Influence of Factors on Release of Antimicrobials from Antimicrobial Packaging Materials

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Antimicrobial packaging materials (films or coatings) (APMs) have aroused great interest among the scientists or the experts specialized in material science, food science, packaging engineering, biology and chemistry. APMs have been used to package the food such as dairy products, poultry, meat (e.g. beef), salmon muscle, pastry dough, fresh pasta, bakery products, fruits, vegetables

and beverages. Some materials have been already commercialized. The ability of APMs to extend the shelf-life of the food depends on the release rate of the antimicrobials (AMs) from the materials to the food. The optimum rate is defined as target release rate (TRR). To achieve TRR, the influencing factors of the release rate should be considered. Herein we reviewed for the first time these factors and their influence on the release. These factors mainly include the AMs, food (or food simulant), packaging materials, the interactions among them, the temperature and environmental relative humidity (RH).

Keywords: antimicrobial, antimicrobial packaging film, controlled release, diffusion, food

INTRODUCTION

Every year the food spoilage causes tremendous economic losses and food-borne diseases arouse the attention of the governments all over the world. Aiming at relieving this problem, the antimicrobials (AMs) are normally added to the surface of the food by spray or dip, or inside the food by addition. Nonetheless these methods have many flaws (Lopez-Rubio et al., 2004; Mastromatteo et al., 2010). Active packaging (AP) has been emerging as an alternative and a better solution (Ozdemir and Floros, 2004). AP actively changes the condition of the packages to extend the shelf-life and improve the safety or sensory properties of the food during storage (Vermeiren et al., 1999). As a promising form of AP, antimicrobial AP has been explored and several options have been proposed to the food industry (Arvanitoyannis and Stratakos, 2012; Chen et al., 2012a; Lopez-Rubio et al., 2004). To inhibit the growth of microorganisms, antimicrobial substances have to reach the cells, which means that the antimicrobial agents either have to be released from the packaging materials (Han, 2005; Sung et al., 2013) or being in direct contact with the food (Aznar et al., 2012; Cran et al., 2010; Mascheroni et al., 2011; Mastromatteo et al., 2011; Zactiti and Kieckbusch, 2009). Using this technique, the antimicrobial effect can be achieved with fewer AMs compared to the traditional methods.

The release rate of the AMs is one of the key factors affecting the efficiency. If it is too slow, food spoilage may occur. If it is too fast, the AMs contained in the packaging may be consumed rapidly, reaching the minimum inhibitory concentration (MIC) in too short time. It is time

consuming and expensive to determine the release rates of AMs into the food because most foodstuffs are comprised of a complex mixture of substances such as water, carbohydrates, fats, lipids, proteins, vitamins, fibres and minerals. Normally the mathematical models are used to estimate the release profiles. These models are based on release mechanisms such as diffusion, swelling, dissolution or degradation, or the combination of them. These models can be divided into two categories, i.e. Fickian diffusion models (Licciardello et al., 2013; Torres et al., 2014; Yu et al., 2016) and non-Fickian diffusion models (Conte et al., 2013; Han et al., 2008; Suppakul et al., 2011). In these models, diffusion coefficient is a key factor, which was predicted by Piringer and his colleagues for the first time in polyolefins (Bane et al., 1996; Brandsch et al., 2002; Piringer, 1994). An alternative method is molecular dynamics simulation (MSD), a computer simulation technique based on classical molecular mechanics, provides a new way to simulate the diffusion process. MSD has been used for the investigation of diffusion of small molecules in polymer (Li et al., 1997; Oliver and Damian, 1999). We investigated the diffusion process of 13 kinds of small molecules in amorphous PET and the influence of types of polypropylene material on diffusion based on MSD (Wang et al., 2010, 2012). All these methods can help to predict the release profile to optimize antimicrobial systems, estimate concentration profiles and predict the concentration of AMs on the surface of the food to monitor if it is above MIC. The optimum rate providing the longest induction period is defined as target release rate (TRR) (Zhu, 2008). The aim of controlled release packaging (CRP) is to obtain TRR. CRP acts

as a delivery system offering an appropriate release of active compounds over time in a controlled manner in order to maintain the required concentration of AMs over the food (LaCoste et al., 2005).

As mentioned before, the release of AMs from CRP materials can be influenced by many factors, such as the AMs (e.g. molecular weight, size, polarity and initial concentration in the film), the food (or simulant) (e.g. polarity, fat content, ionic strength and pH), packaging materials (e.g. polarity, thickness, pore size, porosity, glass transition temperature (GTT), the additives, the plasticization, degree of the crosslinking, crystallization, swelling and film-preparation methods), interactions among above factors, storage time, the temperature and environmental relative humidity (RH) (Chalier et al., 2009; Cozzolino et al., 2013; Jipa et al., 2012; Narayanan et al., 2013; Neo et al., 2013; Ouattara et al., 2000; Uz and Altinkaya, 2011; *Zactiti* and Kieckbusch, 2009). By carefully tuning these factors, there will be a better chance to achieve TRR. Herein these factors are reviewed for the first time.

Commonly-used AMs can be classified as synthetic or natural (Kuorwel et al., 2011; Sung et al., 2013). Synthetic AMs include metal ions, metallic nanoparticles (NPs) and metal oxide NPs, ethyl lauroyl arginate (LAE), organic acids and their salts etc. (Imran et al., 2010; Nerín et al., 2016). Natural AMs are environmental friendly and comprise the enzymes, peptides, antibiotics, essential oils (EOs), natural extracts and naturally occurring polymers such as chitosan. Natural AMs, ZnO, LAE, organic acids and their salts are considered as generally recognized as safe

(GRAS) by Food and Drug Administration (FDA). These AMs act against a wide range of Gram-negative bacteria, Gram-positive bacteria, yeasts, moulds and fungi seen in Table 1. The AMs can be incorporated into the packaging materials by using active labels, embedding/surface modification of the material or by coating the packaging material (Akrami et al., 2015; Becerril et al., 2007; Gutiérrez et al., 2009a, 2009b, 2010 and 2011; López et al., 2007; Narayanan et al., 2013; Otero et al., 2014; Rodríguez-Lafuente et al., 2007a and 2007b). Other technologies such as extrusion are still far from this field, as the high temperature involved in the process degrades the AMs and causes significant losses by evaporation. We recently developed a new approach, in which the antimicrobial agents are incorporated in the adhesive used for building multilayer structures. The system has been studied and optimized not only *in vitro* but also *in vivo* for tomato puree (Gherardi et al., 2016).

