Antimicrobial polymeric materials for packaging applications: A review

Eun-Soo Park

Green Energy and Material Team, Young Chang Silicone Co., Ltd., (Gasan-dong) 205-16, Gasandigital 1-ro, Geumcheon-gu, Seoul 153-803, Korea

In recent years, antimicrobial packaging has attracted much attention from the food industry because of the increase in consumer demand for minimally processed, preservative-free products. Antimicrobial packaging can be considered an emerging technology that could have a significant impact on shelf life extension and food safety. Many classes of antimicrobial compounds have been evaluated in film structures, synthetic polymers and edible films. New antimicrobial packaging materials are continually being developed. Many of them exploit natural agents to control common food-borne microorganisms. The present review will be restricted to food packaging applications only, including a brief outline of some antimicrobial polymeric packaging systems, recent developments and future prospects.

Keywords: microbial; infection; antimicrobial; polymer; packaging

1. Introduction

The microbial contaminated polymeric materials could serve as important sources of cross-infections, causing a variety of serious consequences in medical devices, hospital equipment, water purification and delivery systems, bio-protective equipment. Even though they cannot be directly assimilated by microorganisms, microbes can grow and propagate using bioassimilable contaminants on the surface of the polymeric materials. One possible way to avoid microbial contamination is to develop them that possess antimicrobial activities [1-8]. The polymeric materials with resistance to microbial colonization and pathogenic microorganism spreading (antimicrobial polymers) have been one of the examples of the active material functionality. The antimicrobial polymers are expected to protect against negative impact of the pathogenic microorganisms, which can seriously affect the society from the viewpoint of both health damages and unwanted economical loads connected with that. They have usually been prepared by compounding antimicrobial agents into ordinary synthetic polymers. However, many of the antimicrobial agents steadily permeate out from the polymer matrices, giving rise to poisonous influences on the human body. Covalent bonding of antimicrobial pharmacophores to polymer matrices would reduce or eliminate the permeation problems, which can be done either by polymerization of monomers possessing antimicrobial activity or by direct chemical anchoring of pharmacophores onto functional groups of the ordinary synthetic polymers [3]. Moreover, increased efficiency, selectivity, and handling safety are additional benefits which may be realized [4]. Many novel antimicrobial agents have been synthesized by chemical means [9] or by microbial fermentation [10] and wait to be compounded or chemically anchored to polymers [9, 10]. Antimicrobial agents used in antimicrobial-processed products are classified into organic, inorganic and natural organic compounds. Organic antimicrobial agents raise health concerns and many of them do not have sufficient antimicrobial activity. Polymeric antibacterial agents can significantly reduce loss of antimicrobial activity associated with volatilization, photolytic decomposition, dissolution, and permeation [4]. On the other hand, inorganic antimicrobial agents employ Ag, Cu, and Zn compounds and are excellent in safety and antimicrobial activity. These metalic compounds are used in many types of household and medical products due to their good balance between antimicrobial activity and endurance. However, patients with metal allergy due to Cu or Zn have been reported [11]. Antimicrobial polymeric materials could find a successful application such as coating on glassy polymers, food packaging, sanitary, or medical application, antimicrobial agents are prepared by introducing antimicrobial functional groups into the polymer molecules to protect the polymeric materials against harmful microorganisms in spite of the lower antimicrobial activity compared to the respective monomers. This chapter reviews the different types of antimicrobial polymeric materials developed for packaging applications, recent developments and future prospects. Special emphasis will be on the advantages/disadvantages of each technology.

2. Antibacterial polymeric packaging

Polymeric packaging fulfils the diverse role from protecting products, preventing spoilage, contamination, extending shelf life, ensuring safe storage thereby helping to make them readily available to consumers in our day to day life. The term antimicrobial packaging encompasses any packaging techniques used to control microbial growth in a food product. These include packaging materials and edible films and coatings that contain antimicrobial agents and also techniques that modify the atmosphere within the package [12]. In this section, a brief description of polymeric packaging material, food-borne pathogen and antimicrobial polymer-based food packaging material is presented.

2.1 Polymeric packaging material

Packaging materials provide a means to preserve, protect, merchandise, market and distribute foods. They play a significant role in how these products reach the consumers in a safe and wholesome form without compromising quality. The relationship between the food and contact with the packaging material continuously interact and contribute to changes that can occur over time in these products [13]. It is therefore important that several factors are considered when choosing the right package for a particular food product. Generally, the packaging material may either be rigid or flexible. Rigid containers include glass and plastic bottles and jars, cans, pottery, wood boxes, drums, tins, plastic pots and tubes. They give physical protection to the food inside that is not provided by flexible packaging. Flexible packaging is a major group of materials that includes polymer films, papers, foil and some types of vegetable fibres and cloths that can be used to make wrappings, sacks and sealed or unsealed bags [13].

The polymers are made up of large, organic molecules that can be formed into a variety of useful products, they are fluid, moldable, heat sealable, easy to print, and can be integrated into production processes where the package is formed, filled, and sealed in the same production line [14]. Flexible and semi-rigid containers made of polymers are gradually replacing the traditional metal cans and glass jars for packaged shelf-stable foods. Unlike metal cans and glass jars, they are relatively permeable to gases, water vapour, and other small penetrate molecules. Therefore, polymer materials used for packaging oxygen sensitive foods should possess low oxygen permeability [14]. In addition to the high barrier requirement, materials for polymeric packages should possess various other characteristics such as mechanical strength, heat resistance, puncture resistance, chemical resistance, transparency, gloss, printability and compliance with relevant food contact legislation [15].

The packaging industry is the largest user of polymers; more than 90 % of flexible packaging is made of them, compared to only 17 % of rigid packaging. Barrier resins are generally being employed for polymer containers by modifications to improve product protection and make them more cost effective [13]. Polymer films are mainly used as packaging materials for food products, consumer goods, and liquid and bulk chemical and petrochemical products, as well as for household purposes. Typical polymer film production technologies are blown and cast extrusion. Blown film manufacturing involves using a jet of air to blow the molten polymer through a circular blown film die. The melted plastic then forms a continuous tube, which is inflated, flattened by rollers, and cut to length-resulting in double-thickness film. Cast film is manufactured by extruding the melted polymer through a flat die or slot-forming a thin sheet or film. After extrusion, it is attached to the surface of a chilled (rotating) roller so that it is cooled extremely fast. It is the surface of the rotating roller that gives cast film its characteristic smooth and clear appearance. While cast film can be produced at much higher line speeds, there is higher waste along with little orientation in the cross direction [16]. Barrier packaging would not be what it is today had it not been for the discovery of the multilayer structure. Prior to the development of co-extrusion technology, multilayer films were produced by laminating thin polymer layers together. While this process of lamination worked, it was found to be slow and not very efficient. Co-extrusion involves combining two or more layers of melted plastic into a single extruded web [16]. Materials used in the production of packaging films include cellulose and its esters, polyolefins, polyvinyls, polystyrene (PS), polyesters and polyamides.

The plain cellulose is a glossy transparent film that is odourless, tasteless and biodegradable. It is tough and puncture resistant, although it tears easily. It has dead-folding properties that make it suitable for twist-wrapping (e.g. sugar confectionery). However, it is not heat sealable and the dimensions and permeability of the film vary with changes in humidity. It is used for foods that do not require a complete moisture or gas barrier, including fresh bread and some types of sugar confectionery [17]. Cellulose acetate is a clear, glossy transparent, sparkling film that is permeable to water vapour, odours and gases and is mainly used as a window material for paperboard cartons [18].

The most widely used commercial polyolefins are polyethylene (PE), polypropylene (PP), and poly(ethylene-*co*-vinyl acetate) (EVA). PE is classified according to its density as low density PE (LDPE), linear low density PE (LLDPE), medium density PE (MDPE), and high density PE (HDPE). LDPE film is heat sealable, inert, odour free and shrinks when heated. It is a good moisture barrier but is relatively permeable to oxygen and is a poor odour barrier. It is less expensive than most films and is therefore widely used for bags, for coating papers or boards and as a component in laminates. LDPE is also used for shrink- or stretch wrapping. Stretch wrapping uses thinner LDPE (25 - 38 μm) than shrink-wrapping (45 - 75 μm), or alternatively, LLDPE is used at thicknesses of 17 - 24 μm [17]. The cling properties of both films are adjusted to increase adhesion between layers of the film and to reduce adhesion between adjacent packages [19]. HDPE is stronger, thicker, less flexible and more brittle than LDPE and a better barrier to gases and moisture. Sacks made from HDPE have high tear and puncture resistance and have good seal strength. They are waterproof and chemically resistant and are increasingly used instead of paper or sisal sacks. PP is a clear glossy film with a high strength and puncture resistance. It has a moderate barrier to moisture, gases and odours, which is not affected by changes in humidity. It stretches, although less than PE. It is used in similar applications to LDPE. Oriented PP is a clear glossy film with good optical properties and a high tensile strength and puncture resistance [20]. It has moderate permeability to gases and odours and a higher barrier to water vapour, which is not affected by changes in humidity. It is widely used to pack biscuits, snack foods and dried foods [21].

