Phytochemicals, Plant Secondary Metabolites, Possessing Antimicrobial Properties. The Battle against Microbial Pathogens: Basic Science, Technological Advances and Educational Programs. Spain: FORMATEX, 185-92.

Leopoldini, M., Russo, N., & Toscano, M. (2011). The molecular basis of working mechanism of natural polyphenolic antioxidants. *Food Chemistry*, *125*(2), 288-306.

Li J, Ye F, Lei L, Zhao G. (2018). Combined Effects of Octenylsuccination and OreganoEssential Oil on Sweet Potato Starch Films with an Emphasis on Water Resistance. *International Journal of Biological Macromolecules*, 115, 547-553.

Li, B., Zhao, Y., Liu, C., Chen, Z., & Zhou, D. (2014). Molecular pathogenesis of Klebsiella pneumoniae. *Future microbiology*, *9*(9), 1071-1081.

Li, H., & Parry, J. W. (2011). Phytochemical compositions, antioxidant properties, and colon cancer antiproliferation effects of Turkish and Oregon hazelnut. *Food and Nutrition Sciences*, *2*(10), 1142.

Li, J., Ye, F., Liu, J., & Zhao, G. (2015). Effects of octenylsuccination on physical, mechanical and moisture-proof properties of stretchable sweet potato starch film. *Food Hydrocolloids*, *46*, 226-232.

Lima VN, Oliveira-Tintino CD, Santos ES, Morais LP, Tintino SR, Freitas TS, Geraldo YS, Pereira RLS, Cruz RP, Menezes IRA, Coutinho HD. (2016). Antimicrobial and Enhancement of the Antibiotic Activity by Phenolic Compounds: Gallic Acid, Caffeic Acid and Pyrogallol. *Microbial Pathogenesis, 99*, 56-61.

Liu Y, Wei S, Liao M. (2013). Optimization of Ultrasonic Extraction of Phenolic Compounds from *Euryale ferox* Seed Shells using Response Surface Methodology. *Industrial Crops and Products, 49*, 837-843.

Livermore, D. M. (2012). Current epidemiology and growing resistance of gram-negative pathogens. *The Korean journal of internal medicine*, *27*(2), 128.

Locatelli, M., Travaglia, F., Coïsson, J. D., Martelli, A., Stevigny, C., & Arlorio, M. (2010). Total antioxidant activity of hazelnut skin (Nocciola Piemonte PGI): Impact of different roasting conditions. *Food chemistry*, *119*(4), 1647-1655.

Longato, E., Meineri, G., Peiretti, P. G., Gai, F., Viuda-Martos, M., Pérez-Álvarez, J. Á., ... & Fernández-López, J. (2019). Effects of hazelnut skin addition on the cooking, antioxidant and sensory properties of chicken burgers. *Journal of food science and technology*, *56*(7), 3329-3336.

López-Córdoba, A., Medina-Jaramillo, C., Piñeros-Hernandez, D., & Goyanes, S. (2017). Cassava starch films containing rosemary nanoparticles produced by solvent displacement method. *Food Hydrocolloids*, *71*, 26-34.

Lopez-Romero, J. C., González-Ríos, H., Borges, A., & Simões, M. (2015). Antibacterial effects and mode of action of selected essential oils components against Escherichia coli and Staphylococcus aureus. *Evidence-Based Complementary and Alternative Medicine*, *2015*.

Lopez-Silva, M., Bello-Perez, L. A., Agama-Acevedo, E., & Alvarez-Ramirez, J. (2019). Effect of amylose content in morphological, functional and emulsification properties of OSA modified corn starch. *Food Hydrocolloids*, *97*, 105212.

Lou Z, Wang H, Rao S, Sun J, Ma C, Li J. (2012). *p*-Coumaric Acid Kills Bacteria Through Dual Damage Mechanisms. *Food Control, 25*(2), 550-554.

Lou, Z., Wang, H., Rao, S., Sun, J., Ma, C., & Li, J. (2012). p-Coumaric acid kills bacteria through dual damage mechanisms. *Food control*, *25*(2), 550-554.

Lou, Z., Wang, H., Zhu, S., Ma, C., & Wang, Z. (2011). Antibacterial activity and mechanism of action of chlorogenic acid. *Journal of food science*, *76*(6), M398-M403.

Luchese, C. L., Abdalla, V. F., Spada, J. C., & Tessaro, I. C. (2018). Evaluation of blueberry residue incorporated cassava starch film as pH indicator in different simulants and foodstuffs. *Food Hydrocolloids*, *82*, 209-218.

Magill, S. S., Edwards, J. R., Bamberg, W., Beldavs, Z. G., Dumyati, G., Kainer, M. A., ... & Ray, S. M. (2014). Multistate point-prevalence survey of health care–associated infections. *New England Journal of Medicine*, *370*(13), 1198-1208.

Mandalari, G., Bisignano, C., D'Arrigo, M., Ginestra, G., Arena, A., Tomaino, A., & Wickham, M. S. J. (2010). Antimicrobial potential of polyphenols extracted from almond skins. *Letters in applied microbiology*, *51*(1), 83-89.

Mandalari, G., Bisignano, C., D'Arrigo, M., Ginestra, G., Arena, A., Tomaino, A., & Wickham, M. S. J. (2010). Antimicrobial potential of polyphenols extracted from almond skins. *Letters in applied microbiology*, *51*(1), 83-89.