Packaging materials basically include non-biodegradable petroleum-based films, biodegradable and/or edible films seen in Table 1 (Campos et al., 2011; Raheem, 2012). The former mainly includes polyethylene terephthalate (PET), polyethylene (PE), ethylene-vinyl alcohol (EVOH) copolymer, polyvinyl chloride (PVC), polyamide (PA), polypropylene (PP), ethylene vinyl acetate (EVA) copolymer, poly(butylene adipate-co-terephthalate) (PBAT) and ionomer. The latter mainly includes polylactic acid (PLA), polyvinyl alcohol (PVOH), polycaprolactone (PCL), polyhydroxybutyrate (PHB), polysulfosuccinate, polyhydroxyalkanoate (PHA), polysaccharides (starch, chitosan, sodium alginate, cellulose and pectin), proteins (soy

protein isolate (SPI), zein, wheat gluten (WG)) and beeswax (BW). Most biodegradable and/or edible polymer materials are water-soluble and can easily swell leading to rapid release of the AMs (Del Nobile et al., 2008; Higueras et al., 2013; Hu et al., 2012; Mayachiew et al., 2010; Sanchez-Gonzalez et al., 2011; Souza et al., 2013). Although EVOH is not biodegradable, it is highly hydrophilic which can be plasticized by the sorption of water (Cerisuelo et al., 2012). There are many film-preparation methods like solution casting, coating, injection/compression-molding, extrusion, coextrusion, extrusion blowing and electrospinning producing sub-micro or nanofibrous materials (Kriegel et al., 2008; Mascheroni et al., 2013; Neo et al., 2013).

Generally speaking the release rate can be increased by higher temperature, higher initial AM concentration, lower tortuosity, higher porosity, larger average pore size and lower GTT (Narayanan et al., 2013; Uz and Altinkaya, 2011). The GTT can be reduced by swelling and plasticization, while it can be increased by cross-linking, restricting polymer chain mobility (de Souza et al., 2010; Fabra et al., 2014; Fajardo et al., 2014; Mastromatteo et al., 2011). All these factors that influence the release rate will be discussed in detail hereinafter.

FACTORS INFLUENCING THE KINETICS

Metals and Metal Oxides

Among the metals with antimicrobial properties, without a doubt silver occupies the first position. Silver ions at concentration of 10^{-9} to 10^{-6} mol L^{-1} can act against a variety of bacteria,

yeasts and molds (Maillard and Hartemann, 2013). The release of Ag^+ ions from the packaging materials is based on ionic exchange between Ag^+ ions and cations/protons in the food (or food simulant) (Fernandez et al., 2010). Higher acidity and ionic strength of the food (or food simulant) normally lead to a higher release (Busolo et al., 2010; Fernandez et al., 2010; Martínez-Abad et al., 2012, 2013a, 2014a). The film matrix plays an important role in the release. The plasticization induced by high RH and/or partial acid hydrolysis by an acidic simulant might facilitate the release of Ag^+ ions from PLA or easily swollen EVOH (Martínez-Abad et al., 2012). The film-processing method is another factor. Compared to the compression films prepared by melt/compression, the cast films prepared by solution-casting/solvent evaporation were less compact and more irregularly structured, favoring solvent accessibility and the ionic exchange of Ag^+ ions (Fernández et al., 2010). For melt/compression method, the addition of the substances such as surfactant to the film matrix (e.g. PLA) led to a better distribution of the silver salt favoring the release (Martínez-Abad et al., 2014a). For solution casting method, different solvents can be chosen to tune the release of Ag^+ ions. For example, Martínez-Abad et al. prepared silver-infused PLA films with solvents such as tetrahydrofuran (THF) or the mixture of THF and dimethylformamide (DMF) (Martínez-Abad et al., 2013a). Since $AgNO_3$ dissolves worse in THF than in the mixture, it has a higher tendency to agglomerate on the surface of the film favoring the release. The coating can tune the release by changing its thickness and/or composition. When the coating serves as barrier layer, increase of its thickness is unfavorable for

the release of AMs from the coated film. Martínez-Abad et al. coated BW on Ag^+-loaded PLA film to avoid the burst release at the initial stage (Martínez-Abad et al., 2014b).

Metallic-based nanocomposite antimicrobial packaging materials have received much attention in recent years (Llorens et al., 2012). Most commonly-used metallic-based nanocomposites contain nanosilver. Nanosilver food packaging is now commercially available in several countries (Silvestre et al., 2011). According to the official definition in Europe, the NPs should have at least one dimension less than 100 nm size (Benn et al., 2010). The NPs show substantially different physicochemical and biological properties compared to conventionally sized particles because of their high surface/volume ratios (Chaudhry et al., 2008). It was proposed that the release of nanomaterials from polymeric nanocomposites was via passive diffusion, desorption and dissolution probably assisted by matrix degradation (Duncan and Pillai, 2015). NPs within the surface layer diffuse first (Huang et al., 2011; Sotiriou et al., 2012). It is believed that the antimicrobial action takes place with the release of Ag^+ ions to the packaged product. This mechanism involves the previous oxidation of silver into the ions, which probably occurs either from the released nanosilver or from those silver NPs on the packaging surface (Echegoyen and Nerín, 2013). The NPs with smaller size can oxidize more easily favorable for the release (Auffan et al., 2009; Conte et al., 2013). As expected, higher fill percentage of silver NPs in the film or coating led to higher release rate (Cushen et al., 2013; Sadeghnejad et al., 2014). Corona air plasma promotes adhesion when printing, coating or laminating. The surface

modification of polymer films (e.g. low density polyethylene (LDPE) film) by corona air plasma increased the hydrophilicity of the films thus providing better binding efficiency with metal NPs (e.g. nanosilver) from colloidal solution (Sadeghnejad et al., 2014). An increase in time and power of corona treatment is favorable for the release. Sanchez-Valdes et al. used different film-forming methods (e.g. spraying, casting and lamination) to deposit PE-Ag nanocomposite layer on a five-layer film (Sanchez-Valdes et al., 2009). They found that more voids in the layer facilitate the diffusion of water and silver led to higher release rate of Ag^+ ions. The method of spraying produced more voids in that layer followed by casting while no apparent voids were found for lamination. The addition of montmorillonite (MMT) can change the structure and the morphology of the film thus influencing the release of AMs. In some cases MMT is unfavorable for the release of AMs due to nanoclay silicate layers and their agglomerates (Barzegar et al., 2014). MMT can be used as the supporting material of silver in the nanocomposite films (e.g. chitosan) in order to achieve steady and progressive release of Ag^+ ions (Lavorgna et al., 2014).

There are other metal AMs such as nano-ZnO (Emamifar et al., 2012; Espitia et al., 2012), nano copper (Conte et al., 2013) and nano-TiO_2 (Lin et al., 2014). We investigated the influence of the additives (e.g. the antioxidants and light stabilizers) in the films on the release of nanosilver and nano-TiO_2 to food simulants (Lin et al., 2014; Su, et al., 2015). The addition of the mixture of four additives was unfavorable for the release of nanosilver but favorable for the release of nano-TiO_2. Probably the additives inhibited the oxidation of nanosilver while had no

obvious effect on nano-TiO_2. Further investigation will be made on the interaction mechanism between different types of additives and the nanometals.

