

Potential Formulation of Cinnamic acid Nanoemulsion for Application in Fruits and Vegetables Preservation

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Abstract

Cinnamic acid (CA) is a naturally occurring phenolic compound found in various plant sources and has attracted a great deal of interest over the years due to its diverse antimicrobial, antioxidant, antifungal, and anti-inflammation properties. With this advantages, trans-cinnamic acid (trans-CA) could become a potential natural antimicrobial compound. However, CA is exceedingly hydrophobic with a very poor water solubility of 0.29 g/L and a partition coefficient ($P_{\text{octane/water}}$) of 2.41. As such this poor solubility which contributes to its low bioavailability needs to be addressed so that its full potential can be exploited. To address this problem, one effective strategy is to incorporate it into a carrier nanoemulsion delivery system. To the best of our knowledge, the formulation of CA nanoemulsion has not been explored before. Therefore, the objective of the current review article is to report on the existing potential to formulate an oil-in-water (o/w) nanoemulsion of CA that can be applied in the fruits and vegetables industry to control and maintain their freshness that normally deteriorates due to damages caused by minimal processing methods such as peeling, slicing, dicing and shredding and so forth. It has already been demonstrated that nanotechnology can be used as a hurdle technology to control the growth of foodborne pathogens but its combination with other preservation and intelligent packaging technologies may be the most effective approach to guarantee food safety and extension of shelf life as well as maintaining the sensory attributes of fruits and vegetables.

Keywords: Cinnamic acid, antimicrobial compound, nanoemulsion, preservation, shelf life.

Introduction

There has been an increased demand for naturally occurring antimicrobials from plants that can serve as alternatives in controlling pathogenic and spoilage microorganisms and enhance the shelf-life of foods. In recent years the use of naturally occurring antimicrobial compounds has gained considerable attention from both consumers and the food industry because of the concerns associated with the potential side effects caused by synthetic antimicrobials on health and the emergence of antibiotic-resistant bacteria (Tajkarimi *et al.*, 2010; Bajpai *et al.*, 2012; Rebolleda *et al.*, 2015; Almadiy *et al.*, 2016; Jafari and McClements, 2017; Zahi *et al.*, 2017). The development of this consumption trend has prompted researchers to search for new alternative sources for natural compounds that can be applied in food preservation due to their perceived “green nature” as well as potential antimicrobial properties against a varied range of foodborne pathogens thereby enhancing the shelf-life of foods (Gyawali and Ibrahim, 2014; Fu *et al.*, 2016). Food antimicrobial compounds can be naturally present or purposefully added to foods, food packaging, food contact

surfaces and processing environments to inhibit the growth or inactive spoilage and pathogenic microorganisms whose metabolic products can cause food poisoning or impart adverse off-flavors and texture changes (Davidson, 2001; Davidson *et al.*, 2013). Plants have been reported to be rich sources of antimicrobials, many of which are phenolic compounds found in the essential oils of flowers, leaves, seeds and bulbs. Some studies have reported that plant essential oils from some phenol-rich compounds like carvacrol, eugenol and thymol generally exhibit enhanced antibacterial and antibiofilm effects against *Escherichia coli* O157:H7, *Salmonella typhimurium*, *Listeria monocytogenes* and *Pseudomonas fluorescens* (Lambert *et al.*, 2001; Devi *et al.*, 2010; Hamed *et al.*, 2012; Wu *et al.*, 2014; Hu *et al.*, 2016; Moon and Rhee, 2016; Myszka *et al.*, 2016; Miladi *et al.*, 2017). Nanoemulsions are conventional emulsions that contain very small particles (1-100 nm) formed by dispersing one liquid into another immiscible liquid using suitable emulsifiers (Rao and McClements, 2011). They are kinetically stable to particle aggregation and gravitational separation and are also transparent colloidal dispersions, which makes

them suitable for a wide range of practical applications (Solans *et al.*, 2005; Guerra-Rosas *et al.*, 2017). Their small particle size also offers them long-term stability and high optical clarity that enables their incorporation into food products without altering the products optical properties (Qian and McClements, 2011; McClements, 2012). Nanoemulsions can be formulated using high-energy methods such as high-pressure valve homogenization, microfluidization or sonication and low-energy methods such as phase inversion temperature or spontaneous emulsification. The use of the inexpensive low-energy methods to produce nanoemulsion has currently gained popularity because usage of costly specialized equipment such as the homogenizer is not mandatory.