Martin, N. H., Trmčić, A., Hsieh, T. H., Boor, K. J., & Wiedmann, M. (2016). The evolving role of coliforms as indicators of unhygienic processing conditions in dairy foods. *Frontiers in microbiology*, *7*, 1549.

Martin, R. M., & Bachman, M. A. (2018). Colonization, infection, and the accessory genome of Klebsiella pneumoniae. *Frontiers in cellular and infection microbiology*, *8*, 4.

Masina N, Choonara YE, Kumar P, du Toit LC, Govender M, Indermun S, Pillay V. (2016). A Review of the Chemical Modification Techniques of Starch. *Carbohydrate Polymers*, *157*, 1226-1236.

McGuinness, W. A., Malachowa, N., & DeLeo, F. R. (2017). Focus: infectious diseases: vancomycin resistance in Staphylococcus aureus. *The Yale journal of biology and medicine*, *90*(2), 269.

Medina-Jaramillo C, Gonzalez Seligra P, Goyanes S, Bernal C, Famá L. (2015). Biofilms Based on Cassava Starch Containing Extract of Yerba Mate as Antioxidant and Plasticizer. *Starch-Stärke*, *67*(9-10), 780-789.

Medina-Juárez, L. A., Molina-Quijada, D. M. A., Agustin-Salazar, S., Valenzuela, L. R., Molina-Domínguez, C. C., & Gámez-Meza, N. (2018). Chemical evaluation and antioxidant capacity of Western and Wichita pecan nut cultivars [Carya illinoinensis (Wangenh.) K. Koch]. *Rivista Italiana delle Sostanze Grasse*, 111-118.

Moghadas, B., Dashtimoghadam, E., Mirzadeh, H., Seidi, F., & Hasani-Sadrabadi, M. M. (2016). Novel chitosan-based nanobiohybrid membranes for wound dressing applications. *Rsc Advances*, *6*(10), 7701-7711.

Montella, R., Coïsson, J. D., Travaglia, F., Locatelli, M., Malfa, P., Martelli, A., & Arlorio, M. (2013). Bioactive compounds from hazelnut skin (Corylus avellana L.): Effects on Lactobacillus plantarum P17630 and Lactobacillus crispatus P17631. *Journal of functional foods*, *5*(1), 306-315.

Müller, L. G., Pase, C. S., Reckziegel, P., Barcelos, R. C., Boufleur, N., Prado, A. C. P., ... & da Rocha, J. B. T. (2013). Hepatoprotective effects of pecan nut shells on ethanol-induced liver damage. *Experimental and toxicologic pathology*, *65*(1-2), 165-171.

Murray PR, Rosenthal KS, Pfaller MA. (2015). *Medical Microbiology*. Elsevier Health Sciences.

Musdja MY, Hapsari MA, Agusta, A. (2018). Comparison of Activity and Inhibitory Mechanism between (+)-Catechin and Water Extract of Gambier (Uncaria Gambir Roxb.) Against Some Bacteria. *Scientific Journal of PPI-UKM, 4*(2), 55-60.

Nakayama M, Shimatani K, Ozawa T, Shigemune N, Tomiyama D, Yui K, Katsuki M, Ikeda K, Nonaka A, Miyamoto T. (2015). Mechanism for the Antibacterial Action of Epigallocatechin Gallate (EGCg) on Bacillus subtilis. Bioscience, Biotechnology, and Biochemistry, 79(5), 845-854.

Nakayama, M., Shimatani, K., Ozawa, T., Shigemune, N., Tsugukuni, T., Tomiyama, D., ... & Miyamoto, T. (2013). A study of the antibacterial mechanism of catechins: Isolation and

identification of Escherichia coli cell surface proteins that interact with epigallocatechin gallate. *Food control*, *33*(2), 433-439.

Naseri, A., Shekarchizadeh, H., & Kadivar, M. (2019). Octenylsuccination of sago starch and investigation of the effect of calcium chloride and ferulic acid on physicochemical and functional properties of the modified starch film. *Journal of Food Processing and Preservation*, *43*(3), e13898.

Navon-Venezia, S., Kondratyeva, K., & Carattoli, A. (2017). Klebsiella pneumoniae: a major worldwide source and shuttle for antibiotic resistance. *FEMS microbiology reviews*, *41*(3), 252-275.

Nguyen, T. H., Park, M. D., & Otto, M. (2017). Host response to Staphylococcus epidermidis colonization and infections. *Frontiers in cellular and infection microbiology*, *7*, 90.

Nguyen, V. T. (2017). Recovering bioactive compounds from agricultural wastes. *Recovering bioactive compounds from agricultural wastes.*

Nicolle LE. (2014). Catheter Associated Urinary Tract Infections. *Antimicrobial Resistance and Infection Control, 3*(1), 23.

Nicu, A. I., Pirvu, L., Stoian, G., & Vamanu, A. D. R. I. A. N. (2018). Antibacterial activity of ethanolic extracts from Fagus sylvatica L. and Juglans regia L. leaves. *Farmacia*, *66*(3), 483-486.

No, J., & Shin, M. (2019). Preparation and characteristics of octenyl succinic anhydride-modified partial waxy rice starches and encapsulated paprika pigment powder. *Food chemistry*, *295*, 466-474.

Nogueira, G. F., Soares, C. T., Cavasini, R., Fakhouri, F. M., & de Oliveira, R. A. (2019). Bioactive films of arrowroot starch and blackberry pulp: Physical, mechanical and barrier properties and stability to pH and sterilization. *Food chemistry*, *275*, 417-425.