The released metal in the food or food simulants from nanometal polymeric composites might include different species such as metal ions and the NPs with various sizes and shape. However frequently-used determination methods of metals in food or food simulants are atomic absorption spectroscopy (AAS) and inductively coupled plasma mass spectrometry (ICP-MS) by which the total amount of the metal can be determined (Conte et al., 2013; Emamifar et al., 2012; Fernández et al., 2010; Song et al., 2011). More recently we found that the use of ICP-MS in single particle mode demonstrated that nanoparticles can be also analyzed by this emission technique (Echegoyen and Nerín, 2013; Echegoyen et al., 2016). Another technique, the field-flow fractionation (FFF), has been used to separate particles, colloids and macromolecules with the sizes ranging from 1nm to micron scale (Liu et al., 2012). The FFF can be combined with a wide variety of detectors such as scanning electron microscopy (SEM), transmission electron microscopy (TEM), ultraviolet spectroscopy (UV), diode array detection (DAD), multi-angles light scattering (MALS), dynamics light scattering (DLS), inductively coupled plasma atomic emission spectrometry (ICP-AES) and ICP-MS etc. Based on the same principle the asymmetric flow field-flow fractionation (AsFlFFF) coupled to UV-VIS or ICP-MS has been used for the determination of the size and size distribution of nanosilver particles (Bolea et al., 2014) and nanoselenium (Palomo et al., 2016; Vera et al., 2016). These techniques have a

promising future in the investigation of the release of nanometal species.

Organic Acids and Their Salts

Organic acids used in antimicrobial packaging usually contain lactic, gallic, propionic, acetic, sorbic and formic acids. The most commonly-used salts are potassium sorbate (Psb) and sodium benzoate (SB), which are normally used in the preservation of dairy products and dough (Jipa et al., 2012; Martínez et al., 2013; Mondal et al., 2015; Neo et al., 2013; Ouattara et al., 2000; Rivero et al., 2013; Smulders et al., 2013; Uz and Altinkaya, 2011; Yu et al., 2016; Zactiti and Kieckbusch, 2009). These organic acids are often determined by high performance liquid chromatography (HPLC) or acid/base titration while Psb and SB are determined by ultraviolet/Visual (UV/VIS) spectrophotometry.

The release of organic acids from the packaging materials to the water is very fast because they are soluble in water (Neo et al., 2013). The released organic acids can decrease pH value of the food or food simulants (Rivero et al., 2013). Normally solution casting method is used to obtain edible or biodegradable films containing these AMs (Jipa et al., 2012; Martínez et al., 2013; Neo et al., 2013; Ouattara et al., 2000; Rivero et al., 2013; Yoshida et al., 2010; Zactiti and Kieckbusch, 2009). When compression-moulding method is used, it is important to control the film-forming temperature especially for volatile acids (e.g. formic acid) in order to obtain higher initial concentration of these acids in the films (Martínez et al., 2013). The formation of multi-component composite films can provide better packaging properties. The change of the

ratio of these compounds can tune the release rate of AMs (Jipa et al., 2012; Yu et al., 2016). We studied the release profile of Psb from low-methoxy pectin/carboxymethylcellulose (CMC) composite films to 95% ethanol (Yu et al., 2016). We found that the release rate increased with the increase of CMC in the films due to higher swelling degree. The addition of the emulsifier to the film matrix can influence the release. The diffusion coefficients of Psb from palmitic acid/chitosan emulsion films was found to be higher than those from chitosan films probably due to the increased distance between chitosan chains induced by the palmitic acid favoring for the release (Yoshida et al., 2010). The addition of MMT to poly(butylene adipate-co-terephthalate (PBAT) promoted the release of SB because of the rough and ragged surface providing increased surface area for better accessibility of SB (Mondal et al., 2015). β-cyclodextrin (β-CD) with hydrophobic cavity can act as antimicrobial delivery carrier for extended release of AMs (Chen and Liu, 2016). Birck et al. combined the methods of cross-linking and encapsulation by β-CD to prolong the release of SB (Birck et al., 2016). Chemical modification such as cross-linking can decrease the release rate of Psb or SB (Birck et al., 2016; Zactiti and Kieckbusch, 2009). Salts (e.g. calcium chloride) or acids (e.g. citric acid) can be chosen as the crosslinkers according to various film matrices. As expected, longer cross-linking time and higher proportion of crosslinkers result in higher degree of the crosslinking, which is unfavorable for the release (Zactiti and Kieckbusch, 2009). When solution casting method is used, higher film-forming parameters such as the content of film matrix (e.g. cellulose acetate (CA)) in casting solution,

wet casting thickness and drying temperature cause smaller pore size and porosity of the film unfavorable fore the release of AMs (e.g. Psb) (Uz and Altinkaya, 2011).

Enzymes, Peptides and Antibiotics

Some enzymes, peptides and antibiotics can act as AMs. Frequently-used ones include lysozyme, glucose oxidase (GOX), nisin, natamycin, ethyl lauroyl arginate and peptides, which can be determined by UV/VIS spectrophotometry, HPLC, enzyme linked immunosorbent assay (ELISA) and agar diffusion method (Chollet et al., 2009; de Souza et al., 2010; Hanusova et al., 2013; Manso et al., 2014; Mastromatteo et al., 2011; Nithya et al., 2013). AMs in this category are temperature-sensitive, thus normally solution casting method is used to prepare the edible or biodegradable films containing these AMs. Among these AMs, lysozyme is one of the most studied natural protein biopreservative and is effective against gram-positive bacteria (Sung et al., 2013). Positively charged lysozyme can be incorporated into negatively charged polymers for stronger interaction. These polymers include microfibrillated cellulose (MFC) (i.e. nano-sized cellulose fibrils), low methoxyl pectin and protein etc. (Bayarri et al., 2014; Cozzolino et al., 2013; Fajardo et al., 2014). Neutral matrix (e.g. paper, PVOH and PET) can be either modified by increasing anionic density with negatively charged surface treated spelt bran or anionic polyelectrolytes such as CMC and polygalacturonic acid (PGA) (Mascheroni et al., 2010; Mastromatteo et al., 2011), or by surface modification induced by low temperature plasma for better adhesive properties with sol–gel coating containing lysozyme (Corradini et al., 2013). The

formation of complex between lysozyme and the film matrix (e.g. neutral but highly polar starch film) is unfavorable for the release (Fabra et al., 2014). Cross-linking with different concentration of cinnamaldehyde was used to avoid swelling-induced burst release of lysozyme from gliadin films to phosphate buffer (Fajardo et al., 2014). The influence of food simulants on the release of lysozyme was investigated (Bayarri et al., 2014; Mascheroni et al., 2010). Food simulant containing pectinase caused the breakdown of lysozyme/ low methoxyl pectin complexes leading to the dramatic release of lysozyme (Bayarri et al., 2014). Food simulants such as anionic detergent or high salt solution caused the release of a large amount of lysozyme from cellulose-based paper due to chemical forces including electrostatic interaction among them (Mascheroni et al., 2010). The release of lysozyme to the agar gel was limited compared to that to liquid simulants because of high molecular weight of lysozyme (Fabra et al., 2014). The plasticizers are added to the film matrix to increase the flexibility and elasticity of the films, which can also influence the release. Most frequently-used plasticizers in the preparation of edible and/or biodegradable films are glycerin, polyethylene glycol (PEG) and sorbitol. Higher content of them in the films normally increase the solubility of the films in water-containing food (or simulants) leading to higher release of AMs. However the influence of plasticizers varies from case to case. For example, when zein–wax composite films and zein–oleic acid blend films were plasticized with catechin, catechin reduced the porosity of the films resulting in decreased release rate of lysozyme (Arcan and Yemenicioglu, 2013). Meanwhile wax increased the