Recent studies have shown that converting antimicrobial compounds as well as essential oils into nanoemulsions significantly improved their antibacterial activities (Ghosh *et al.*, 2013; Sugumar *et al.*, 2013; Moghimi *et al.*, 2016; Zhang *et al.*, 2017). Moreover, encapsulation of functional molecules within nanoparticles as a delivery system of antimicrobials in food has already been investigated (McClements *et al.*, 2009; Fu *et al.*, 2016). However, the integration of antimicrobial compounds in food systems still presents a considerable drawback due to their poor water solubility which affects their antimicrobial properties since sufficient concentrations cannot be achieved in aqueous phase (Gaysinsky *et al.*, 2007; Salvia-Trujillo *et al.*, 2015). As such, several food phenol-rich antimicrobial agents, mostly essential oils such as basil oil, carvacrol, eugenol, and thymol have been encapsulated in nanoemulsions to retard spoilage and pathogenic microorganisms in food systems such as fresh lettuce, cooked meat sausages, zucchini, milk and fruit juices (Ghosh *et al.*, 2013; Shah *et al.*, 2013; Ghosh *et al.*, 2014; Donsì *et al.*, 2014; Bhargava *et al.*, 2015; Fu *et al.*, 2016; Chen *et al.*, 2017).

Cinnamic acid (CA), 3-Phenyl-2-propenoic acid, is a naturally occurring phenolic compound found in various plants, fruits and vegetable sources such as cinnamon, cloves, black pepper, coriander, turmeric and so forth, and has a generally recognized as safe status (FDA, 2013) (Shi, 2017). Therefore CA has a long history of human exposure and uses. Previous studies have shown that CA can exist as both *cis*- and *trans*-forms in nature. The *trans*-CA is usually the predominant form in nature (>99%) because it is much more stable than the *cis*-isomer (Liu and Feng, 2015; Turner *et al.*, 1993). However, CA is exceedingly hydrophobic with a very poor water solubility of 0.29 g/L and a partition coefficient ($P_{\text{octane/water}}$) of 2.41 (Patel *et al.*, 2014). As such this poor solubility which contributes to its low bioavailability needs to be addressed so that its full potential can be exploited. To address this problem, one effective strategy is to incorporate it into a carrier nanoemulsion delivery system.

To the best of our knowledge, the formulation of CA nanoemulsion has not been explored before. Therefore, the objective of the current review article is to report on the existing potential to formulate an oil-in-water (o/w) nanoemulsion of CA that can be applied in the fruits and vegetables industry to control and maintain their freshness that normally deteriorates due to damages caused by minimal processing methods such as peeling, slicing, dicing and shredding and so forth. These processing operations usually shorten the shelf life of fresh-cut fruits and vegetables by a series of typical symptoms, such as tissue softening, cut surface browning, decreased nutritional value, presence of off-flavor and microbiological spoilage during storage. Moreover, the increased cases in recently reported foodborne disease outbreaks associated with fresh-cut produce are a serious concern towards public health.

Nanotechnology as Applied in Fruits and Vegetables Preservation

Nanotechnology is an emerging field of study that offers use of new techniques and materials with one or more dimensions that are in the range of 1-100 nm in length capable of prolonging food shelf life (Mihindukulasuriya and Lim, 2014). Encapsulation of bioactive compounds within nanoparticles may lead to improved protection against chemical or biochemical degradation as well as preventing their adverse interactions with other food ingredients. The encapsulation can also mask undesirable flavor profiles (Jafari and McClements, 2017). The use of silver nanoparticles in fruits and vegetables preservation as a promising antimicrobial material against a large number of microorganisms has been reported (Duan *et al.*, 2008; Kuorwel *et al.*, 2015). The silver ions inside the cell can disrupt or kill the microorganisms by a series of damages, including DNA damage, activation of antioxidant enzymes, depletion of antioxidant molecules (e.g., glutathione), binding of proteins and structural changes in the cell wall and nuclear membrane (McShan *et al.*, 2014; Mastromatteo *et al.*, 2015). Silver-PVP nanoparticles coating have been reported to maintain the quality of green asparagus, leading to an extended shelf life of 25 d at 2°C and 20 d at 10°C, respectively, whereas those of the controls were 15 days at 2°C and 10 d at 10°C, respectively (An *et al.*, 2008). A cellulose silver nanoparticle hybrid material combined with modified atmospheric packaging was also used for the preservation of fresh-cut melon stored at 4°C for 10 d (Fernandez *et al.*, 2010). This hybrid material also retarded the senescence of the fresh-cut melon, presented a remarkably lower yeast counts and maintained a juicier melon appearance after 10 days of storage thereby prolonging the shelf life of fresh-cut melon by 5 d compared to the controls.