Poly(ethylene-*co*-vinyl alcohol) (EVOH) has one of the lowest oxygen permeability reported among polymers commonly used in packaging. EVOH is a semi-crystalline copolymer of ethylene and vinyl alcohol monomer units. Commercial production of EVOH is generally a two-step process involving free radical polymerization of ethylene and vinyl acetate followed by saponification. The acetate functional groups in EVA copolymers are converted into hydroxyl groups during a saponification process. Only polyvinyl alcohol (PVOH) has oxygen permeability lower than that of EVOH. However, PVOH is soluble in water and difficult to process by melt extrusion because its melting point is close to its heat degradation temperature. The melting point of PVOH is about 180 - 190 °C, while it thermally degrades at temperatures around 150 °C [22]. Therefore PVOH has limited use in food packaging. Data from EVAL Americas (Houston, TX) indicates that oxygen permeability of EVOH (EVAL® resin with 27 mol% ethylene) is about 0.006 cc·mil/100 in^2·day·atm at 23 °C. It is especially important for refrigerated and shelf-stable foods where oxygen deteriorates the quality of packaged products and reduces their shelf life. EVOH accounts for a majority of thermoplastic barrier materials used for rigid or semi-rigid retortable food containers. However it is of limited use in flexible packages or lid films for rigid trays used for packaging thermally processed shelf-stable low acid foods due to its moisture sensitivity [23]. EVOH is hydrophilic, absorbing a significant amount of moisture when directly exposed to humid conditions, leading to an increase in its oxygen permeability. Thus the performance of EVOH as a barrier material in food packages depends upon the processing and storage conditions to which the packages are exposed. Despite the problems of moisture sensitivity, EVOH is still a preferred barrier material for various packaging applications, accounting for about 70 - 75 % of barrier resin used for retortable rigid containers [24].

Two most important polyvinyl polymers for food packaging applications are poly(vinyl chloride) (PVC) and poly(vinylidene chloride) (PVDC). PVC is most commonly used for clear wrapping because of its cheap cost and stretching capabilities as well as being easy to extrude into sheets. It exhibits excellent thermoformability, high flexural strength, good chemical resistance and low permeability to oils. These properties make PVC the material of choice for blister packaging [25]. PVC film can be found in stretch wrap for industrial and pallet wrap, shrink wrap, some bags and liners, labels and blood bags. It also is used exclusively to package fresh red meats. That is because it is semi-permeable, which, as mentioned earlier, means that just enough oxygen can pass through the film to keep the meat fresh and maintain its bright red colour. PVDC is a synthetic resin produced by the polymerization of vinylidene chloride. It is used principally in clear, flexible, and impermeable polymer food wrap. The oxygen permeability of high barrier PVDC is about 0.08 cc·mil/100 in^2·day·atm at 23 °C [26]. PVDC is very strong and is therefore used in thin films. It has a high barrier to gas and water vapour and is heat shrinkable and heat sealable. The gas barrier properties of PVDC are not affected by moisture, and PVDC itself has relatively low water vapour transmission rate. The thickness normalized water vapour transmission rate of saran XU-32024 PVDC is 0.06 g·mil/100 in^2·day. However, the use of PVDC is challenged by several issues that include cost, processing difficulties, and environmental concerns. PVDC homopolymer has a melting point of 198 - 205 °C and decomposes at around 210 °C, which makes the polymer difficult to process [27]. On the other hand, copolymers of PVDC have lower melting points of about 140 - 175 °C, making melt processing feasible. Because of the fairly narrow range of feasible processing temperatures for PVDC, its co-extrusion with polymers that require high processing temperatures such as nylon 6 (260 - 290 °C) and polyethylene terephthalate (PET) (280 - 310 °C) becomes difficult [28].

PET is a strong, lightweight synthetic resin and the most common type of polyester. PET is becoming the package of choice for many food products, particularly beverages and mineral waters. The main reasons for its popularity are the properties of glass-like transparency coupled with adequate gas barrier properties for retention of carbonation. The three major packaging applications of PET are as containers (bottles, jars and tubs), semi-rigid sheet for thermoforming (trays and blisters) and thin oriented films (bags and snack food wrappers). PET bottles and jars are manufactured by the process of injection stretch blow moulding [29]. Semi-rigid transparent PET sheet, the precursor for thermoforming PET articles, is made by extruding a ribbon of molten PET polymer onto a series of cooling and compressing rolls. The cooled sheet is then stored before feeding through a thermoforming line, which heats the sheet, stamps, forms, and cuts out the article all in one process. Manufacture of thin, biaxially oriented PET film is a much more demanding operation, which develops fully the properties of the PET [30]. The excellent thermal properties of PET film allow it to be processed and used over a wider temperature range (-70 to +150 °C) than most common packaging films. They can be used in the demanding sterilisation processes based on steam, ethylene oxide and radiation. These are ideal for retort packaging, dual ovenable lidding and ‘boil in the bag’ applications [29].

Polyamides are clear, strong films over a wide temperature range (from -60 to 200 °C) that have low permeability to gases and are grease proof. However, the films are expensive to produce, require high temperatures to heat seal, and the permeability changes at different storage moistures. They are used with other polymers to make them heat sealable at lower temperatures and to improve the barrier properties, and are used to pack meats and cheeses [31]. They may be processed into film by blown or cast film process, oriented or non-oriented. Nylon 6 is a widely used polyamide for the production of flexible packaging film, in most cases combined with polyolefins as a component of a multilayer structure.

Furthermore multilayer films are coated with other polymers or aluminum to improve their barrier properties or to impart heat sealability. For example a nitrocellulose coating on both sides of cellulose film improves the barrier to oxygen, moisture and odors, and enables the film to be heat sealed when broad seals are used. Package films made from cellulose that has a coating of vinyl acetate are tough, stretchable and permeable to air, smoke and moisture. They are used for packaging meats before smoking and cooking. A thin coating of aluminum (metallization) produces a very good barrier to oils, gases, moisture, odors and light. This metallized film is less expensive and more flexible than plastic/aluminum foil laminates [32]. Common films on the market are polymer multilayer films which combine PE, PP, nylon, EVOH and PET.

2.2 Food-borne pathogen

In general, infectious pathogens may enter the body and invade or colonize host tissues. This requires some time usually greater than 8 h for onset of illness. Toxigenic pathogens create food "poisoning" situations by producing an enterotoxin in the food. Incubation times for onset of disease from toxigenic microbes are often shorter than for invasive pathogens and can be as little as 1 h, as in the case of staphylococcal enterotoxin-induced illness. The short incubation time in comparison to the infectious pathogens results because the agent of illness, the toxin, is pre-formed in the food and ingested. Illness is not contingent upon the organism migrating to the intestinal tract implanting and growing [33]. Selected examples of food-borne pathogens in various foods as follow.

Salmonella species are gram-negative rod-shaped bacteria of the Enterobacteriaceae family. Despite great advances in molecular genetic approaches to identification and characterization these organisms are still serologically defined, i.e., by their somatic (O) and (usually) flagellar (H) and sometimes capsular (Vi) antigens. Over approximately 2,400 different serotypes are known to exist. *Salmonella* can cause a number of disease syndromes including typhoid fever from *Salmonella typhi*. However, other strains of *Salmonella* cause gastroenteritis, bacteremia, and enteric or paratyphoid fever [34]. Symptoms include abdominal pain, diarrhea, occasionally with mucous or blood. Nausea and vomiting often occur but are rarely severe or protracted. A fever of 38 - 39 °C is common, often after a chill. In many instances the disease resolves within 48 h. However, it can last with diarrhea and low-grade fever for 10 - 14 days. In severe cases dehydration may lead to hypotension, cramps, oliguria, and uremia. Symptoms are often more severe in infants and adults over 60 years of age. Fatalities rarely exceed 1 % of the affected population and are generally limited to infants, elderly, and debilitated individuals [34].