hydrophobicity and tortuosity of the films also resulted in decreased release rate of lysozyme. Supercritical assisted phase inversion technique is supposed to be able to prepare membranes with controlled morphology and porosity (Baldino et al., 2014). When CO_2 density increased, smaller pores were produced in the membrane leading to the decrease of the release rate of lysozyme. Nisin is the most widely used bacteriocin in active food packaging and is effective against gram-positive bacteria, which has higher affinity toward hydrophilic material (Cha and Chinnan, 2003; Jamshidian et al., 2010). The release of nisin depends on the composition of the film, pH and ionic strength of the simulants (Wang et al., 2015a; Wang et al., 2015b). Nanocomposite films (e.g. PLA/cellulose nanocrystals (CNC)) allowed a slow controlled release of nisin during storage (Salmieri et al., 2014). Da Silva et al. found that chemical interaction between natamycin and chitosan reduced the release rate of natamycin to water from alginate/chitosan composite films. (da Silva et al., 2012). Wang et al found that the release of nisin from chitosan/poly (L-lactic acid) (PLLA) increased with the decrease of chitosan/ PLLA ratio (Wang et al., 2015a). In acidic simulants with decreasing pH, the increasing electrostatic repulsion between both positively-charged nisin and chitosan favored the release of nisin. Meanwhile the increased ionic strength was unfavorable for the release. Chollet et al. studied the release of nisin to agarose gels from PE-based films coated with nisin-loaded hydroxypropyl methylcellulose (HPMC) (Chollet et al., 2009). They found that purer nisin and higher fat content of gels facilitated the release. Smart AP provides a controlled antimicrobial effect by

releasing AMs only on demand by changing the temperature (Fuciños et al., 2015). Fuciños et al. prepared polysaccharide-based (GA) films containing natamycin-loaded smart thermosensitive poly(N-isopropylacrylamide) (PNIPA)/acrylic acid (AA) nanohydrogels (Fuciños et al., 2015). The release of natamycin was fast at 37℃ due to the collapse of nanohydrogels. GOX was immobilized on PA or ionomer films by chemical interaction (Hanusova et al., 2013). Its release was due to the cleavage of the covalent bonds of peptide linkers, which was enhanced by acid hydrolysis. Less GOX was released from PA films than from ionomer films because GOX bound more strongly to PA films. The release of the peptide of *Bacillus licheniformis* Me 1, an efficient peptide against common food-borne pathogens, was better controlled from cellulose film than from LDPE film (Nithya et al., 2013).

Essential Oils

EOs are lipid fractions obtained from plants such as basil, citronella, thyme, oregano, cinnamon, clove and rosemary (Kuorwel et al., 2011). They are commonly-used AMs and also have antioxidant ability, preferably used for the preservation of meat, fish and their products (Tongnuanchan and Benjakul, 2014). Major antimicrobial compounds in EOs include carvacrol, thymol, linalool, methylchavicol, eugenol, isoeugenol, allyl isothiocyanate (AITC), cinnamaldehyde, perillaldehyde and vanillin, which are determined mainly by UV/VIS spectrophotometry, FTIR, gas chromatography flame ionization detector (GC-FID), gas chromatography mass spectrometry (GC-MS), HPLC, HPLC-diode array detector (DAD)-MS,

Ultra-performance liquid chromatography (UPLC)-DAD and UPLC-MS (Aznar et al., 2012; Cerisuelo et al., 2013; Chen et al., 2012b; Gutiérrez et al., 2010; Han et al., 2008; Martínez-Abad et al., 2013b; Nerín, 2012; Sánchez-García, 2008). There are a huge number of publications dealing with antimicrobial properties of EOs and their major components. But the main difficulties in their use in packaging materials reside in both the efficient incorporation in the packaging and the controlled release. For a better efficiency, several approaches such as encapsulation or chemical bonds with the polymers have been explored. Unfortunately most of the publications deal with in vitro tests and very few applied the new packaging to real food (Carrizo et al., 2015; Gutiérrez et al., 2009b; Montero et al., 2011; Otero et al., 2014; Rodríguez-Lafuente et al., 2009 and 2010). Some of the most relevant publications are discussed below.

The properties of EOs components are crucial factors for the release. EOs components are slightly soluble in water and highly soluble in organic solvents or olive oil (Rodriguez et al., 2013). Therefore the release is slower to water than to hydrophobic solution (Chen et al., 2012b; Cran et al., 2010; Hu et al., 2012; Torres et al., 2014). We studied the release of basil, citronella, oregano or rosemary EOs from a coated PP film to a stack of virgin PP films (Licciardello et al., 2013). They found that the release of EO components depended more on the molecular weight/molar volume and polarity than on their initial concentrations in coated PP films. They also found that diffusion coefficient of higher polar geraniol was higher in non-polar PP virgin

films than that of citronellal despite of their same molecular weight. Similarly the release of higher polar linalool from non-polar LDPE film to isooctane was faster than that of methylchavicol despite of their similar molecular weight (Suppakul et al., 2011). We found that the release of eugenol from SPI films to olive oil was relatively easier than the release of isoeugenol due to the structural difference (Chen et al., 2012b). Microencapsulation of AMs enables their controlled release. Guarda et al. studied the release of carvacrol and thymol from the gum arabic microcapsules coated on corona-treated LDPE (Guarda et al., 2011). The release of non-crystallisable carvacrol was faster than that of crystallisable thymol since crystallites hampered the diffusion of molecules through the wall of gum arabic. Wu et al prepared gelatin films incorporated with cinnamon essential oil (CEO) nanoliposomes. The release of CEO nanoliposomes to corn oil was sustained because hydrophobic groups of gelatin formed a shelter around the external layer of nanoliposomes which increased their stability.