Nostro, A., Scaffaro, R., D'Arrigo, M., Botta, L., Filocamo, A., Marino, A., & Bisignano, G. (2013). Development and characterization of essential oil component-based polymer films: a potential approach to reduce bacterial biofilm. *Applied microbiology and biotechnology*, *97*(21), 9515-9523.

Nour, V., Trandafir, I., & Cosmulescu, S. (2012). HPLC determination of phenolic acids, flavonoids and juglone in walnut leaves. *Journal of chromatographic science*, *51*(9), 883-890.

Nouri L, Nafchi AM. (2014). Antibacterial, Mechanical, and Barrier Properties of Sago Starch Film Incorporated with Betel Leaves Extract. *International Journal of Biological Macromolecules*, *66*, 254-259.

Olaechea PM, Insausti J, Blanco A, Luque P. (2010). Epidemiología e Impacto de las Infecciones Nosocomiales. *Medicina Intensiva, 34*(4), 256-267.

Oliveira, I., Sousa, A., Ferreira, I. C., Bento, A., Estevinho, L., & Pereira, J. A. (2008). Total phenols, antioxidant potential and antimicrobial activity of walnut (Juglans regia L.) green husks. *Food and chemical toxicology*, *46*(7), 2326-2331.

Oliveira, I., Sousa, A., Valentão, P., Andrade, P. B., Ferreira, I. C., Ferreres, F., ... & Pereira, J. A. (2007). Hazel (Corylus avellana L.) leaves as source of antimicrobial and antioxidative compounds. *Food chemistry*, *105*(3), 1018-1025.

Orona-Castillo I, Sangerman-Jarquín DM, Fortis-Hernández M, Vázquez-Vázquez C, Gallegos-Robles MÁ. (2013). Producción y Comercialización de Nuez Pecanera (*Carya illinoensis* Koch) en el Norte de Coahuila, México. *Revista Mexicana de Ciencias Agrícolas, 4*(3), 461-476.

Osmon DR, Berbari EF, Berendt AR, Lew D, Zimmerli W, Steckelberg JM, Rao N, Hanssen A, Wilson WR. (2013). Diagnosis and Management of Prosthetic Joint Infection: Clinical Practice Guidelines by the Infectious Diseases Society of America. *Clinical Infectious Diseases, 56*(1), e1-e25.

Osorio, E., Flores, M., Hernández, D., Ventura, J., Rodríguez, R., & Aguilar, C. N. (2010). Biological efficiency of polyphenolic extracts from pecan nuts shell (Carya Illinoensis), pomegranate husk (Punica granatum) and creosote bush leaves (Larrea tridentata Cov.) against plant pathogenic fungi. *Industrial Crops and Products*, *31*(1), 153-157.

Othman M, San Loh H, Wiart C, Khoo TJ, Lim KH, Ting KN. (2011). Optimal Methods for Evaluating Antimicrobial Activities from Plant Extracts. *Journal of Microbiological Methods*, *84*(2), 161-166.

Ottenio, M., Tran, D., Annaidh, A. N., Gilchrist, M. D., & Bruyère, K. (2015). Strain rate and anisotropy effects on the tensile failure characteristics of human skin. *Journal of the mechanical behavior of biomedical materials*, *41*, 241-250.

Ovando-Martínez M, Bello-Pérez LA, Whitney K, Osorio-Díaz P, Simsek S. (2011). Starch Characteristics of Bean (*Phaseolus vulgaris* L.) Grown in Different Localities. *Carbohydrate Polymers*, *85*(1), 54-64.

Ovando-Martínez M, Whitney K, Ozsisli B, Simsek S. (2017). Physicochemical Properties of Octenyl Succinic Esters of Cereal, Tuber and Root Starches. *Journal of Food Processing and Preservation, 41*(1), e12872.

Özdemir, K. S., Yılmaz, C., Durmaz, G., & Gökmen, V. (2014). Hazelnut skin powder: A new brown colored functional ingredient. *Food Research International*, *65*, 291-297.

Paczosa, M. K., & Mecsas, J. (2016). Klebsiella pneumoniae: going on the offense with a strong defense. *Microbiol. Mol. Biol. Rev.*, *80*(3), 629-661.

Pang, Z., Raudonis, R., Glick, B. R., Lin, T. J., & Cheng, Z. (2018). Antibiotic resistance in Pseudomonas aeruginosa: mechanisms and alternative therapeutic strategies. *Biotechnology advances*.

Pappas PG, Lionakis MS, Arendrup MC, Ostrosky-Zeichner L, Kullberg BJ. (2018). Invasive Candidiasis. *Nature Reviews Disease Primers, 4,* 18026.

Pelissari, F. M., Ferreira, D. C., Louzada, L. B., dos Santos, F., Corrêa, A. C., Moreira, F. K. V., & Mattoso, L. H. (2019). Starch-Based Edible Films and Coatings: An Eco-friendly Alternative for Food Packaging. In *Starches for Food Application* (pp. 359-420). Academic Press.

Pelvan, E., Olgun, E. Ö., Karadağ, A., & Alasalvar, C. (2018). Phenolic profiles and antioxidant activity of Turkish Tombul hazelnut samples (natural, roasted, and roasted hazelnut skin). Food chemistry, 244, 102-108.

Pelvan, E., Olgun, E. Ö., Karadağ, A., & Alasalvar, C. (2018). Phenolic profiles and antioxidant activity of Turkish Tombul hazelnut samples (natural, roasted, and roasted hazelnut skin). *Food chemistry*, *244*, 102-108.