Listeria monocytogenes (*L. monocytogenes*) is a Gram-positive rod-shaped bacterium. It is the agent of listeriosis, a serious infection caused by eating food contaminated with the bacteria. The very widespread distribution of this organism in the natural environment coupled with its resistance to freezing, growth in the presence of 10 % salt, survival in concentrated brine solutions, and its ability to grow at 1 - 45 °C (optimum at 35 - 37 °C) makes control of this organism in the processing environment challenging. Eradication of this organism from ready-to-eat meat and poultry processing environments is unlikely given current technology [35]. Hence, implementation of rigorous controls is essential to prevent processed food contamination. Two types of listeriosis are recognized - (a) an invasive form that can be life threatening in newborn infants, the elderly, and immunocompromised adults and (b) a less common self-limiting gastrointestinal illness. In the gastrointestinal form, flu-like symptoms such like diarrhea, vomiting, fever, may occur 18 - 24 h after ingestion of the contaminated food [33].

Campylobacter species are gram-negative, spiral-shaped rods and typically motile. The *Campylobacter* genus consists of 14 species. The most common food-borne species are *Campylobacter jejuni* and *Campylobacter coli*. Members of the genus are susceptible to environmental stresses and are considered to be relatively fragile. Because of these concerns, this organism can be difficult to isolate in the laboratory. The most common type of illness caused by *Campylobacter* spp. is gastroenteritis referred to as campylobacteriosis. Enteric symptoms are caused by a thermolabile toxin [35]. Infections are usually self-limiting, and treatments typically include fluid and electrolyte replacement. Antibiotic treatments may be used in severe cases [36].

Staphylococcus aureus (*S. aureus*) is a common bacterial pathogen causing staphylococcal food poisoning a leading cause of food-borne intoxication worldwide. Staphylococcal food poisoning is not attributed to ingestion of live bacterial cells but rather acquired from ingesting one or more heatstable pre-formed staphylococcal enterotoxins in foods contaminated with enterotoxin producing strains of staphylococci, principally, *S. aureus*. This type of food poisoning is classified as intoxication since it does not require growth of the bacterium in the host. Indeed, numerous outbreaks have been caused by foods in which the organism has been killed but the heat-stable toxin remained. Staphylococcal enterotoxins are unique because they are not destroyed by heating including canning. *S. aureus* causes food poisoning by releasing enterotoxins into the food and toxic shock syndrome by release of superantigens into the bloodstream. In humans, *S aureus* causes various suppurative (pus-forming) infections including superficial skin lesions, boils, styes, and furunculosis as well as more serious infections such as pneumonia, mastitis, phlebitis, meningitis, and urinary tract infections; and deep-seated infections, such as osteomyelitis and endocarditis [33].

Bacillus cereus (*B. cereus*) is a gram-positive, spore-forming rod-shaped microorganism. The spores of *B. cereus* can survive most cooking processes. Mainly prolific as an aerobic vegetative cell, survival in anaerobic conditions is also possible. Germination of spores to high populations of viable cells may produce a toxin in foods or in human intestines, causing gastrointestinal illness. Fried rice is a common source of illness caused by *B. cereus*. It is frequently present in uncooked rice, their heat-resistant spores can survive and germinate after cooking and a heat-stable enterotoxin may be produced that can survive further heating such as stir frying. Toxin production is enhanced by the presence of protein such as eggs or meat [33]. Foods with high fat content may also have a protective effect. Therefore, the enterotoxin may be present in the food or it may be produced after ingestion within the small intestine. *B. cereus* strains can produce two types of food-borne illness: diarrheal and emetic. The diarrheal illness is often associated with meat products, soups, potatoes and other starchy vegetables, puddings, and sauces. Onset times may occur 8 - 16 h after ingestion of food containing the microorganisms and/or toxin. Abdominal pain, diarrhea, and possibly nausea and vomiting may ensue. Illness usually lasts for 12 - 14 h and complications are rare [33].

Clostridium botulinum (*C. botulinum*), a gram-positive, anaerobic, rod-shaped bacterium, consists of four physiological diverse groups (groups I - IV) that share the common feature of producing the extremely potent botulinum neurotoxins. Food-borne botulism is an intoxication involving the consumption of food containing botulinal toxin produced during the growth of these organisms in food. Groups responsible for food-borne botulism in humans include group I and group II whereas groups III and IV affect primarily non-human animal hosts. Botulinal intoxication can range from a mild illness, that may be disregarded or misdiagnosed, to a serious disease that can be fatal within 24 h. Rapidity of onset and severity of disease depend on the rate and amount of toxin absorbed with roughly half the annual cases of food-borne botulism being attributed to type [33].

Escherichia coli (*E. coli*) is a gram-negative, non-spore-forming short rod-shaped bacterium capable of growth and gas production at 45.5 °C in lactose-containing medium. *E. coli* produce a toxin(s) after it implants in the colon and colonizes it resulting in illness. Pre-formed toxins have not been shown to occur in foods or cause human disease. It is a difficult organism to manage from a public health standpoint, because of its low infectious dose which may be, in part, related to its substantial acid tolerance and ability to survive low pHs sometimes found in the stomach. [33]. Despite the relatively low number of illnesses compared to other food-borne microbes, there are an estimated 2,100 hospitalizations and 61 deaths, putting it fourth in the number of annual food-borne illness related deaths below non-typhoidal *Salmonella* (553 deaths), *L. monocytogenes* (499 deaths), and *Campylobacter* (99 deaths) [37].

Clostridium perfringens (*C. perfringens*) is a mesophilic bacterium. The lowest temperature for growth is around 20 °C and the highest is around 50 °C. The optimum growth temperatures are between 37 and 45 °C. The organism's generation time at 45 °C under optimal conditions can be as rapid as 7 min allowing *C. perfringens* to quickly multiply in foods where it may form discrete microscopic colonies of high population. The organism's ability to form heat-resistant spores also contributes to its ability to cause food poisoning. The illness occurs when people swallow these bacteria or their spores which then multiply and produce toxin in the small intestine. Symptoms of *C. perfringens* type A food poisoning appear between 6 and 24 h (usually 8 - 12 h) after eating contaminated food and then resolve spontaneously within the next 12 - 24 h. The symptoms consist of the sudden onset of acute abdominal pain followed by diarrhea. Nausea is common, but fever and vomiting are usually absent. Death rates from *C. perfringens* type A food poisoning are low, however, fatalities do occur in elderly or in debilitated persons [37].

Enterobacter sakazakii (*E. sakazakii*) is a gram-negative, non-sporulating, rod-shaped, opportunistic bacterium that has been historically distinguished from *E. cloacae* based on its ability to produce yellow pigment, and, as of 1980, comprised a distinct species within the genus Enterobacteriaceae family. Enterobacteriaceae based on DNA-DNA hybridization and phenotypic characteristics [38]. The pathogen has been reported as growing between 4 and 47 °C [38] and has been implicated in sporadic cases of neonatal sepsis and meningitis, associated with necrotizing enterocolitis in infants and, in rare instances, has been implicated in infections in immunocompromised adults [39].

2.3 Antimicrobial polymer-based food packaging material

Foods contamination leading to spoilage and growth of pathogenic microorganisms can happen when exposed to environment during slaughtering, processing, packaging and shipping. Although traditional food preservation methods such as drying, heating, freezing, fermentation and salting can extend food shelf life, it is not consummate especially to inhibit the growth of pathogenic microorganisms that may endanger consumers' health. Even fresh produce, which is displayed unpackaged at the store, must be transported out of the store in some type of container. Packaging provides protection of food from adulteration by water, gases, microorganisms, dust, and punctures, to name a few [40]. Most food packaging systems represent either a package/food system or a package/headspace/food system. A package/food system is a solid food product in contact with the packaging material, or a low-viscosity or liquid food without headspace. Diffusion between the packaging material and the food and partitioning at the interface are the main migration phenomena involved in this system. Package/headspace/food systems are represented by foods packed in flexible packages, cups, and cartons. Evaporation or equilibrated distribution of a substance among the headspace, packaging material and/or food has to be considered as a part of main migration mechanisms to estimate the interfacial distribution of the substance [41].