Film matrix influences the release of EOs components according to its polarity (or hydrophilicity) and morphology. We found strong interaction between SPI films and polar EOs components (e.g. thymol, cinnamaldehyde, vanillin, eugenol and isoeugenol) slowed down the release (Chen et al., 2012b; Hu et al., 2012). Water insoluble WG-based bioplastics are more suitable for controlled release of oregano EOs to water than water soluble egg-white (EW)-based bioplastics (Martínez et al., 2013). Martínez-Abad et al. showed that the release of cinnamaldehyde was controlled by PCL matrix rather than by the concentration of

cinnamaldehyde (Martínez-Abad et al., 2013b). Han et al. reported that the release of cinnamaldehyde from PA coating on LDPE films was faster to more acidic simulants because PA coating hydrolyzed faster (Han et al., 2008). We found that the release of carvacrol, thymol and cinnamaldehyde from PP films was faster than that from EVOH coated PE films because polar EVOH strongly retained the polar EOs compounds (Gutiérrez et al., 2010). Del Nobile et al. found that the diffusion of thymol depended more on micro-voids in the film than on thymol concentration (Del Nobile et al., 2008). Efrati et al. developed thymol-containing single-layer PE films with different crystallinity degree (Efrati et al., 2014b). PE with higher crystallinity degree reduced the release rate due to a higher tortuosity. Besides single-layer films, they also produced three-layer films with thymol-containing PE film as the inner layer and EVA of different polar comonomer percentage as the outer layer. Higher polar comonomer percentage led to stronger interaction between EVA and thymol.

The release of EOs can be controlled by the addition of the substances such as plasticizer, MMT nanoclay, natural fibre (e.g. kenaf or spelt bran), EVA and β-CD (Campos-Requena et al., 2015; Narayanan et al., 2013; Sánchez-García, 2008; Sanchez-Garcia et al., 2010; Shemesh et al., 2015; Tawakkal et al., 2016; Torres-Giner et al., 2014; Tunc and Duman, 2011). Eugenol can serve as antimicrobial and plasticizer. The addition of it can decrease GTT of PHB film resulting in its fast release (Narayanan et al., 2013). The addition of nanoclay to the polymer matrix generally increases the solubility of EOs components (e.g. carvacrol and thymol) and decreases

their release due to a larger tortuosity. Efrati et al. prepared linear low density polyethylene (LLDPE) films containing thymol, nanoclays and foaming agent which could increase the heat stability of thymol (Efrati et al., 2014a). The diffusion coefficient of thymol decreased with the increase of nanoclays. Rodriguez et al. demonstrated that nanoclay in the CA matrix didn't affect much the release rate of thymol since these nanocomposites presented an intercalated structure which produced less tortuosity than the exfoliated structure (Rodriguez et al., 2014). However in some cases nanaclay facilitate the release of EOs components (Mascheroni et al., 2011). Mascheroni et al. prepared the paper with WG coating containing nanoclay and carvacrol and found that the addition of carvacrol and nanoclay disrupted the structure of WG layer, which favored the release of carvacrol. The addition of natural fibres such as kenaf or spelt bran as fillers to the biodegradable matrix (e.g. PLA or zein) can produce environmental friendly biocomposite packaging materials. The micro-voids or micro-channels induced by these fibres in the matrix facilitate the release of thymol (Mastromatteo et al., 2009; Tawakkal et al., 2016). LDPE/EVA films were prepared containing linalool, carvacrol, thymol and methylchavicol respectively (Cran et al., 2010; Suppakul et al., 2011). EVA formed hydrogen bonds with linalool, but EVA reduced the crystallinity of the polymer favoring the release. Therefore the concentration of EVA was optimized for the controlled release of these EOs components. The addition of β-CD to encapsulate AMs normally is beneficial for the controlled release of AMs. Barba et al prepared whey protein isolate (WPI) film with carvacrol encapsulated by β-CD. They

found that β-CD inclusion complex could prolong the release time (Barba et al., 2015). The addition of β-CD to PLA provided a microenvironment to stabilize bound AITC resulting in less free AITC for release (Raouche et al., 2011). Mascheroni et al. prepared nanofibrous pullulan membranes with perillaldehyde encapsulated by β-CD for the controlled release of perillaldehyde (Mascheroni et al., 2013).

Ambient environment conditions such as the temperature and RH are especially important for the volatile EOs (Cerisuelo et al., 2012; Chalier et al., 2009: Kurek et al., 2014; Martínez-Abad et al., 2013b; Martínez et al., 2013; Mascheroni et al., 2011; Tunc and Duman, 2011). The packaging films containing EOs should be processed or stored at milder temperatures and lower RH to prevent their loss. A sustained release of encapsulated AITC from PLA/AITC electrospun-grafted fibers to the air was observed at room temperature while almost no release was observed at temperature lower than 4℃ (Kara et al., 2016). Kurek et al. found that there was more than 98% lost of carvacrol from chitosan matrix after two days of storage at 37℃ with RH＞96% (Kurek et al., 2014). Cerisuelo et al. reported that carvacrol was released from PP/EVOH (carvacrol)/PP multilayer films not only to the salmon but also to the external atmosphere when RH was higher than 60% (Cerisuelo et al., 2013). Therefore for a better performance of these films, RH should be less than 60%. Mascheroni et al. found EOs components encapsulated by β-CD in pullulan membranes only started the release at RH＞90% because of the strong interaction between EOs components and β-CD (Mascheroni et al., 2013).

A special method of near critical and supercritical impregnation was used to load thymol to LLDPE films (Rojas et al., 2015; Torres et al., 2014). The impregnation pressure was the most important parameter influencing the release of thymol. Higher pressure led to higher initial concentration resulting in more released thymol (Torres et al., 2014). Rojas et al prepared LLDPE films containing 2-nonanone, which is the main component of EOs of ruda, by supercritical impregnation (Rojas et al., 2015). They found that a lower depressurization rate of the impregnation process resulted in a higher initial content of 2-nonanone in LLDPE. Another novel method of loading thymol is by thermal inkjet printing. Caro et al. printed chitosan/tripolyphosphate/thymol NPs on chitosan films and chitosan/quinoa-protein films respectively (Caro et al., 2016). They reported that the release of thymol from chitosan films was faster than that from chitosan/quinoa-protein films because the NPs accumulated mainly at the surface of chitosan films but went deeper into the hybrid films due to their higher porosity. The NPs at the surface were more accessible to the solvent leading to a faster release of thymol.

Seldom foods are used in the release study due to their complexity. Lopes et al. studied the release of cinnamaldehyde from cinnamaldehyde /cellulose-derivative polymer into the pastry dough and the bread respectively (Lopes et al., 2014). The release into the pastry dough was higher than that into the bread because the dough contained vegetable fat and also a better contact between the film and the dough.

Chitosan

Chitosan is a kind of polysaccharide biomaterial with a dual role as antimicrobial and packaging film matrix (Dutta et al., 2012). Lago et al. reviewed different analytical methods to characterize and determine chitosan including fourier transform infrared (FTIR), nuclear magnetic resonance (NMR), UV, viscosimetry, elemental analysis, X-Ray Diffraction (XRD), thermogravimetric analysis (TGA), titration, SEM and size exclusion chromatography (SEC) (Lago et al., 2011). The antimicrobial activity of pure chitosan film is based on the released soluble protonated glucosamine species (Fernandez-Saiz et al., 2008; Fernandez-Saiz et al., 2009a; Fernandez-Saiz et al., 2010). More dissolved chitosan led to higher antimicrobial capacity (Fernandez-Saiz et al., 2009b). Fernandez-Saiz et al. reported that there was a substantial loss in the release of protonated glucosamine species as a result of the cross-linking and/or other physical/chemical changes in the biomaterial when the chitosan films were stored at high temperature or RH (Fernandez-Saiz et al., 2009b). Bie et al. found that higher content of starch in PLA/starch/chitosan blended films could increase the hydrophilicity of the film favoring the release of chitosan species (Bie et al., 2013). The release was fast from the surface or near the surface of these films in contact with the water. In contrast, the release from the inner of the film was slow, gradual and therefore sustainable. Lei et al. used atmospheric pressure plasma to irradiate PP layer of PET/PP films for better adhesion with chitosan (Lei et al., 2014). The release rate of protonated glucosamine species from PET/PP films increased with the increase of acidity which makes chitosan more ionized and soluble. The release rate decreased with the

increase of ionic strength and the decrease of ionic mobility.