Combination of nanoparticles with intelligent packaging technologies has also been conducted to preserve fruits and vegetables. Another multifunctional inorganic nanoparticle with potential to inhibit microbial growth is ZnO nanoparticles. A novel polyvinyl chloride film mixed with ZnO nanoparticle powder was developed for preservation of fresh-cut apples and the results showed that the ZnO nanopackaging significantly reduced the decay rate of the fresh-cut apples by 21.9% and improved their shelf-life by 6 days compared to the control sample with PVC film packaging without ZnO (Li *et al.*, 2011). In another study using fresh cut kiwi fruit, it was reported that ZnO nanoparticles coating combined with ultrasound significantly delayed the ripening process by slowing down the mass loss and the softening of the kiwi fruit texture. The combined application of ultrasound and ZnO nanoparticles coating was capable of effectively delaying the senescence and significantly extended the storage shelf-life by 4 d (Meng, 2014). Chawengkijwanich and Hayata (2008) developed a TiO₂ nanoparticle-coated polypropylene packaging film. After one day of storage, a decrease of *E. coli* from 6.4 to 4.9 log CFU g⁻¹ in fresh-cut lettuce packaged in this bag irradiated with UVA light was observed, while that of samples stored in an uncoated polypropylene film bag irradiated with UVA light decreased from 6.4 to 6.1 log CFU g⁻¹.

Recently, due to the formation of a protective atmosphere around fresh fruits and vegetables, there has been increasing interest in the utilization of nanoemulsions and nanoemulsion-based coatings to preserve fresh produce. This novel application is particularly suitable for encapsulation of functional compounds as it prevents their degradation and improves their bioavailability (Silva *et al.*, 2012). These may be oil-in-water (O/W) or water-in-oil (W/O), and either liquid in liquid, or liquid in solid. Their interface may be stabilized by various types of emulsifiers, whose structure and amphiphilicity determine droplet curvature and size. Also the oil type and composition, the surfactant-to-oil ratio, and the presence of cosolvents and cosolutes may affect droplet size and emulsion stability. Nanoemulsions usually result in higher stability in terms of gravitational separation, flocculation, and coalescence of oil droplets and enhanced bioactivity of emulsified oils due to the smaller droplet size and a higher surface area to droplet volume ratio (Kim *et al.*, 2014). Recently, Kim *et al.* (2014) inoculated grape berry with *Salmonella* and *Escherichia coli* and then subjected it to lemongrass oil nanoemulsion. This treatment reduced *Salmonella* and *Escherichia coli* by more than 3.2 and 2.6 log CFU g⁻¹, respectively, without significant changes in its flavor and glossiness. Moreover, this treatment maintained the firmness, phenolic compound concentration and antioxidant activity of grape berry.