The active and intelligent food packaging category is a novel type of packaging compared with traditional methods. Active packaging systems are developed with the goal of extending shelf life for foods and increasing the period of time that the food is high quality. Active packaging technologies include some physical, chemical, or biological action which changes interactions between a package, product, and/or headspace of the package in order to get a desired outcome [42]. In general, the intelligent aspect of food packaging refers to the concept of monitoring information about the quality of the packed food. The purpose of the intelligent system could be to improve the quality or value of a product, to provide more convenience, or to provide tamper or theft resistance [43]. Antimicrobial packaging is a type of active packaging that goes beyond the traditional passive packaging role of protecting and marketing a food product. It interacts with the food in a desirable way to reduce or inhibit microorganism growth on food surfaces [44]. It can take different forms, including: the addition of sachets or pads containing volatile antimicrobials into packages, the incorporation of antimicrobial agents directly into polymers, antimicrobial coatings on polymer surfaces, the immobilization of antimicrobials to polymers by ion or covalent bonds and use of polymers that are inherently antimicrobial activity [45].

In order to absorb or emit gases to a package or headspace, sachets and pads are very commonly used. Sachets or pads within the container have been a successful application of passive technology. Oxygen absorbers, moisture absorbers and ethanol vapour generators are the main types of sachets [46]. Oxygen absorbers are usually made of powdered iron or ascorbic acid. Oxygen absorbers in sachets are commonly found in meat and poultry products, coffee, pizzas, baked goods and dried foods. Water absorbent pads may be used in packages containing meats that are likely to leak after temperature fluctuations. These pads prevent the growth of molds or bacteria by absorbing water into super absorbent polymer granules placed between two layers of micro-porous non-woven polymer [45]. Some sachets are capable of emitting ethanol as an antimicrobial agent to extend the shelf life of high moisture bakery products. However sachets cannot be used in liquid foods. They may not be used in a package made of flexible film, as the film will cling to the sachet and prevent it from performing its function.

The incorporation of antimicrobials direct into polymer is receiving considerable attention as a means of extending the bacterial lag phase, slowing the growth rate of microorganisms and maintaining food quality and safety. This is assumed to control growth of undesirable microorganisms. There are two ways of incorporation of antimicrobials into the packaging materials. One way is the addition of antimicrobial agents into the melt form of polymer and the other is the addition into the wet polymer solution. Many chemical antimicrobial agents can be employed in antimicrobial film systems including organic acids and their salts (sorbates, benzoates, and propionates), parabens, sulfites, nitrites, chlorides, phosphates, epoxides, alcohols, ozone, hydrogen peroxide, diethyl pyrocarbonate, antiobiotics, and bacteriocins [47].

Coating or adsorbing antimicrobials onto polymer surfaces technique is generally used for the antimicrobials which are sensitive to high temperature, such as enzymes, and cannot be used in polymer film processing. Enzymes with antimicrobial activity, such as lysozyme, have low heat tolerance which restricts the application of these compounds to their sorption into the polymer surface, or coating or casting from solutions [47]. Antimicrobial coatings may be developed by incorporating nisin, lactoferrin, sodium diacetate, sorbic acid, and potassium sorbate into a coating material. Films containing nisin, sorbic acid, and potassium sorbate have the ability to inhibit the food-borne pathogen *L. monocytogenes*. Nisin has also been shown to inhibit microorganisms, including *Listeria sp.*, when coated onto methyl cellulose or hydroxypropyl methyl cellulose on LDPE package film [48]. Nisin is a polypeptide produced by microbiological fermentation that remains a prohibitively expensive active ingredient [48].

A rapid release of the antimicrobial compound from the film to the food surface causes its fast consumption in a short period of time, after which the minimum concentration required for the inhibition of microbial growth is not maintained on the food surface. On the other hand, spoilage reactions on the food surface may start if the release rate of the antimicrobial agent from the film is slow. Thus, the controlled release of the active agent for a long period of time is necessary to maintain its minimum inhibitory concentration on the food surfaces. Lysozyme is a naturally occurring antimicrobial that has been incorporated into both monolayer cross-linked PVOH film and a multilayer structure of cross-linked PVOH [49]. The release rate of lysozyme can be controlled through the degree of cross-linking of the polymer matrix with no loss of antimicrobial effectiveness [50]. Antimycotics and antimicrobials have been added to food packaging films to delay outgrowth of mold. Potassium sorbate release from LDPE and HDPE films has been studied in food systems, including American processed and mozzarella cheeses [51]. Sorbate-release from HDPE packaging has enabled processed American cheese to be free of microbial contamination for 5 months at room temperature storage. In other system, known as BioSwitch [52], an antimicrobial is released on command when bacterial growth occurs. The basic concept is that a change in the environment such as pH, temperature, or UV light occurs and the antimicrobial responds accordingly. The external stimulus results in a release of the antimicrobial component of the package. In this system, the antimicrobial is released on command, and the system is active only at specific conditions. This system could potentially increase the stability and specificity of preservation and reduce the amount of chemicals needed in foods. A common example of release on command antimicrobials in food packaging is the inclusion of polysaccharide particles that encapsulate antimicrobial compounds. Many bacteria will digest polysaccharide when they grow, and so if a bacterial contamination occurs, the growth of bacteria will release the antimicrobial compounds and should inhibit subsequent microbial growth [40].

Currently, the majority of antimicrobial polymer materials are produced by either polymer compounding with inorganic or organic antimicrobial agents or by coating polymer surfaces with antimicrobials. However, the general problems with the additive approach are poor compatibility, decrease in mechanical and physical properties, loss of antimicrobial activity and health and environment risk [53]. In addition the use of conventional antimicrobials is associated with the problems of residual toxicity of these agents which can cause more serious problems to the environment. For example, in the case of using these antimicrobial agents in food packaging, there is a risk of diffusion of these agents into the food causing various problems [54, 55]. In water treatment, the most popular treatment method to disinfect and sterilize water is to use chlorine and other related chemicals. However, their residues can become concentrated in the food chain and in the environment as well as the possible formation of halomethane analogues that are suspected of being carcinogenic should lead to the avoidance of their use [54].

Due to the associated problems result from the use of conventional antimicrobial agents; the idea of polymeric antimicrobial agents appeared to be an attractive alternative. Nowadays, there is an increasing interest in selective antimicrobial polymers whose potency against bacteria and non-toxicity towards mammalian cells distinguishes them from most polymeric antimicrobials that are broadly poisonous [56-58]. This technology can be divided into two types: immobilization of antimicrobials to polymers by ion or covalent linkages or use of polymers that are inherently antimicrobial. Some polymers containing an antimicrobial pharmacophore can be prepared by the ionic or covalent bonding of the pharmacophore to polymers. This would require a molecular structure large enough to retain activity on the microbial cell wall even though bound to the polymer. Methyl 2-benzimidazolecarbamate is known to inhibit the growth of fungi very effectively. Park et al. [2] introduced a 2-benzimidazolecarbamoyl moiety to EVOH, imbuing the polymer with antifungal activity. Park et al. [6] also synthesized a polymeric antimicrobial agents by reacting three antimicrobial agents, 4-aminobenzoic acid (ABA), salicylic acid (SA), and 4-hydroxy benzoic acid (HBA) with EVOH. *S. aureus* was more susceptible to the synthesized polymeric antimicrobial agents than *P. aeruginesa*. The antimicrobial activity increased in the order of EVOH-HBA < EVOH-ABA < EVOH-SA. These synthesized antimicrobial polymers can be used to flexible packaging film.

Cationic polymers such as chitosan and poly-L-lysine are inherently antimicrobial and have been used in films and coatings. These polymers interact with negative charges on the cell membrane and cause the leakage of their intracellular components [44]. Synthetic antimicrobial macromolecules which include antimicrobial peptids, polymers and peptide polymer hybrids represent a huge class of molecules which can be used in effective antimicrobial polymer due to their unique biochemical properties. The use of these antimicrobial macromolecules which target the cytoplasmic membrane of microbes is a promising approach to lower the propensity of pathogen resistant development. Antimicrobial N-halamine polymers and coating have been studied extensively to their numerous qualities such as effectiveness toward a broad spectrum of microorganism, long-term stability, regenerability, safety to human and environment and low cost [53].