Chitosan can serve as film matrix to incorporate AMs like LAE, limonene and galangal extract (Higueras et al., 2013; Mayachiew et al., 2010; Sanchez-Gonzalez et al., 2011). Higher concentration of LAE or galangal extract in chitosan films led to a slower release due to the interaction between these AMs and chitosan (Higueras et al., 2013; Mayachiew et al., 2010). AMs-incorporated chitosan films are not suitable to preserve highly non-polar fatty food because of the lack of film hydration. Sanchez-Gonzalez et al. found that the hydration of chitosan films was essential for the release of limonene (Sanchez-Gonzalez et al., 2011). Fernandez-Pan et al. found that the release of carvacrol was faster to 96% ethanol than to olive oil because the films could hydrate better in 96% ethanol (Fernandez-Pan et al., 2015). Higher chitosan molecular weight employed in the film formulation led to higher viscosity of film-forming dispersions, which resulted in larger carvacrol droplets facilitating the release of carvacrol. Chemical or physical cross-linking of chitosan film matrix hinders the release of AMs. Bajpai et al. prepared curcumin-containing chitosan/cellulose micro-crystals films (Bajpai et al., 2015). Cellulose micro-crystals could physically crosslink with chitosan. Higueras et al. prepared chitosan films chemically crosslinked with cinnamaldehyde via imino-covalent bonding. The release of cinnamaldehyde was influenced by the degree of imino bond hydrolysis (Higueras et al., 2015). The drying or storage temperature of the films can lead to thermal cross-linking giving rise to a more compact film structure (Higueras et al., 2015; Mayachiew et al., 2010). Different drying

method of the film can be tried to produce the film with different morphology. For example, low-pressure superheated steam drying (LPSSD) method led to higher porosity facilitating the release of galangal extract (Mayachiew et al., 2010).

CONCLUSION

In the past decade, extensive progress and improvements have been made in the research of antimicrobial packaging. People have realized the importance of controlled release of AMs from the packaging materials. However the mechanisms of the release have not yet been fully understood in some cases. The additives such as antioxidants and light stabilizers in the plastics also influence the release of AMs, but they are rarely studied. TRR is still difficult to achieve. Although more and more APMs have been developed in the labs, few are commercially available due to their applicability and safety. Up till now most investigation of APMs was performed using food simulants instead of real foods. It can be emphasized as well that the concentration of antimicrobial agent optimized in vitro at laboratory scale has to be considerably increased when applying the same approach in vivo. The few studies published on real food all demonstrated that this premise can be considered as a general rule. Meanwhile available AMs are still limited. More natural AMs should be explored such as the extracts of Chinese traditional herbs for example. Biopolymer nanocomposite films have a bright future for their environmental friendliness and satisfying mechanical properties, although barrier properties, general performance and cost are still challenging. Having an antimicrobial packaging does not guaranty

that the packaging and the food are safe and the study of specific migration limit (SML) and non-intentionally added substances (NIAS) should be performed. Despite of all the weakness, the industrialization of the APMs for food preservation is still promising.

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Table 1. Release studies of antimicrobials from films and coatings to food /simulants.

AMs	Film Matrix	Preparation method	Microorganism	Food/Simulant	T (℃)	Ref
Silver ion	PLA	Solution casting/melt mixing	*S. aureus*, *E. coli*	3% acetic acid, water, ethanol (10%, 95%)	20	(Fernández et al., 2010)
Silver ion	PLA	Solution casting	*Salmonella spp.*	2.0×10^{-3} mol/L HNO_3	Room temperature	(Busolo et al., 2010)
Silver ion	PLA	Solution casting	*S. enterica*	Slightly acidified water	Room temperature	(Martínez-Abad et al., 2013a)
Silver ion	EVOH	Solution casting	*L. monocytogenes*,	Slightly acidified water	5, 25, 50	(Martínez-Abad et

			Salmonella.spp.			al., 2012)
Silver ion	PLA	Melt-compounding	*S. enterica*	Water (pH 6)	24	(Martínez-Abad et al., 2014a)
Silver ion	PLA	Solution casting	*S. enterica*	Neutral water, water (pH 2.5)	24	(Martínez-Abad et al., 2014b)
Silver ion	Chitosan/MMT	Solution casting	*P. fluorescens, P. putida*	Water	Room temperature	(Lavorgna et al., 2014)
Nanosilver	PE	Commercial product	*Not mentioned*	4% acetic acid, water, hexane, 95% ethanol	25, 40 ,50	(Huang et al., 2011)

Nanosilver	PE	Commercial product	*Not mentioned*	3% acetic acid, 95% ethanol	20, 40, 70	(Song et al., 2011)
Nanosilver	PVC	Solution casting	*Not mentioned*	Chicken meat	6.6, 7.2, 19.9, 24.1	(Cushen et al., 2013)
Nanosilver	5 layer	Laminating, casting, spraying	*P. oleovorans, A. niger*	Water	Room temperature	(Sanchez-Valdes et al., 2009)
Nanosilver	LDPE	Coating	*S. aureus, E. coli*	Water	Room temperature	(Sadeghnejad et al., 2014)
Nanosilver	PE	Commercial product	*Not mentioned*	3% acetic acid, 50% ethanol	40	(Echegoyen and Nerín, 2013)
Nanosilver	PE	Extrusion blowing	*Not mentione*	3% acetic acid, 50%	20, 40, 70	(Su, et al., 2015)

			d	ethanol		
Nanosilver, nanozinc	LDPE	Melt mixing	*Total yeast, molds*	Orange juice	4	(Emamifar et al., 2012)
Nanocopper	PLA	Drop- casting	*Pseudomonas spp.*	Phosphate buffer (pH 6.8)	Room temperature	(Conte et al., 2013)
Nano-TiO_2	PE	Extrusion blowing	*Not mentioned*	3% acetic acid, 50% ethanol	25, 70, 100	(Lin et al., 2014)
Lactic acid	PA6 film	Soaking	*E. coli*	Water., beef	0-20	(Smulders et al., 2013)
Gallic acid	Zein	Electrospinning	*S. aureus, E. coli, C. albicans*	Water	23	(Neo et al., 2013)
Propionic acid	Chitosan	Solution casting	*S. aureus, Salmonella spp.,*	Phosphate buffer (pH 6.5),	4	(Rivero et al., 2013)