Bhargava *et al.* (2015) achieved an up to 3.4, 2.3, and 3.1 log CFU g⁻¹ reductions in *Listeria monocytogenes*, *Salmonella typhimurium* and *Escherichia coli* of fresh-cut lettuce by 0.05% oregano oil nanoemulsions, respectively. Likewise, nanoemulsion-based edible coatings with lemongrass essential oil contributed to a faster and greater inactivation of *Escherichia coli* of fresh-cut apple during storage time compared with conventional emulsions (Salvia-Trujillo *et al.*, 2015). Unfortunately, although firmness was maintained, significant browning was observed during storage on fresh-cut apples coated with high concentration lemongrass essential oil nanoemulsions. Ghosh *et al.* (2014) formulated eugenol-loaded antimicrobial nanoemulsion using sesame oil, and the nanoemulsion exhibited antibacterial effect on the native cultivable bacteria populations in orange juice. It also showed an enhanced in situ antibacterial activity over the same concentration of sodium benzoate, and better results were obtained at storage temperature of 4°C. Donsì *et al.* (2014) designed carvacrol nanoemulsion and determined the infusion and antimicrobial activity of the emulsions in zucchini samples. When the droplet size of emulsion was below the characteristic size of inter and intracellular interstices, the emulsion exhibited a significantly enhanced effective diffusivity that promoted the antimicrobial action of carvacrol. Recently nanoemulsions from carvacrol and medium chain triglyceride were also shown to be effective at controlling the growth of *Salmonella enterica* and *Escherichia coli* on mung beans and alfalfa seeds (Komaiko and McClements, 2015). Conceivably, nanoemulsion-based delivery systems for essential oils not only enabled a slow and sustained release of the antimicrobial compounds, but also contributed to their incorporation in complex food systems. Essential oil components have the ability to penetrate the cell wall, cytoplasmic membrane, and the mitochondrial membrane structures resulting in the leakage of the cell contents and disruption of proton motive force and ultimately leading to the excessive loss of critical ions and molecules before cell death. Reductions in foodborne bacteria achieved by different nanoemulsions on the different food systems serves as an indication of great potential of plant antimicrobials in enhancing food safety.

Applications of Pure Cinnamic Acid on fruits and Vegetables Preservation

Cinnamic acid (CA) has for a long time been extensively applied in the cosmetics and pharmaceutical industries due to its anticancer, anti-tumor, anti-malaria, antidiabetic, anti-inflammatory properties and as a light penetration inhibitor in sunscreen formulations (Adisakwattana *et al.*, 2004; Chen *et al.*, 2011; Gravina *et al.*, 2011; Patel *et al.*, 2014; Liu and Feng, 2015; Zhu *et al.*, 2016; Oishi *et al.*, 2017).

An extensive variety of food products, together with fragrances, pharmaceuticals, flavors, and polymers, have also been developed with cinnamic acid as either a synthetic intermediate or ingredient. However, recently CA has also attracted some interest in the field of food and nutrition because of its antioxidant and anti-microbial properties (Shi *et al.*, 2005; Sharma and Rao, 2015). CA has also been used as a food additive and condiment in cooking (Wang *et al.*, 2014). Even with its extensive application in the pharmaceutical industry, very few studies have reported the use of pure CA in preservation of fruits and vegetables. However, it has been reported that dipping whole and sliced fruits in cinnamic acid solutions at concentrations of 3–5 mg mL⁻¹ delayed the onset of visible spoilage at both ambient and chill temperatures (Roller *et al.*, 1998). Roller and Seedhar (2002) have also reported that treatment of the kiwi fruits with low concentrations of cinnamic acid at 1 mM prevented the appearance of visible spoilage and inhibited growth of the microbial flora for 5 d at both 4 and 8°C. The aroma of cinnamic acid was detectable in the treated fruit after storage but was not considered unpleasant. No visible colour change was detected on the treated kiwi fruits for the duration of the trial. In the same study, it was also reported that treatment of fresh-cut honeydew melon with 1 mM of cinnamic acid extended the lag phase of the microbial flora from less than 1 day in the untreated controls to 3 d at 8°C and 5 d at 4°C. The viable counts on the treated melon were 6 log cfu g⁻¹ lower on day 3 at 8°C and 4 log cfu g⁻¹ lower on d 5 at 4°C compared with the untreated controls. However, by day 10, all counts were very similar at approximately 8.5 log cfu g⁻¹ irrespective of the treatment received or the storage temperature. These results showed that treatment of honeydew melon with cinnamic acid extended the lag phase, but once initiated growth proceeded at a similar rate in both the treated and the untreated fruits. The characteristic 'spicy' odour of cinnamic acid was less readily detected on the melon than on the kiwi fruit after treatment.