Nanotechnologies are expected to play a major role here, taking into account all additional safety considerations and filling the presently existing gap in knowledge. The potential of polymer nanocomposites as food packaging materials is largely due to the enhanced gas and moisture barrier properties, increased stiffness with lighter weight, strength and thermal stability [59]. The concept of polymer nanocomposites was developed in the late 1980s. Toyota was the first company to commercialise these nanocomposites and to use nanocomposite parts in one of its popular models for several years [60]. Polymer nanocomposites are a class of hybrid materials made from nanoscale particles such as metal oxides, semiconductors, clay minerals, and carbon materials. Several potential applications have been identified so far in various industrial sectors, for example automobiles, construction, aerospace, electronics and electrical, food packaging, and coatings and pigments [59]. Several of these studies are targeted specifically at food or food packaging applications, and a recent publication reviewed the numerous classes of nanomaterial antimicrobials targeted for use in drinking water sterilization [61]. Antimicrobial nanocomposite systems are particularly effective, because of the high surface-to-volume ratio and enhanced surface reactivity of the nanosized antimicrobial agents, making them able to inactivate microorganisms more effectively than their micro- or macro-scale counterparts. They too provide improved strength and barrier properties that are desirable for food packaging. One of the biggest advantages of inorganic nanoparticles (NPs) over molecular antimicrobials is the ease with which the former can be incorporated into polymers to form functional antimicrobial materials [62]. Commonly used or tested antimicrobial nano and nanocomposite materials include metal ions (silver, copper, gold, platinum), metal oxide [titanium dioxide (TiO_2), zinc oxide (ZnO), calcium oxide (CaO), magnesium oxide (MgO)], and modified nanoclays.

Silver has been long known to have microbial inhibition. It has been in use since time immemorial in the form of metallic silver, silver nitrate, silver sulfadiazine for the treatment of burns, wounds and several bacterial infections. But due to the emergence of several antibiotics the use of these silver compounds has been declined remarkably. Nanotechnology is gaining tremendous impetus in the present century due to its capability of modulating metals into their nanosize, which drastically changes the chemical, physical and optical properties of metals. Metallic silver in the form of silver NPs has made a remarkable comeback as a potential antimicrobial agent. The use of silver NPs is also important, as several pathogenic bacteria have developed resistance against various antibiotics. This is especially true due to the controlled release properties of silver NPs [63], which can be engineered to remain potent antimicrobial agents for long periods of time. Thus, silver NP/polymer nanocomposites are attractive materials for use in food packaging materials to preserve shelf life. The antimicrobial activity of these NPs may be related to several mechanisms including, induction of oxidative stress due to generation of reactive oxygen species (ROS) which may cause the degradation of the membrane structure of the cell, release of ions from the surface of NPs that has been reported to cause bacterial death due to binding to cell membrane. However, the mechanism of toxicity is still only partially understood [64]. Silver NPs can damage cell membranes of microorganisms by forming “pits” on their surfaces. Moreover, they may penetrate into the cells to cause DNA damage [65]. Silver ions released from the surface of these NPs can interact with thiol groups in protein to induce bacterial inactivation, condensation of DNA molecules, and loss of their replication ability [64]. Copper is of natural occurrence in plant and animal tissues where it participates in a number of important roles. To certain limits, the human body has mechanisms available for protection against copper toxicity at the cellular, tissue, and organ levels. Although only a few studies have reported the antibacterial properties of copper NPs, they show copper NPs have a significant promise as bactericidal agent [66]. In contrast other NPs, such as platinum, gold, iron oxide, silica and its oxides, and nickel have not shown bactericidal effects in studies with *E. coli* [67, 88]. Yoon et al. [69] reported the antibacterial effects of silver and copper NPs using single representative strains of *E. coli* and *B. subtilis*, where the copper NPs demonstrated superior antibacterial activity compared to the silver NPs.

However gold, silver and platinum are prohibitively expensive to be used on industrial scale. Therefore, current research work focuses metal oxides like titanium dioxide (TiO_2) as effective antibacterial agents for coating on the polymer films [70-72]. TiO_2 is non-toxic and has been approved by the FDA for use in human food, drugs, cosmetics and food contact materials. Unlike silver NPs, the antimicrobial activity of TiO_2 NPs is photocatalyzed and thus TiO_2-based antimicrobials are only active in the presence of UV light. The greater inhibition in the presence of light supports the notion that the antibacterial activity of TiO_2 was related to photocatalytic reactive oxygen species (ROS) production. While cell death with TiO_2 was less pronounced in the dark, it still occurred, indicating that an additional mechanism is involved. Similar results have been reported from mammalian cytotoxicity studies, where TiO_2 exerted oxidative stress in the dark under non-photocatalytic conditions [73]. Currently there is considerable interest in the self-disinfecting property of TiO_2 for meeting hygienic design requirements in food processing and packaging surfaces. For instance, TiO_2 NPs have been found to be effective against common food-borne pathogens including *Salmonella choleraesuis*, *Vibrio parahaemolyticus*, and *L. monocytogenes* under UV illumination but not in the dark [70]. Specifically targeting food-packaging materials, Cerrada et al. ultrasonically dispersed TiO_2 NPs throughout EVOH films and observed their effective photo-activated biocidal properties against nine microorganisms (bacteria and yeasts) cited to be involved in food poisoning and spoilage [74]. Another food packaging study showed that PP films coated with TiO_2 NPs inhibited *E. coli* growth on fresh cut lettuce [75]. In principle, food packaging films incorporating TiO_2 NPs may have the additional benefit of protecting food content from the oxidizing effects of UV irradiation while maintaining good optical clarity, as TiO_2 NPs are efficient short-wavelength light absorbers with high photostability.

Other metal oxide nanopowders of ZnO, CaO and MgO were found to show marked antibacterial activity [76]. The advantage of using these inorganic oxides as antimicrobial agents is that they contain mineral elements essential to humans and exhibit strong activity even when administered in small amounts [77]. Jin et al. [78] studied several approaches (powder, film, PVP capped and coating) for the application of nano-ZnO in food systems and concluded that nano-ZnO exhibits antimicrobial effects against *L.monocytogenes* and *S.enteritidis* in liquid egg white and in culture media. ZnO has found many applications in daily life such as in drug delivery, cosmetics, and medical devices due to its strong antimicrobial effect on a board spectrum of microorganisms. Moreover, it is currently listed by FDA as a generally recognized as safe material. However, the toxicity of ZnO NPs is not directly related to their entering into the cell, rather their intimate contact onto the cell causes changes in the microenvironment in the vicinity of the organism-particle contact area to either increase metal solubilization or to generate ROS that may ultimately damage cell membrane. Moreover, the toxicity of ZnO NPs is not only affected by the light via ROS production, but may also happen in the dark although its mechanism is not yet defined [79]. The antimicrobial properties of MgO NPs were studied and they were found to be highly effective against bacteria. The interaction of MgO NPs with bacteria, subsequently damaging the bacterial surface, has been proposed to explain the antibacterial activity of MgO NPs. Stoimenov et al. [80] suggested that the cell death was caused by the electrostatic interaction between the bacteria surface and MgO NPs. Makhluf et al. [81] demonstrated that nano-MgO exhibited high activity against bacteria due to the interaction of particles and bacteria. MgO NPs could take up halogen gases due to the defect nature of their surface and its positive charge, which resulted in a strong interaction with bacteria, which are negatively charged [80].

Nanoclays have been the most studied nanofillers, due to their high availability, low cost, good performance and good processability. The first publications about applications of polymer/nanoclays composites to food packaging date from the 1990's [59]. The clays for nanocomposites usually are bidimensional platelets with very tiny thicknesses (frequently around 1 nm) and several micrometers in length. Most of the research that has been published so far involved the use of montmorillonite (MMT) clay as the nanocomponent. A wide range of synthetic polymers such as PE, nylon and PVC, and biopolymers such as starch, have been investigated [82]. Barrier properties against oxygen, carbon dioxide, ultraviolet, moisture and volatiles are perhaps the most important properties that a nanocomposite food packaging can offer. Akkapeddi et al. [83] observed significant improvement in the gas barrier properties of nylon 6 in which ultra-thin, nanoscale silicate platelets of high aspect ratio were incorporated via an in-situ polymerisation process. The oxygen barrier properties of nylons were further enhanced by a novel active barrier approach where proprietary polymeric oxygen scavengers were melt blended into nanoscale dispersions of high oxygen scavenging efficiency. In another system, researchers replaced the sodium ions of MMT nanoclays with silver ions and showed antimicrobial activity of these silver nanoclays when dispersed in poly(ε-caprolactone) [84]; nanoclays modified with silver have also been dispersed in poly(lactic acid) to similar effect [85].