Peralta, J., Bitencourt-Cervi, C. M., Maciel, V. B., Yoshida, C. M., & Carvalho, R. A. (2019). Aqueous hibiscus extract as a potential natural pH indicator incorporated in natural polymeric films. *Food Packaging and Shelf Life*, *19*, 47-55.

Percival SL, Suleman L, Vuotto C, Donelli G. (2015). Healthcare-Associated Infections, Medical Devices and Biofilms: Risk, Tolerance and Control. *Journal of Medical Microbiology, 64*(4), 323-334.

Pfister, B., & Zeeman, S. C. (2016). Formation of starch in plant cells. *Cellular and Molecular Life Sciences*, *73*(14), 2781-2807.

Piccinelli, A. L., Pagano, I., Esposito, T., Mencherini, T., Porta, A., Petrone, A. M., ... & Aquino, R. P. (2016). HRMS profile of a hazelnut skin proanthocyanidin-rich fraction with antioxidant and anti-Candida albicans activities. Journal of agricultural and food chemistry, 64(3), 585-595.

Piñeros-Hernandez D, Medina-Jaramillo C, López-Córdoba A, Goyanes S. (2017). Edible Cassava Starch Films Carrying Rosemary Antioxidant Extracts for Potential Use as Active food Packaging. *Food Hydrocolloids, 63*, 488-495.

Piotrowski, J. S., Okada, H., Lu, F., Li, S. C., Hinchman, L., Ranjan, A., ... & Deshpande, R. (2015). Plant-derived antifungal agent poacic acid targets β-1, 3-glucan. *Proceedings of the National Academy of Sciences*, *112*(12), E1490-E1497.

Porto, L. C. S., da Silva, J., Ferraz, A. B., Ethur, E. M., Porto, C. D., Marroni, N. P., & Picada, J. N. (2015). The antidiabetic and antihypercholesterolemic effects of an aqueous extract from pecan shells in wistar rats. *Plant foods for human nutrition*, *70*(4), 414-419.

Porto, L. C. S., da Silva, J., Ferraz, A. D. B. F., Corrêa, D. S., dos Santos, M. S., Porto, C. D. L., & Picada, J. N. (2013). Evaluation of acute and subacute toxicity and mutagenic activity of the aqueous extract of pecan shells [Carya illinoinensis (Wangenh.) K. Koch]. *Food and chemical toxicology*, *59*, 579-585

Prietto, L., Mirapalhete, T. C., Pinto, V. Z., Hoffmann, J. F., Vanier, N. L., Lim, L. T., ... & da Rosa Zavareze, E. (2017). pH-sensitive films containing anthocyanins extracted from black bean seed coat and red cabbage. *LWT*, *80*, 492-500.

Punia, S., Sandhu, K. S., Dhull, S. B., & Kaur, M. (2019). Dynamic, shear and pasting behaviour of native and octenyl succinic anhydride (OSA) modified wheat starch and their utilization in preparation of edible films. *International journal of biological macromolecules*, *133*, 110-116.

Punia, S., Sandhu, K. S., Dhull, S. B., & Kaur, M. (2019a). Dynamic, shear and pasting behaviour of native and octenyl succinic anhydride (OSA) modified wheat starch and their utilization in preparation of edible films. *International journal of biological macromolecules*, *133*, 110-116.

Punia, S., Siroha, A. K., Sandhu, K. S., & Kaur, M. (2019b). Rheological and pasting behavior of OSA modified mungbean starches and its utilization in cake formulation as fat replacer. *International journal of biological macromolecules*, *128*, 230-236.

Qin, Y., Liu, Y., Yong, H., Liu, J., Zhang, X., & Liu, J. (2019). Preparation and characterization of active and intelligent packaging films based on cassava starch and anthocyanins from Lycium ruthenicum Murr. *International journal of biological macromolecules*, *134*, 80-90.

Qin, Y., Liu, Y., Yong, H., Liu, J., Zhang, X., & Liu, J. (2019). Preparation and characterization of active and intelligent packaging films based on cassava starch and anthocyanins from Lycium ruthenicum Murr. *International journal of biological macromolecules*.

Quirós-Sauceda AE, Ayala-Zavala JF, Olivas GI, González-Aguilar GA. (2014). Edible Coatings as Encapsulating Matrices for Bioactive Compounds: A Review. *Journal of Food Science and Technology*, *51*(9), 1674-1685.

Radha Krishnan K, Babuskin S, Rakhavan KR, Tharavin R, Azhagu Saravana Babu P, Sivarajan M, Sukumar M. (2015). Potential Application of Corn Starch Edible Films with Spice Essential Oils for the Shelf Life Extension of Red Meat. *Journal of Applied Microbiology*, *119*(6), 1613-1623.

Ramalhosa, E., Delgado, T., Estevinho, L., & Pereira, J. A. (2011). Hazelnut (Corylus avellana L.) cultivars and antimicrobial activity. In *Nuts and Seeds in Health and Disease Prevention* (pp. 627-636). Academic Press.

Ramirez LS, Castaño DM. (2009). Metodologías para Evaluar *in vitro* la Actividad Antibacteriana de Compuestos de Origen Vegetal. *Scientia et Technica*, *2*(42).

Re R, Pellegrini N, Proteggente A, Pannala A, Yang M, Rice-Evans C. (1999). Antioxidant Activity Applying an Improved ABTS Radical Cation Decolorization Assay. *Free Radical Biology and Medicine, 26*(9), 1231-1237.