			Candida spp., Penicilliu m spp.	pastry dough		
Acetic acid, Propionic acid	Chitosan	Solution casting	*Not mentione d*	Phosphat e buffer (pH 5.7, 6.4, 7.0)	4, 10, 24	(Ouattara et al., 2000)
Sorbic acid	Monolayer (PVOH/BC), monolayer coated with BC	Solution casting	*E. coli*	Water	25	(Jipa et al., 2012)
Formic acid, oregano EOs	Wheat gluten protein, egg-white albumen protein	Compression molding	*A. niger, C. kefyr, B. cereus, E. coli*	Water	Room temperat ure	(Martínez et al., 2013)

Psb	Sodium alginate	Solution casting	*Not mentioned*	Water	25	(Zactiti and Kieckbusch, 2009)
Psb	CA	Solution casting	*Not mentioned*	Water	4	(Uz and Altinkaya, 2011)
Psb	Chitosan	Solution casting	*Not mentioned*	Water	Room temperature	(Yoshida et al., 2010)
Psb	Potato starch/MMT	Solution casting	*A. niger*	Potato dextrose agar	25	(Barzegar et al., 2014)
Psb	Pectin/carboxymethyl cellulose	Solution casting	*Not mentioned*	95% ethanol	4, 25, 40 60	(Yu et al., 2016)
SB	PBAT/MMT	Solution casting	*S. aureus*, *B. subtilis*	Water	25	(Mondal et al., 2015)

SB	PVOH/citric acid, PVOH/citric acid/cyclodextrin	Solution casting	*S. aureus*, *E. coli*, *Candida*	Water	37	(Birck et al., 2016)
Lysozyme	PVOH +surface treated or not treated spelt bran	Solution casting	*Not mentioned*	Water	Room temperature	(Mastromatteo et al., 2011)
Lysozyme	Sodium caseinate	Solution casting	*S. aureus*	Sodium acetate buffer (pH 3.0-5.8)	4, 25	(de Souza et al., 2010)
Lysozyme	Gliadin	Solution casting	*L. innocua*	Phosphate buffer (pH 6.2)	20	(Fajardo et al., 2014)
Lysozyme	Isolate pea	Solution casting	*L.*	agar gel	10, 25	(Fabra et

	protein , corn starch		*monocytogenes*			al., 2014)
Lysozyme	Zein-wax composite film, zein-oleic acid blend film	Solution casting	*L. innocua*	Water	4	(Arcan and Yemenicioglu, 2013)
Lysozyme	CA	Solution casting	*E. coli, B. amyloliquefaciens*	Water	4	(Gemili et al., 2009)
Lysozyme	Cellulose based paper	Prepared according to international standard ISO 5269-2:2004	*Not mentioned*	0.5 mol/L NaCl, 8 mol/L urea, 1% sodium dodecylsulphate	Room temperature	(Maschero ni et al., 2010)
Lysozyme	Cellulose	Prepared	*E. coli, L.*	Solution	4, 10, 23	(Maschero

	based paper	according to international standard ISO 5269-2:2004	*innocua*	(pH 4-7), NaCl content (0.2-2 M)		ni et al., 2012)
Lysozyme	MFC	Solution casting	*Not mentioned*	Water, 10 wt.% ethanol	6, 20	(Cozzolino et al., 2013)
Lysozyme	PVOH, PET	Dip coating	*M. lysodeikticus*	Buffered solution (pH 6.2)	4, 25	(Corradini et al., 2013)
Lysozyme	Low methoxyl pectin	Solution casting	*Not mentioned*	Imidazole –acetate buffer (pH 7.0)	Room temperature	(Bayarri et al., 2014)
Lysozyme	CA	Supercritical assisted phase inversion	*M. lysodeikticus*	Water	Room temperature	(Baldino et al., 2014)
Glucose oxidase	PA or ionomer	Film on surface of reaction	*E. coli, P. fluoresce*	3% acetic acid,	23	(Hanusova et al.,

		mixture	*ns, L. helveticus, L. innocua*	phosphate buffer (pH 7.0, 4.5)		2013)
Nisin	HPMC coated PE/PA/PE film	Coating	*K. rhizophila*	Agarose gels	25	(Chollet et al., 2009)
Nisin	Chitosan/PLA	Solution casting	*S. aureus*	Water	25	(Wang et al., 2015a)
Nisin	Chitosan/PVOH	Solution casting	*S. aureus*	Water	25	(Wang et al., 2015b)
Nisin	PLA/CNC	Compression molding	*L. monocytogenes*	Agar culture medium	4	(Salmieri et al., 2014)
Natamycin	GA-PNIPA-AA	Solution casting	*P. commune*	Water, agar	5,10,37	(Fucinos et al., 2015)
Natamycin	Sodium	Solution casting	*Not*	Water	25	(da Silva

	alginate with or without chitosan		*mentioned*			et al., 2012)
Peptide of bacillus licheniformis Me 1	LDPE, cellulose	Soaking, coating by spreading	*M. luteus, L. monocytogenes, S. aureus, B. cereus , S. typhimurium*	Phosphate buffer (pH 3.0, 7.0, 9.0)	4, 25, 37	(Nithya et al., 2013)
Basil, citronella, oregano and rosemary EOs	PP	Coating	*Not mentioned*	9 layers of virgin PP	40	(Licciardello et al., 2013)
Oregano,	PP, EVOH,	Commercial	*Not*	Ethanol	20	(Aznar et

citral and cinnamon EOs	PET	product	*mentioned*	(10%, 95%)		al., 2012)
Cinnamon, oregano and clove EOs	PE/EVOH	Coextrusion	*B. cereus, S. Aureus, L. monocytogenes etc.*	Water, 3% acetic acid, 10% ethanol and isooctane	40	(López et al., 2016)
Cinnamon EO	Cassava starch/ nanoclay	Solution casting	*P. commune, E. amstelodami*	Water	Room temperature	(Souza et al., 2013)
Cinnamon EO	Gelatin	Solution casting	*E. coli, S. aureus, B. subtilis, A. niger*	Corn oil	4, 40	(Wu et al., 2015)