The antimicrobial and antioxidant property of cinnamic acid, was also illustrated for its inhibitory effects on the diphenolase activity of mushroom tyrosinase (Shi *et al.*, 2005). Aromatic carboxylic acids, including benzoic acid, cinnamic acid, p-coumaric acid, ferulic acid and sinapic acid, were reported as effective polyphenol oxidase inhibitors (Raju and Bawa, 2006). In a recent study by (Sharma and Rao, 2015), the effects of incorporating cinnamic acid as an antioxidant agent into xanthan gum based edible coating on the quality attributes of fresh-cut Asian pear (*Pyrus pyrifolia* L. cv. 'Nashpati') and European pear (*Pyrus communis* L. cv. 'Babughosha') stored at 4°C was investigated. The results showed that application of xanthan coating enriched with cinnamic acid on both fresh-cut pear varieties inhibited the activity of browning

related enzymes, polyphenol oxidase and peroxidase, thereby preventing total phenolics oxidation into melanin compounds and delayed browning incidence and extended their shelf-life up to 4 d and 8 d of storage period, respectively. Changes regarding the sensory attributes of coated and uncoated fresh-cut pear cultivars, indicated that application with xanthan gum either alone or supplemented with cinnamic acid had no negative impact on their taste and odor. The addition of cinnamic acid into xanthan gum coating formulation also slightly reduced the growth of total mesophilic bacteria by 0.25 log cfu g⁻¹ during the 8 d of storage time.

All these studies demonstrated that cinnamic acid could be used as a preservative to delay spoilage and maintain the quality attributes of fresh-cut fruits and vegetables at refrigeration and chill temperatures without adverse sensory consequences. Cinnamic acid as a phenolic compound is well known for its role in defense mechanism of plants against pathogenic microbes. Therefore, like other phenolics, cinnamic acid has a lipophilic property that plays a crucial role in its antimicrobial effect. Lipophilic compounds have been reported to cause structural and functional damage of microbial cells by disrupting membrane permeability and osmotic balance of the cell, eventually causing leakage of various substances such as ions, ATP, nucleic acids and amino acids leading to cell death, indicating an irreversible damage to the cytoplasmic membranes of bacteria (Moghimi *et al.*, 2016; Zahi *et al.*, 2017). The importance of the hydroxyl groups in phenolic compounds are also important in the inhibitory action over microorganism as they promote the delocalization of electrons, which then act as proton exchangers and reduce the gradient across the cytoplasmic membrane of bacterial cells (Martínez-Graciá *et al.*, 2015).

Future prospects of Cinnamic Acid Nanoemulsion Formulation for Application in Fruits and Vegetables

Cinnamic acid as a naturally occurring phenolic compound has a generally recognized as safe status. As already reported, pure CA application in food has only been limited to application in some fruits and vegetables preservation by either coating or dipping them without any effect on their sensorial properties. As such, CA nanoemulsion formulation has not been reported before. However, CA is exceedingly hydrophobic and has a very poor water solubility which makes it difficult to use in preparation of an oil-in-water nanoemulsion. This draw back affects its antimicrobial efficacy since sufficient concentrations cannot be achieved in aqueous phase. Therefore it will be necessary to first dissolve it in an organic solvent so as to address its solubility problem. It is expected that CA nanoemulsion would exhibit a higher antimicrobial activity than that of the pure compound due to the subcellular size of nanoemulsions

effectively crossing the bacterial cell walls and destabilizing the lipid envelope of the treated microorganisms on the fruits and vegetables' surfaces. The much larger surface area of nanoparticles would promote a greater contact with cell membranes, as well as greater capacity for absorption and migration. Hence, nano-sized materials frequently present different properties than that of the normal sized materials. Therefore, CA nanoemulsion formulation has potential to be used as an alternative natural preservative to extend the shelf life of fresh cut fruits and vegetables.

Conclusion

The fresh-cut fruits and vegetables industry is expected to continue expanding rapidly in the coming years and hence there is still urgent need of improved technologies for shelf life extension. It has already been demonstrated that nanotechnology can be used as a hurdle technology to control the growth of foodborne pathogens but its combination with other preservation and intelligent packaging technologies may be the most effective approach to guarantee food safety and extension of shelf life as well as maintaining the sensory attributes of fruits and vegetables. Therefore, future studies should aim at improving shelf life, organoleptic quality and nutritional value of fresh-cut produce by reasonable combinations of these novel technologies. Also studies on the fate of pathogenic organisms on fruit and vegetables treated with cinnamic acid nanoemulsion would be essential to ensure that the elimination of the spoilage flora does not inadvertently enhance the survival of pathogens.

Acknowledgements

This study was funded by the National Natural Science Foundation of China (grant no.31201433 and 31401532) and Postgraduate Scientific Research Innovation Project of Jiangsu Province (No.KYLX15_1139).

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