CNTs are some of the most attractive nanomaterials because of their unusual physicochemical, mechanical, and electrical properties as well as their broad range of potential applications [86]. Early studies indicated that the CNT size and surface area are important material characteristics from a toxicological perspective [88, 88]. As the size of CNTs decreases, the specific surface area increases, leading to increased opportunity for interaction and uptake by living cells.

This characteristic could result in adverse biological effects that otherwise would not be possible with the same material in a larger form [87, 88]. Kang et. al. [86] provide the evidence that the size (diameter) of CNTs is a key factor governing their antibacterial effects and that the likely main CNT-cytotoxicity mechanism is cell membrane damage by direct contact with CNTs. Experiments with well-characterized single-walled CNTs (SWNTs) and multi-walled CNTs (MWNTs) demonstrate that SWNTs are much more toxic to bacteria than MWNTs. Gene expression data show that in the presence of both MWNTs and SWNTs, *E. coli* expresses high levels of stress-related gene products, with the quantity and magnitude of expression being much higher in the presence of SWNTs.

Complex nanoscale architectures with antibacterial activity have also been developed; for example, Ho et al. covalently attached vancomycin molecules to the surface of gold NPs and showed that they have killing power more potent than vancomycin on its own, even against vancomycin-resistant bacterial strains [89], and Yang et al. [90] functionalized lysozyme-coated PS NPs with selective antibodies and demonstrated efficient bactericidicity against the common food pathogen *L. monocytogenes*. Bi et al. [91] loaded carbohydrate (phytoglycogen) NPs with nisin and showed that they exhibit sustained antimicrobial activity against plated *L. monocytogenes* with efficacy that lasts several times longer than free nisin.

3. Future prospects

Future trends and safety issues research and development in the field of polymeric packaging materials are very dynamic and develop in relation with the search for producing safer materials and environment friendly food packaging solutions. Looking to the future of flexible films, there are already foreseen consumer and development trends as well as continuing innovations in the field. The greater need for materials that fight infection will give incentive for discovery and use of antimicrobial polymer.

Nanotechnology has demonstrated a great potential to provide important changes in the food packaging sector. An on-going trend in the packaging market is the development of materials which possess high barrier properties. Due to the excellent barrier properties, polymer nanocomposite has major applications in food packaging industries for processed meats, cheese, confectionary and cereals as it enhances the shelf life of food materials. Consumer demands are also driving research and development for alternatives to petroleum-based packaging materials including those with recyclable or edible properties, as well as those materials made from renewable/sustainable agricultural products. Antimicrobial nanocomposites are promising to expand the use of biodegradable polymers, since the addition of antimicrobial nanoreinforcements has been related to improvements in overall performance of biopolymers, making them more competitive in a market dominated by non-biodegradable materials. Novel biodegradable biopolymer based nanocomposite films are also developed as environmentally friendly material to reduce polymer waste. The application of biopolymers, bio-based polymers, edible gels, films, or coatings incorporated with nanosized antimicrobials have the potential to find practical applications in the food industry. There is continuing research regarding biodegradable/ compostable films and the push to make them more widely available and utilized.

Furthermore several nanostructures can be useful to provide active and/or intelligent properties to food packaging systems, as exemplified by antimicrobial properties, oxygen scavenging ability, enzyme immobilization, or indication of the degree of exposure to some detrimental factor such as inadequate temperatures or oxygen levels. So, nanocomposites may not only be used to passively protect foods against environmental factors, but also to incorporate desirable properties to the packaging system so it may actually enhance stability of foods, or at least to indicate their eventual inadequation to be consumed. They can also be designed to incorporate and deliver active substances into biological systems, at low cost and with limited environmental impact. For example, create a bacteria-repellent surface in packaging film which changes colour in the presence of harmful microorganism or toxins [92]. These types of unique characteristics could be used for a wide range of minimally processed and processed food products. Moreover polymer nanotechnology is the future for the global packaging industry. Once production and material costs are reduced, companies will be using this technology to increase their product's stability and shelf life so that higher quality products can be delivered to their customers while saving money. Research continues into other types of antimicrobial nanofillers, allowing new nanocomposite structures with different improved properties that will further advance the use of them in many antimicrobial packaging applications.

4. Conclusions

Food quality and safety are major concerns in the food industry. In many food industrial processes, food is packaged prior to the application of the preservation technology in order to optimize preservation processes and minimize product manipulation. Therefore, the package is incorporated in the same production line and the preservation technologies are applied to the already packaged product. Antimicrobial packaging can be considered an emerging technology that could have a significant impact on shelf life extension and food safety. Use of antimicrobial agents in food packaging can control the microbial population and target specific microorganisms to provide higher safety and quality products. Many classes of antimicrobial compounds have been evaluated in film structures, synthetic polymers and edible films.

The characteristics of some antimicrobial polymeric packaging systems are reviewed in this chapter. The need to package foods in a versatile manner for transportation and storage, along with the increasing consumer demand for fresh, convenient, and safe food products presages a bright future for antimicrobial polymeric packaging.