Mustard EO	Cellulose sulfate+β-CD	Solution casting	*E. coli, S. aureus, B. subtilis, A. niger*	Water	Room temperature	(Chen and Liu, 2016)
Cinnamaldehyde	PCL	Solution casting	*S. enterica, L. monocytogenes*	Air	Room temperature	(Martínez-Abad et al., 2013b)
Cinnamaldehyde	Cellulose-derivative polymer	Solution casting	*Salmonella spp., B. cereus, Mesophilic aerobic, yeast, mould, coliform*	Pastry dough, bread	8, 23	(Lopes et al., 2014)
Cinnamaldeh	Chitosan	Solution casting	*S. aureus,*	MHB	Room	(Higueras

yde			*E. coli, L. monocytogenes*		temperature	et al., 2015)
Cinnamaldehyde	Polyester/ aluminum /polyethylene	Modified commercial products	*E. coli* and *Saccharomyces cereviase*	3% acetic acid	60	(Gherardi et al., 2016)
Trans-cinnamaldehyde	PA coated LDPE	Coating	*Not mentioned*	10 wt.% ethanol (pH 4, 7, 10)	4-35	(Han et al., 2008)
Carvacrol	WG coated paper	Coating	*E. coli, B. cinerea*	Air	30	(Maschero ni et al., 2011)
Carvacrol	SPI coated paper	Coating	*Not mentioned*	Air	5, 20, 30	(Chalier et al., 2009)
Carvacrol	EVOH	Coating	*Not*	Air	23	(Cerisuelo

	coated PP		*mentioned*			et al., 2012)
Carvacrol	MC/MMT	Solution casting	*E. coli, S. aureus, B. cinerea*	Air	15-45	(Tunc and Duman, 2011)
Carvacrol	PP/EVOH/PP	Coextrusion	*Not mentioned*	Salmon muscle	4	(Cerisuelo et al., 2013)
Carvacrol	chitosan	Solution casting	*Not mentioned*	Air	4, 20, 37	(Kurek et al., 2014)
Carvacrol	LDPE/MMT	Melt processing	*B. cinerea*	Air	18	(Campos-Requena et al., 2015)
Carvacrol	LDPE/MMT	Melt processing	*E. coli, L. innocua*	Air	Room temperature	(Shemesh et al., 2015)

Carvacrol	WPI	Solution casting	*not mentioned*	50% ethanol	25	(Barba et al., 2015)
Carvacrol	Chitosan	Solution casting	*P. fragi, S. putrefaciens , A. hydrophila*	olive oil, 96% ethanol	25	(Fernandez-Pan et al., 2015)
Thymol	Zein	Solution casting	*B. cereus, C. lusitaniae, Pseudomonas spp., S. thermophilus*	Buffered water (pH 7)	25	(Del Nobile et al., 2008)
Thymol	PCL,	Solution casting	*Not*	Air	24	(Sánchez-

	PCL/nanoclay		*mentioned*			García, 2008)
Thymol	Zein/spelt bran	Solution casting	*Not mentioned*	Water	Room temperature	(Mastromatteo et al., 2009)
Thymol	LLDPE	Near critical and supercritical fluid impregnation	*Not mentioned*	Ethanol (10%, 95%)	40	(Torres et al., 2014)
Thymol	LLDPE+MMT	Extrusion	*E. coli*	Air	40	(Efrati et al., 2014a)
Thymol	LLDPE	Cast extrusion	*E. coli*	Air	Room temperature	(Efrati et al., 2014b)
Thymol	PLA/zein (or zein hybrid) fiber/PLA	Electrospinning +compression	*L. monocytogenes*	Air	Room temperature	(Torres-Giner et al., 2014)
Thymol	PLA, PLA/kenaf	Melt blending and	*Not mentione*	Air	Non-isothermal	(Tawakkal et al.,

		compression molding	*d*			2016)
Thymol	CA/organoclay	Solution casting	*L. innocua*	95% ethanol	40	(Rodriguez et al., 2014)
Thymol	Chitosan, chitosan/quinoa-protein	Inkjet printing	*L. innocua, S. aureus, S. typhimurium, E. aerogenes, P. aeruginosa, E. coli,*	Water	20	(Caro et al., 2016)
Eugenol	PHB	Solution casting	*S. aureus, E. coli, S. typhimurium, B.*	Water, 3% acetic acid, 50 %	37	(Narayanan et al., 2013)

			cereus, A. flavus, A. niger, Penicilliu m sp., R. solani	ethanol, n-hexane		
Eugenol, isoeugenol	SPI	Solution casting	*Not mentione d*	Olive oil	5-60	(Chen et al., 2012b)
Perillaldehyd e	Pullulan+β-CD	Electrospinning	*Not mentione d*	Air	23	(Maschero ni et al., 2013)
Thymol,cinna maldehyde, vanillin	SPI	Solution casting	*Not mentione d*	Olive oil	5-60	(Hu et al., 2012)
Carvacrol , thymol, cinnamaldehy de	PP, PE/EVOH	Commercial product by coating	*L. monocyto genes, S. choleraes*	Agar	Room temperat ure	(Gutiérrez et al., 2010)

			uis, C. albicans, A. flavus			
Thymol, carvacrol	BOPP/gum arabic microcapsules coating	Coating	*E. coli, S. aureus, L. innocua, S. cerevisiae, A. niger*	Water	4	(Guarda et al., 2011)
Thymol,cinnamaldehyde	CA/organoclay	Solution casting	*L. innocua*	Ethanol (10%, 95%)	40	(Rodriguez et al., 2013)
Linalool, methylchavicol	LDPE+EVOH	Extrusion blowing	*Not mentioned*	Isooctane	4-25	(Suppakul et al., 2011)
Linalool, carvacrol, thymol	LDPE+EVOH	Compression molding, extrusion blowing	*Not mentioned*	Ethanol (15%, 95%), isooctane	25	(Cran et al., 2010)

2-nonanone	LLDPE	Supercritical fluid impregnation	*Not mentioned*	10% ethanol	40	(Rojas et al., 2015)
AITC	PLA+ β -CD	Extrusion，thermomoulding	*B. cinerea*	PDA medium	50	(Raouche et al., 2011)
AITC	PLA	Solution casting	*L. innocua, E. coli*	Air	-20, 3, 22	(Kara et al., 2016)
Chitosan	Gliadin/chitosan	Solution casting	*S. aureus*	MHB medium	37	(Fernandez-Saiz et al., 2008)
Chitosan	Chitosan	Solution casting	*S. aureus, Salmonella spp.*	MHB medium	37	(Fernandez-Saiz et al., 2009b)
Chitosan	PLA/starch	Extrusion	*E. coli, S. aureus*	Agar culture medium	Room temperature at RH 90%	(Bie et al., 2013)

Chitosan	PET/PP	Assemble by plasma treatment	*E. coli, S. aureus, B. subtilis*	Acetic acid solution	5-45	(Lei et al., 2014)
LAE	Chitosan	Solution casting	*Bacteria, yeasts, fungi*	Water	4, 28	(Higueras et al., 2013)
Limonene	Chitosan	Solution casting	*Not mentioned*	Water, ethanol (10%, 50%, 95%), isooctane	20	(Sanchez-Gonzalez et al., 2011)
Galangal extract	Chitosan	Solution casting	*S. aureus*	MHA medium	37	(Mayachiew et al., 2010)
Curcumin	Chitosan/cellulose microcrystals	Solution casting	*E. coli*	Physiological fluid	37	(Bajpai et al., 2015)

*Abbreviation: Nitrocellulose (NC) ; Mueller-Hinton broth (MHB); methyl cellulose (MC); high density polyethylene (HDPE) ; Mueller-Hinton agar (MHA); potato dextrose agar (PDA)