Rebelo, R., Fernandes, M., & Fangueiro, R. (2017). Biopolymers in medical implants: a brief review. *Procedia engineering*, *200*, 236-243.

Rempe CS, Burris KP, Lenaghan SC, Stewart Jr CN (2017). The Potential of Systems Biology to Discover Antibacterial Mechanisms of Plant Phenolics. *Frontiers in Microbiology, 8,* 422.

Ren W, Cheng W, Wang G, Liu Y. (2017). Developments in Antimicrobial polymers. *Journal of Polymer Science Part A: Polymer Chemistry*, *55*(4), 632-639.

Robbins, K. S., Gong, Y., Wells, M. L., Greenspan, P., & Pegg, R. B. (2015). Investigation of the antioxidant capacity and phenolic constituents of US pecans. Journal of functional foods, 15, 11-22.

Robbins, K. S., Ma, Y., Wells, M. L., Greenspan, P., & Pegg, R. B. (2014). Separation and characterization of phenolic compounds from US pecans by liquid chromatography–tandem mass spectrometry. Journal of agricultural and food chemistry, 62(19), 4332-4341.

Rodríguez-Pérez, C., Quirantes-Piné, R., Uberos, J., Jiménez-Sánchez, C., Peña, A., & Segura-Carretero, A. (2016). Antibacterial activity of isolated phenolic compounds from cranberry (Vaccinium macrocarpon) against Escherichia coli. *Food & function*, *7*(3), 1564-1573.

Rojhan, M., & Nouri, L. (2018). Antimicrobial, Physicochemical, Mechanical, and Barrier Properties of Tapioca Starch Films Incorporated with Eucalyptus Extract. *Journal of Chemical Health Risks*, *3*(3).

Romero-Bastida, C. A., Zamudio-Flores, P. B., & Bello-Perez, L. A. (2011). Antimicrobianos en películas de almidón oxidado de plátano: Efecto sobre la actividad antibacteriana, microestructura, propiedades mecánicas y de barrera. *Revista mexicana de ingeniería química*, *10*(3), 445-453.

Ruiz-Bustos E, Velazquez C, Garibay-Escobar A, García Z, Plascencia-Jatomea M, Cortez-Rocha MO, Hernandez-Martínez J, Robles-Zepeda RE. (2009). Antibacterial and Antifungal Activities of Some Mexican Medicinal Plants. *Journal of Medicinal Food, 12*(6), 1398-1402.

Russo, T. A., & Marr, C. M. (2019). Hypervirulent Klebsiella pneumoniae. *Clinical microbiology reviews*, *32*(3), e00001-19.

Sabaté Brescó, M., Harris, L. G., Thompson, K., Stanic, B., Morgenstern, M., O'Mahony, L., ... & Moriarty, T. F. (2017). Pathogenic Mechanisms and host Interactions in *Staphylococcus epidermidis* Device-Related Infection. *Frontiers in Microbiology*, *8*, 1401.

Saibabu, V., Fatima, Z., Ahmad, K., Khan, L. A., & Hameed, S. (2019). Octyl gallate triggers dysfunctional mitochondria leading to ROS driven membrane damage and metabolic inflexibility along with attenuated virulence in Candida albicans. *Medical mycology*.

Salaheen, S., Nguyen, C., Hewes, D., & Biswas, D. (2014). Cheap extraction of antibacterial compounds of berry pomace and their mode of action against the pathogen Campylobacter jejuni. *Food Control*, *46*, 174-181.

Salazar-Holguín, H. D., & Cisneros-Robledo, M. E. (2016). Resistencia a los antimicrobianos de agentes causales de las principales infecciones nosocomiales. *Revista Médica del Instituto Mexicano del Seguro Social*, *54*(4), 462-471.

Salehi, H., Mehrasa, M., Nasri-Nasrabadi, B., Doostmohammadi, M., Seyedebrahimi, R., Davari, N., ... & Siavash, M. (2017). Effects of nanozeolite/starch thermoplastic hydrogels on wound healing. *Journal of research in medical sciences: the official journal of Isfahan University of Medical Sciences*, *22*.

Salgado, P. R., Ortiz, C. M., Musso, Y. S., Di Giorgio, L., & Mauri, A. N. (2015). Edible films and coatings containing bioactives. *Current Opinion in Food Science*, *5*, 86-92.

Sanguinetti, M., Posteraro, B., & Lass-Flörl, C. (2015). Antifungal drug resistance among Candida species: mechanisms and clinical impact. *Mycoses*, *58*, 2-13.

Santos, F. O., Angélico, E. C., da Costa, J. G. M., Rodrigues, F. F., Rodrigues, O. G., & de Medeiros, R. S. (2013). Antibacterial evaluation of Anacardium occidentale (Linn)(Anacardiaceae) in semiarid Brazil. *African Journal of Biotechnology*, *12*(30).

Secretaría de Agricultura, Ganadería, Desarrollo Rural, Pesca y Alimentación (SAGARPA). (2017). Se Incrementa 83 por ciento la Producción de Nuez en México. Comunicado de Prensa. B003-CSCH01-2017.

Segura-Campos, M., Chel-Guerrero, L., & Betancur-Ancona, D. (2008). Synthesis and partial characterization of octenylsuccinic starch from Phaseolus lunatus. *Food Hydrocolloids*, *22*(8), 1467-1474.