References

[1] Park ES, Moon WS, Song MJ, Kim MN, Chung KH, Yoon JS. Antimicrobial activity of phenol and benzoic acid derivatives. International Biodeterioration & Biodegradation. 2001; 47:209-14.
[2] Park, ES, Lee HJ, Park HY, Kim MN, Chung KH, Yoon JS. Antifungal effect of carbendazim supported on poly(ethylene-*co*-vinyl alcohol) and epoxy resin. Journal of Applied Polymer Science. 2001; 80:728-36.
[3] Moon WS, Kim JC, Chung KH, Park ES, Kim, MN, Yoon, JS. Antimicrobial activity of a monomer and its polymer based on quinolone. Journal of Applied Polymer Science. 2003; 90:1797-801.
[4] Kim JH, Park ES, Shim JH, Kim MN, Moon WS, Chung KH, Yoon. JS. Antimicrobial activity of p-hydroxyphenyl acrylate derivatives. Journal of Agricultural and Food Chemistry. 2004; 52:7480-83.
[5] Yang HS, Park ES. Mechanical properties and antimicrobial activity of silicone rubber compounds containing acrylated norfloxacin and its polymer. Macromolecular Materials and Engineering. 2006; 291:621-28.
[6] Park ES, Kim HK, Shim JH, Kim MN, Yoon JS. Synthesis and properties of polymeric biocides based on poly ethylene-*co*-vinyl alcohol. Journal of Applied Polymer Science. 2004; 93:765-70.
[7] Park ES, Kim HS, Kim MN, Yoon JS. Antibacterial activities of polystyrene-*block*-poly(4-vinyl pyridine) and poly(styrene-*random*-4-vinyl pyridine). European Polymer Journal. 2004; 40:2819-822.
[8] Park ES. Mechanical properties and antibacterial activity of peroxide-cured silicone rubber foams. Journal of Applied Polymer Science. 2008; 110:1723-29.
[9] Maeda T, Manabe Y, Yamamoto M, Yoshida M, Ojazaki K, Nagamune H, Kourai H. Synthesis and antimicrobial characteristics of novel biocides, 4,4′-(1,6-Hexamethylene dioxydicarbonyl)bis(1-alkylpyridinium iodide)s. Chemical and Pharmaceutical Bulletin. 1999; 47:1020-23.
[10] Raaska L, Alakomi HL, Salonen MS, Sandholm TM. Antagonistic activity of *Staphylococcus siderophores* and chemical biocides against *Bacillus subtilis* in a paper-machine environment. Journal of Industrial Microbiology & Biotechnology. 1999; 22:27-32.
[11] Nakashima H, Miyano N, Takatuka T. Elution of metals with artificial sweat/saliva from inorganic antimicrobials/processed cloths and evaluation of antimicrobial activity of cloths. Journal of Health Science. 2008; 54:390-99.
[12] Cha DS, Chinnan MS. Biopolymer-Based Antimicrobial Packaging: A Review. Critical Reviews in Food Science and Nutrition. 2004; 44:223-37.
[13] Raheem D. Application of plastics and paper as food packaging materials - An overview. Emirates Journal of Food and Agriculture. 2012; 25:177-88.
[14] Marsh K, Bugusu B. Food packaging roles, materials and environmental issues. Journal of Food Science. 2007; 72:39-55.
[15] Sidwell JA. Food Contact Polymeric Materials. England: Rapra Technology; 1992; 6(1): Report 61.
[16] Hoppe E. Flexible Packaging: Innovations and Developments, University of Wisconsin‐Stout. 2009 Italian Packaging Technology Award. Available from: http://www.iopp.org/files/public/UWStoutErinHoppe.pdf.
[17] Allahvaisi S, Polypropylene in the Industry of Food Packaging. In: Dogan F, edtor. Polypropylene, Rijeka: InTech; 2012.
[18] Chiellini E. Environmentally-compatible Food Packaging. Cambridge: Woodhead Publishing; 2008.
[19] Allahvaisi S, Fellows PJ, Axtell BL. Appropriate Food Packaging: Materials and methods for small businesses. 2nd Ed. Bourton: Practical Action Publishing; 2003.
[20] Bowditch TG, Penetration of Polyvinyl Choloride and Polypropylene Packaging Films by Ephestia cautella (Lepidoptera: Pyralidae) and Plodia interpunctella (Lepidoptera: Pyralidae) Larvae, and Tribolium confusom (Coleoptera: Tenebrionidae). Journal of Economic Entomology. 1997; 90(4):1028-101.
[21] Hirsch A, Flexible Food Packaging. New York: Van Nostrand Reinhold; 1991.
[22] Holland BJ, Hay JN. The thermal degradation of poly(vinyl alcohol). Polymer. 2001; 42: 6775-83.
[23] Mokwena KK,Tang J, Ethylene Vinyl Alcohol: A Review of Barrier Properties for Packaging Shelf Stable Foods. Critical Reviews in Food Science and Nutrition, 2012; 52:640-50.
[24] Burke P. High barrier polymeric materials for increased shelf life. US Army Natick RD & E Center. Activities Report: Research and Development. 1990: 42:76-9.
[25] Pearson RB. PVC as a food packaging material. Food Chemistry. 1982; 8:85-96.
[26] Brown WE.Vinylidine chloride copolymers. In: The Wiley Encyclopedia of Packaging Technology, Baker M, Eckroth D (Eds.), Hobokken: John Wiley & Sons; 1986. p. 692-6.
[27] Valentas KJ, Rotstein E, Singh RP, Handbook of Food Engineering Practice. Boca Raton: CRC Press; 1997.
[28] Massey LL. Permeability Properties of Plastics and Elastomers: A Guide to Packaging and Barrier Materials. PDL Handbook Series. Plastic Design Library. New York: William Andrew Publishing; 2003.
[29] Packaging Materials: 1. Polyethylene Terephthalate (PET) for Food Packaging Applications. Washington, DC: International Life Sciences Institute, 2000; p. 11-12.
[30] DuPont Publications: Technical data sheets on PET Melinex films, 1997.
[31] Paine FA, Paine HY. A Handbook of Food Packaging, 2nd Edition, London: Blackie Academic and Professional; 1992.
[32] Lamberti M., Escher F. Aluminium foil as a food packaging material in comparison with other materials. Food Reviews International. 2007; 23:407-33.
[33] Behling RG, Eifert J, Erickson MC, Gurtler JB, Kornacki JL, Line E. Radcliff R, Ryser ET, Stawick B, Yan Z. Selected Pathogens of Concern to Industrial Food Processors: Infectious, Toxigenic, Toxico-Infectious, Selected Emerging Pathogenic

Bacteria In Kornacki JL, editors. Principle of Microbiological Troubleshooting in the industrial Food Processing Environment. New York: Springer; 2010.
[34] Hanes D. Nontyphoid Salmonella, Chapter 9. In: Miliotis MD, Bier JW (eds) International Handbook of Foodborne Pathogens. New York: Marcel Dekker; 2003, p.137-49.
[35] Tompkin RB, Scott VN, Bernard DT, Sveum WH, Gombas KS. Guidelines to prevent post-processing contamination from Listeria monocytogenes. Dairy, Food and Environmental Sanitation. 1999; 19:551-62.
[36] Altekruse SF, Stern NJ, Fields PI, Swerdlow DL. Campylobacter jejuni - An emerging foodborne pathogen. Emerging Infectious Diseases. 1999; 5:28-35.
[37] Mead PS, Slutsker L, Dietz V, McCraig LF, Bresse JS, Shapiro C, Griffin PM, Tauxe RV. Food-related illness and death in the United States. Emerging Infectious Diseases. 1999; 5:607-25.
[38] Farmer JJ, Asbury MA, Hickman FW, Brenner DJ, and the Enterobacteriaceae Study Group Enterobacter sakazakii, new species of Enterobacteriaceae isolated from clinical specimens. International Journal of Systematic Bacteriology. 1980; 30:569-84.
[39] Gurtler JB, Kornacki JL, Beuchat LR, Enterobacter sakazakii: A coliform of increased concern to infant health. International Journal of Food Microbiology. 2005; 104:1-34.
[40] Huff K. Active and Intelligent Packaging: Innovations for the Future. Department of Food Science & Technology. Virginia Polytechnic Institute and State University, Blacksburg, Va, 2008; p. 1-13.
[41] Quintavalla S, Vicini L. Antimicrobial food packaging in meat industry. Meat Science. 2002; 62:373-80.
[42] Yam KL, Takhistov PT, Miltz J. Intelligent packaging: concepts and applications. Journal of Food Science. 2005; 70: R1-R10
[43] Robertson GL. Active and intelligent packaging. In Food packaging: principles and practice-2nd ed. Boca Raton: CRC Press; 2006, Chap. 14.
[44] Soares NFF, Pires ACS, Camilloto GP, Santiagosilva P, Espitia PJP, Silva WA. Recent patents on active packaging for food application. Recent Patents on Food, Nutrition & Agriculture. 2009; 1:171-8.
[45] Appendini P, Hotchkiss JH. Review of antimicrobial food packaging. Innovative Food Science and Emerging Technologies. 2002; 3(2):113-26.
[46] Edelstein S, Gerals B, Crutchley Bushell T, Gundersen G. Food and Nutrition at Risk in America: Food Insecurity, Biotechnology, Food Safety, and Bioterrorism. Burlington: Jones & Bartlett Publishers, 2009.
[47] Ozdemir M, Floros JD. Active food packaging technologies. Critical Reviews in Food Science and Nutrition. 2004: 44:185-93.
[48] Brody AL. Active packaging becomes more active. Food Technology. 2005; 59:82-4.
[49] Buonocore GG, Conte A, Corbo MR, Sinigaglia M, Del Nobile MA, Mono- and multilayer active films containing lysozyme as antimicrobial agent. Innovative Food Science and Emerging Technologies. 2005; 6:459-64.
[50] Buonocore GG, Sinigaglia M, Corbo MR, Bevilacqua A, Notte EL, Nobile MAD. Controlled release of antimicrobial compounds from highly swellable polymers. Journal of Food Protection. 2004; 67:1190-94.
[51] Han JH. Antimicrobial food packaging. Food Technology 2000; 54:56-65.
[52] De Jong AR, Boumans H, Slaghek T. Van Veen J, Rijk R, Van Zandvoort M. Active and intelligent packaging for food: is it the future?. Food Additives & Contaminants: Part A. 2005; 22:975-9
[53] Arora S, Yadav V, Kumar P, Gupta R, Deepak Kumar D. Polymer Based Antimicrobial Coatings as Potential Biomaterial: A Review. International Journal of Pharmaceutical Sciences Review and Research . 2013; 23:279-90.
[54] Li G, Shen J. A study of pyridinium-type functional polymers. IV. Behavioral features of the antibacterial activity of insoluble pyridinium type polymers. Journal of Applied Polymer Science. 2000; 78:676-84.
[55] Kenawy ER, Mahmoud YAG, Biologically active polymers, 6 synthesis and antimicrobial activity of some linear copolymers with quaternary ammonium and phosphonium groups. Macromolecular Bioscience. 2003; 3:107-16.
[56] Gabriel GJ, Maegerlein JA, Nelson CF, Dabkowski JM, Eren T, Nsslein K, Tew GN. Comparison of facially amphiphilic versus segregated monomers in the design of antibacterial copolymers. Chemistry - A European Journal. 2009; 15:433-9.
[57] Kenawy ER, Worley SD, Broughton R. The chemistry and applications of antimicrobial polymers: A state-of-the-art review. Biomacromolecules. 2007; 8:1359-84.
[58] Subramanyam E, Mohandoss S, Shin HW: Synthesis, characterization, and evaluation of antifouling polymers of 4-acryloyloxybenzaldehyde with methyl methacrylate. Journal of Applied Polymer Science. 2009; 112:2741-9.
[59] Ray S, Quek SY, Easteal A, Chen XD.The Potential Use of Polymer-Clay Nanocomposites in Food Packaging. International Journal of Food Engineering. 2006; 2:1-11.
[60] Collister J. Commercialisation of polymer nanocomposites. In Krishnamoorti R, Vaia RA, editors. Polymer nanocomposites synthesis, charcterisation and modelling. American Chemical Society, Washington, USA, 2002.
[61] Li Q, Mahendra S, Lyon DY, Brunet L, Liga MV, Li D, Alvarez PJ. Antimicrobial nanomaterials for water disinfection and microbial control: potential applications and implications. Water Research. 2008; 42:4591-602.
[62] Althues H, Henle J, Kaskel S. Functional inorganic nanofillers for transparent polymers. Chemical Society Reviews. 2007; 36:1454-65.
[63] Roe D, Karandikar B, Bonn-Savage N, Gibbins B, Roullet JB. Antimicrobial surface functionalization of plastic catheters by silver nanoparticles. Journal of Antimicrobial Chemotherapy. 2008; 61:869-76.
[64] Emamifar A, Kadivar M, Shahedi M, Solaimanianzad S. Effect of nanocomposite packaging containing Ag and ZnO on inactivation of Lactobacillus plantarum in orange juice. Food Control. 2011; 22:408-13.
[65] Morones JR, Elechiguerra JL, Camacho A, Holt K, Kouri JB, Ramírez JT, Yacaman MJ. The bactericidal effect of silver nanoparticles. Nanotechnology. 2005; 16:2046-52.
[66] Cioffi N, Torsi L, Ditaranto N, Tantillo G, Ghibelli L, Sabbatini L. Copper nanoparticle/polymer composites with antifungal and bacteriostatic properties. Chemistry of Materials. 2005; 17:5255-62.
[67] Williams DN, Ehrman SH, Holoman TRP. Evaluation of the microbial growth response to inorganic nanoparticles. Journal of Nanobiotechnology. 2006; 4:3.