Selvaraj, S., Krishnaswamy, S., Devashya, V., Sethuraman, S., & Krishnan, U. M. (2015). Influence of membrane lipid composition on flavonoid–membrane interactions: Implications on their biological activity. *Progress in lipid research*, *58*, 1-13.

Shah U, Naqash F, Gani A, Masoodi FA. (2016). Art and Science Behind Modified Starch Edible Films and Coatings: A Review. *Comprehensive Reviews in Food Science and Food Safety*, *15*(3), 568-580.

Shahidi, F., Alasalvar, C., & Liyana-Pathirana, C. M. (2007). Antioxidant phytochemicals in hazelnut kernel (Corylus avellana L.) and hazelnut byproducts. *Journal of Agricultural and Food Chemistry*, *55*(4), 1212-1220.

Shao D, Li J, Li J, Tang R, Liu L, Shi J, Huang Q, Yang H. (2015). Inhibition of Gallic Acid on the Growth and Biofilm Formation of *Escherichia coli* and *Streptococcus mutans*. *Journal of Food Science, 80*(6), M1299-M1305.

Shih FF, Daigle KW. (2003). Gelatinization and Pasting Properties of Rice Starch Modified with 2-Octen–1-ylsuccinic Anhydride. *Food/Nahrung*, *47*(1), 64-67.

Signoretto, C., Marchi, A., Bertoncelli, A., Burlacchini, G., Papetti, A., Pruzzo, C., ... & Spratt, D. A. (2014). The anti-adhesive mode of action of a purified mushroom (Lentinus edodes) extract with anticaries and antigingivitis properties in two oral bacterial pathogens. *BMC complementary and alternative medicine*, *14*(1), 75.

Silva-Weiss, A., Bifani, V., Ihl, M., Sobral, P. J. A., & Gómez-Guillén, M. C. (2013a). Structural properties of films and rheology of film-forming solutions based on chitosan and chitosan-starch blend enriched with murta leaf extract. Food hydrocolloids, 31(2), 458-466.

Silva-Weiss, A., Ihl, M., Sobral, P. J. A., Gómez-Guillén, M. C., & Bifani, V. (2013b) Natural additives in bioactive edible films and coatings: functionality and applications in foods. *Food Engineering Reviews*, *5*(4), 200-216.

Simões, D., Miguel, S. P., Ribeiro, M. P., Coutinho, P., Mendonça, A. G., & Correia, I. J. (2018). Recent advances on antimicrobial wound dressing: A review. *European Journal of Pharmaceutics and Biopharmaceutics*.

Simsek S, Whitney K, Ohm JB. (2013). Analysis of Cereal Starches by High-Performance Size Exclusion Chromatography. *Food Analytical Methods*, *6*(1), 181-190.

Simsek, S., Ovando-Martinez, M., Marefati, A., Sjöö, M., & Rayner, M. (2015). Chemical composition, digestibility and emulsification properties of octenyl succinic esters of various starches. *Food Research International*, *75*, 41-49.

Singh, D., Narayanamoorthy, S., Gamre, S., Majumdar, A. G., Goswami, M., Gami, U., ... & Subramanian, M. (2018). Hydroxychavicol, a key ingredient of Piper betle induces bacterial cell death by DNA damage and inhibition of cell division. *Free Radical Biology and Medicine*, *120*, 62-71.

Singleton VL, Rossi JA. (1965). Colorimetry of Total Phenolics with Phosphomolybdic-Phosphotungstic Acid Reagents. *American Journal of Enology and Viticulture, 16*(3), 144-158.

Slatnar, A., Mikulic-Petkovsek, M., Stampar, F., Veberic, R., & Solar, A. (2014). HPLC-MSn identification and quantification of phenolic compounds in hazelnut kernels, oil and bagasse pellets. Food research international, 64, 783-789.

Slobodníková L, Fialová S, Rendeková K, Kováč J, Mučaji P. (2016). Antibiofilm Activity of Plant Polyphenols. *Molecules, 21*(12), 1717.

Smeriglio, A., Mandalari, G., Bisignano, C., Filocamo, A., Barreca, D., Bellocco, E., & Trombetta, D. (2016). Polyphenolic content and biological properties of Avola almond (Prunus dulcis Mill. DA Webb) skin and its industrial byproducts. *Industrial Crops and Products*, *83*, 283-293.

Song, F., Koo, H., & Ren, D. (2015). Effects of material properties on bacterial adhesion and biofilm formation. *Journal of dental research*, *94*(8), 1027-1034.

Stefani, S., Campana, S., Cariani, L., Carnovale, V., Colombo, C., Lleo, M. M., ... & Taccetti, G. (2017). Relevance of multidrug-resistant Pseudomonas aeruginosa infections in cystic fibrosis. *International Journal of Medical Microbiology*, *307*(6), 353-362.

Stepanović S, Ćirković I, Ranin L. (2004). Biofilm Formation by *Salmonella* spp. and *Listeria monocytogenes* on Plastic Surface. *Letters in Applied Microbiology, 38*(5), 428-432.

Sticchi, C., Alberti, M., Artioli, S., Assensi, M., Baldelli, I., Battistini, A., ... & Cenderello, N. (2018). Regional point prevalence study of healthcare-associated infections and antimicrobial use in acute care hospitals in Liguria, Italy. *Journal of Hospital Infection*, *99*(1), 8-16.

Stoica P, Chifiriuc MC, Rapa M, Lazăr V. (2017). Overview of Biofilm-Related Problems in Medical Devices. *In Biofilms and Implantable Medical Devices* (pp. 3-23).

Streeter, K., & Katouli, M. (2016). Pseudomonas aeruginosa: A review of their Pathogenesis and Prevalence in Clinical Settings and the Environment. *Infection, Epidemiology and Microbiology*, *2*(1), 25-32.

Struve, C., Roe, C. C., Stegger, M., Stahlhut, S. G., Hansen, D. S., Engelthaler, D. M., ... & Krogfelt, K. A. (2015). Mapping the evolution of hypervirulent Klebsiella pneumoniae. *MBio*, *6*(4), e00630-15.

Suleyman G, Alangaden, GJ. (2016). Nosocomial Fungal Infections: Epidemiology, Infection Control, and Prevention. *Infectious Disease Clinics, 30*(4), 1023-1052.

Suleyman, G., Alangaden, G., & Bardossy, A. C. (2018). The role of environmental contamination in the transmission of nosocomial pathogens and healthcare-associated infections. *Current infectious disease reports*, *20*(6), 12.

Sun, L., Liao, K., Hang, C., & Wang, D. (2017). Honokiol induces reactive oxygen species-mediated apoptosis in Candida albicans through mitochondrial dysfunction. *PLoS One*, *12*(2), e0172228.

Sweedman MC, Tizzotti MJ, Schäfer C, Gilbert RG. (2013). Structure and Physicochemical Properties of Octenyl Succinic Anhydride Modified Starches: A Review. *Carbohydrate Polymers*, *92*(1), 905-920.

Taş, N. G., & Gökmen, V. (2015). Bioactive compounds in different hazelnut varieties and their skins. *Journal of Food Composition and Analysis, 43*, 203-208.

Taş, N. G., & Gökmen, V. (2017). Phenolic compounds in natural and roasted nuts and their skins: A brief review. *Current Opinion in Food Science*, *14*, 103-109.

Tizzotti, M. J., Sweedman, M. C., Tang, D., Schaefer, C., & Gilbert, R. G. (2011). New 1H NMR procedure for the characterization of native and modified food-grade starches. *Journal of Agricultural and Food Chemistry*, *59*(13), 6913-6919.

Tong SY, Davis JS, Eichenberger E, Holland TL, Fowler VG. (2015). *Staphylococcus aureus* Infections: Epidemiology, Pathophysiology, Clinical Manifestations, and Management. *Clinical Microbiology Reviews*, *28*(3), 603-661.

Torres, F. G., Commeaux, S., & Troncoso, O. P. (2013). Starch-based biomaterials for wound-dressing applications. *Starch-Stärke*, *65*(7-8), 543-551.

Trentin, D. S., Silva, D. B., Frasson, A. P., Rzhepishevska, O., Da Silva, M. V., Pulcini, E. D. L., ... & Giordani, R. B. (2015). Natural green coating inhibits adhesion of clinically important bacteria. *Scientific reports*, *5*, 8287.

Turner RM, Bowers JE, Burgess TL. (2005). Sonoran Desert Plants: An Ecological Atlas. *University of Arizona Press*.

u Nisa, I., Ashwar, B. A., Shah, A., Gani, A., Gani, A., & Masoodi, F. A. (2015). Development of potato starch based active packaging films loaded with antioxidants and its effect on shelf life of beef. *Journal of Food Science and Technology,* 52(11), 7245-7253.

Vázquez G, González-Alvarez J, Santos J, Freire MS, Antorrena G. (2009). Evaluation of Potential Applications for Chestnut (*Castanea sativa*) Shell and Eucalyptus (*Eucalyptus globulus*) Bark Extracts. *Industrial Crops and Products, 29*(2-3), 364-370.

Vázquez G, González-Alvarez J, Santos J, Freire MS, Antorrena G. (2009). Evaluation of Potential Applications for Chestnut (*Castanea sativa*) Shell and Eucalyptus (*Eucalyptus globulus*) Bark Extracts. *Industrial Crops and Products, 29*(2-3), 364-370.

Velásquez-Barreto, F. F., Bello-Pérez, L. A., Yee-Madeira, H., & Velezmoro Sánchez, C. E. (2019). Esterification and Characterization of Starch From Andean Tubers. *Starch-Stärke*, *71*(1-2), 1800101.

Versino F, Lopez OV, Garcia MA, Zaritzky NE. (2016). Starch-Based Films and Food Coatings: An Overview. *Starch-Stärke*, *68*(11-12), 1026-1037.

Villa F, Cappitelli F. (2013). Plant-Derived Bioactive Compounds at Sub-Lethal Concentrations: Towards Smart Biocide-Free Antibiofilm Strategies. *Phytochemistry Reviews*, *12*(1), 245-254.

Vogler, E. A. (1998). Structure and reactivity of water at biomaterial surfaces. Advances in colloid and interface science, 74(1-3), 69-117.

Volova, T. G., Shumilova, A. A., Shidlovskiy, I. P., Nikolaeva, E. D., Sukovatiy, A. G., Vasiliev, A. D., & Shishatskaya, E. I. (2018). Antibacterial properties of films of cellulose composites with silver nanoparticles and antibiotics. *Polymer Testing*, *65*, 54-68.

Wang J, Su L, Wang S. (2010). Physicochemical Properties of Octenyl Succinic Anhydride-Modified Potato Starch with Different Degrees of Substitution. *Journal of the Science of Food and Agriculture*, *90*(3), 424-429.