[68] Ruparelia JP, Duttagupta SP, Chatterjee AK, Mukherji SM. A comparative study on disinfection potential of nanosilver and nanonickel. Technical poster, Proceedings of the 9th Annual Conference of the Indian Environmental Association (Envirovision-2006), entitled Advances in Environmental Management and Technology, Goa, India, 2006 Sep 21-23.
[69] Yoon K, Byeon JH, Park J, Hwang J. Susceptibility constants of Escherichia coli and Bacillus subtilis to silver and copper nanoparticles. Science of the Total Environment. 2007; 373:572-5.
[70] Kim B, Kim D, Cho D, Cho S. Bactericidal effect of TiO2 photocatalyst on selected food-borne pathogenic bacteria. Chemosphere. 2003; 52:277-81.
[71] Robertson JMC, Robertson PKJ, Lawton LA. A comparison of the effectiveness of TiO2 Journal of Photochemistry and Photobiology A: Chemistry. 2005; 175:51-6.
[72] Fu G, Vary PS, Lin CT. Anatase TiO2 nanocomposites for antimicrobial coatings. The Journal of Physical Chemistry B. 2005; 109:8889-98.
[73] Adams LK, Lyon DY, Alvarez PJJ. Comparative eco-toxicity of nanoscale TiO2, SiO2, and ZnO water suspensions. Watter Research, 2006; 40:3527-32.
[74] M. L. Cerrada, C. Serrano, M. Sánchez-Chaves, M. Fernández-García, F. Fernández-Martín, A. de Andrés, R.J.J. Riobóo, A. Kubacka, M. Ferrer, M. Fernández-García. Biodegradable Polycaprolactone-Titania Nanocomposites: Preparation, Characterization and Antimicribial properties. Advanced Functional Materials. 2008; 18:9249-66
[75] Chawengkijwanich C, Hayata Y. Development of TiO2 powder-coated food packaging film and its ability to inactivate Escherichia coli in vitro and in actual tests. International Journal of Food Microbiology. 2008; 123:288-92.
[76] Yamamoto O. Influence of particle size on the antibacterial activity of zinc oxide. International Journal of Inorganic Materials. 2001; 3:643-46.
[77] Sawai J, Yoshikawa T. Quantitative evaluation of antifungal activity of metallic oxide powders (MgO, CaO and ZnO) by an indirect conductimetric assay. Journal of Applied Microbiology, 2004; 96:803-9.
[78] Jin T, Sun D, Su JY, Zhang H, Sue HJ. Antimicrobial efficacy of zinc oxide quantum dots against Listeria monocytogenes, Salmonella enteritidis, and Escherichia coli O157:H7. Journal of Food Science. 2009: 74:46-52.
[79] Emamifar A, Kadivar M, Shahedi M, Solaimanianzad S. Evaluation of nanocomposite packaging containing Ag and ZnO on the shelf life of fresh orange juice. Innovative Food Science & Emerging Technologies. 2010; 11:742-48.
[80] Stoimenov PK, Klinger RL, Marchin GL, Klabunde KJ, Metal oxide nanoparticles as bactericidal agents. Langmuir 2002; 18:6679-86.
[81] Makhluf S, Dror R, Nitzan Y, Abramovich Y, Jelinek R, Gedanken A. Microwave-assisted synthesis of nanocrystalline MgO and its use as a bacteriocide. Advanced Functional Materials, 2005; 15: 1708-15.
[82] Lange J, Wyser Y. Recent innovations in barrier technologies for plastic packaging-a review. Packaging Technology and Science. 2003; 16:149-58.
[83] Akkapeddi K, Socci E, Kraft T, Facinelli J, Worley D. A new family of barrier nylons based on nanocomposites and oxygen scavengers. 61st Annual Technical Conference - Society of Plastics Engineers. 2003; 3: 3845-8.
[84] Incoronato AL, Buonocore GG, Conte A, Lavorgna M, Del Nobile MA. Active systems based on silver-montmorillonite nanoparticles embedded into bio-based polymer matrices for packaging applications. Journal of Food Protection. 2010; 73:2256-62.
[85] Busolo MA, Fernandez P, Ocio MJ, Lagaron JM. Novel silver-based nanoclay as an antimicrobial in polylactic acid food packaging coatings. Food additives & contaminants. Part A, Chemistry, analysis, control, exposure & risk assessment. 2010; 27:1617-26.
[86] Kang S, Herzberg M, Rodrigues DF, Elimelech M. Antibacterial Effects of Carbon Nanotubes: Size Does Matter! Langmuir 2008; 24:6409-13.
[87] Nel A, Xia T, Madler L, Li N. Toxic potential of materials at the nanolevel. Science. 2006; 311(5761):622-7.
[88] Jia G, Wang HF, Yan L, Wang X, Pei RJ, Yan T, Zhao YL, Guo XB (2005) Cytotoxicity of carbon nanomaterials: single-wall nanotube, multi-wall nanotube, and fullerene. Environmental Science & Technology. 2005; 39:1378-83.
[89] Gu H, Ho PL, Tong E, Wang L, Xu B: Presenting vancomycin on nanoparticles to enhance antimicrobial activities. Nano Letters. 2003; 3:1261-63.
[90] Yang H, Qu L, Wimbrow A, Jiang X, Sun YP. Enhancing antimicrobial activity of lysozyme against Listeria monocytogenes using immunonanoparticles. Journal of Food Protection. 2007; 70(8):1844-9.
[91] Bi L, Yang L, Narsimhan G, Bhunia AK, Yao Y. Designing carbohydrate nanoparticles for prolonged efficacy of antimicrobial peptide. Journal of Controlled Release. 2011; 150(2):150-6.
[92] Moraru CI, Panchapakesan CP, Huang QR, Takhistov P, Liu S, Kokini JL. Nanotechnology: A new frontier in food science. Journal of Food Technology. 2003; 57:24-9.