Wang, C., He, X., Fu, X., Huang, Q., & Zhang, B. (2016). Substituent distribution changes the pasting and emulsion properties of octenylsuccinate starch. *Carbohydrate polymers*, *135*, 64-71.

Whitney K, Reuhs, BL, Martinez, MO, Simsek S. (2016). Analysis of Octenylsuccinate Rice and Tapioca Starches: Distribution of Octenylsuccinic Anhydride Groups in Starch Granules. *Food Chemistry*, *211*, 608-615.

Wohrley, J. D., & Bartlett, A. H. (2019). The Role of the Environment and Colonization in Healthcare-Associated Infections. In *Healthcare-Associated Infections in Children* (pp. 17-36). Springer, Cham.

Won, C., Jin, Y. I., Chang, D. C., Kim, M., Lee, Y., Ganesan, P., ... & Chang, Y. H. (2017). Rheological, pasting, thermal and retrogradation properties of octenyl succinic anhydride modified potato starch. *Food Science and Technology*, *37*(2), 321-327.

Wu, Y., Bai, J., Zhong, K., Huang, Y., Qi, H., Jiang, Y., & Gao, H. (2016). Antibacterial activity and membrane-disruptive mechanism of 3-p-trans-coumaroyl-2-hydroxyquinic acid, a novel phenolic compound from pine needles of Cedrus deodara, against Staphylococcus aureus. *Molecules*, *21*(8), 1084.

Wyres, K. L., & Holt, K. E. (2016). Klebsiella pneumoniae population genomics and antimicrobial-resistant clones. *Trends in microbiology*, *24*(12), 944-956.

Xie, Y., Yang, W., Tang, F., Chen, X., & Ren, L. (2015). Antibacterial activities of flavonoids: structure-activity relationship and mechanism. *Current Medicinal Chemistry*, *22*(1), 132-149.

Yazid, N. S. M., Abdullah, N., Muhammad, N., & Matias-Peralta, H. M. (2018). Application of Starch and Starch-Based Products in Food Industry. *Journal of Science and Technology*, *10*(2).

Yeo, I. S., Kim, H. Y., Lim, K. S., & Han, J. S. (2012). Implant surface factors and bacterial adhesion: a review of the literature. *The International journal of artificial organs*, *35*(10), 762-772.

Yuan, B., Lu, M., Eskridge, K. M., Isom, L. D., & Hanna, M. A. (2018). Extraction, identification, and quantification of antioxidant phenolics from hazelnut (Corylus avellana L.) shells. Food chemistry, 244, 7-15.

Zamudio-Flores PB, Ochoa-Reyes E, Ornelas-Paz JDJ, Tirado-Gallegos JM, Bello-Pérez LA, Rubio-Ríos A, Cárdenas-Felix RG. (2015). Caracterización Fisicoquímica, Mecánica y Estructural de Películas de Almidones Oxidados de Avena y Plátano Adicionadas con Betalaínas. *Agrociencia*, *49*(5), 483-498.

Zaragoza R, Ramírez P, López-Pueyo MJ. (2014). Infección Nosocomial en las Unidades de Cuidados Intensivos. *Enfermedades Infecciosas y Microbiología Clínica, 32*(5), 320-327

Zaragoza-Lira MM, Preciado-Rangel P, Figueroa-Viramontes U, García-Hernández JL, Fortis-Hernández M, Segura-Castruita MÁ, Lagarda-Murrieta A, Madero-Tamargo E. (2011). Aplicación de Composta en la Producción del Nogal Pecanero. *Revista Chapingo*. Serie Horticultura, 17(SPE1), 33-37.

Zeppa, G., Belviso, S., Bertolino, M., Cavallero, M. C., Dal Bello, B., Ghirardello, D., ... & Gerbi, V. (2015). The effect of hazelnut roasted skin from different cultivars on the quality attributes, polyphenol content and texture of fresh egg pasta. *Journal of the Science of Food and Agriculture*, *95*(8), 1678-1688.

Zhang, B., Mei, J. Q., Chen, B., & Chen, H. Q. (2017). Digestibility, physicochemical and structural properties of octenyl succinic anhydride-modified cassava starches with different degree of substitution. *Food chemistry*, *229*, 136-141.

Zhang, L., Xu, S. G., Liang, W., Mei, J., Di, Y. Y., Lan, H. H., ... & Wang, H. Z. (2015). Antibacterial activity and mode of action of Mentha arvensis ethanol extract against multidrug-resistant Acinetobacter baumannii. *Tropical Journal of Pharmaceutical Research*, *14*(11), 2099-2106.

Zhang, X., Liu, J., & Huang, X. (2017). Bioactive components of nuts and their health effects. *Journal of Food Safety and Quality*, *8*(7), 2606-2614.

Zhishen J, Mengcheng T, Jianming W. (1999). The Determination of Flavonoid Contents in Mulberry and Their Scavenging Effects on Superoxide Radicals. *Food Chemistry, 64*(4), 555-559.

Zhu F. (2015). Interactions between Starch and Phenolic Compound. *Trends in Food Science & Technology, 43*(2), 129-143.

Zhu F. (2017). Encapsulation and Delivery of Food Ingredients Using Starch Based Systems. *Food Chemistry*, *229*, 542-552.

Zhu, J., Jiang, G., Song, G., Liu, T., Cao, C., Yang, Y., ... & Hong, W. (2019). Incorporation of ZnO/bioactive glass nanoparticles into alginate/chitosan composite hydrogels for wound closure. *ACS Applied Bio Materials*.