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## REVIEW

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### Introduction

In recent years, nanotechnology has significantly impacted food packaging materials, addressing challenges in both food preservation and environmental considerations.<sup>1</sup> Packaging materials are widely acknowledged for their crucial role in protecting food products, preventing degradation from physical, chemical, or biological factors, and ensuring overall quality during storage and handling.<sup>2</sup> In this context, the integration of nanotechnology with encapsulation techniques has led to advanced methods for creating innovative food sector devices with potential benefits across various aspects of food science.<sup>3</sup>

Nanomaterials are attracting attention from researchers for their versatile applications in the food industry. Their morphology, size, and distribution contribute to novel and enhanced properties compared to their bulk counterparts from which they originate.<sup>4,5</sup> In this sense, a wide variety of nanoparticles (NPs) derived from metal or inorganic metallic oxidebased nanomaterials, including silver, copper, zinc oxide, and titanium dioxide, along with nanostructured materials such as

# Nanotechnology in food packaging materials: role and application of nanoparticles

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Global concerns about food security, driven by rising demand, have prompted the exploration of nanotechnology as a solution to enhance food supply. This shift comes in response to the limitations of conventional technologies in meeting the ever-increasing demand for food products. Consequently, nanoparticles play a crucial role in enhancing food production, preservation, and extending shelf life by imparting exceptional properties to materials. Nanoparticles and nanostructures with attributes like expansive surface area and antimicrobial efficacy, are versatile in both traditional packaging and integration into biopolymer matrices. These distinctive qualities contribute to their extensive use in various food sector applications. Hence, this review explores the physicochemical properties, functions, and biological aspects of nanoparticles in the context of food packaging. Furthermore, the synergistic effect of nanoparticles with different biopolymers, alongside its different potential applications such as food shelf-life extenders, antimicrobial agents and as nanomaterials for developing smart packaging systems were summarily explored. While the ongoing exploration of this research area is evident, our review highlights the substantial potential of nanomaterials to emerge as a viable choice for food packaging if the challenges regarding toxicity are carefully and effectively modulated.

starch, cellulose, chitosan, and montmorillonite (MMT)6,7 have been widely employed in food packaging materials as they demonstrate enhancements in water and gas resistance, mechanical strength and thermal properties.8 However, it should be noted that this will also depend on the concentration in which they are used. Besides, nanomaterials enhance the properties of packaging materials including durability, flexibility, barrier properties, and optical properties.9 For instance, some nanostructures such as cellulose nanocrystal (CNC) and cellulose nanofiber (CNF) were found to greatly improve tensile strength and water vapor permeability of chitosan and whey protein isolate.9,10 Additionally, nanomaterials are extensively employed as antimicrobials to reduce microbial spoilage of packaged foods. In this sense, nanoparticles including copper nanoparticles and silver nanoparticles improved the antibacterial properties, thermal properties, and antioxidant activity when added into agar-based films and CNC, respectively.<sup>11,12</sup> Similarly, nanocellulose and nisin based-hydrogel microparticles reduced the growth of L. monocytogenes.13 Nanomaterials are additionally used in intelligent packaging systems to detect microbial contamination, chemical contaminants, or gases indicative of spoilage or quality deterioration in packaged food products.14 In this context, silver nanoparticles (Ag NPs) were reported to effectively detect the lactic acid in fresh milk when incorporated into cysteine and histidine.15 Likewise, titanium

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dioxide nanoparticles (TiO<sub>2</sub> NPs) were employed to check the freshness of meat, showing promising results in the evaluation of the oxidation activity of xanthine oxidase.<sup>16</sup>

As previously evidenced, nanotechnology possesses a great potential to improve innovative products and processes in the food sector which could offer an excellent opportunity to replace non-degradable plastic packaging materials. However, although there are many review papers aiming to discuss the application of nanotechnology in food packaging context, review papers particularly centered on the utilization of nanoparticles such as silver, zinc oxide, titanium dioxide, copper oxide, graphene oxide, and carbon nanotubes are hard to find. Due to the previously mentioned necessity, the present paper comprehensively reviews the applications of the previously mentioned nanomaterials as antimicrobial packaging systems and sensors to guarantee food safety as well as extend their shelf life. An attempt has also been made to acknowledge the positive impacts of nanomaterials on the properties of biofilms when incorporated into them.

## Food packaging roles and contribution of nanomaterials

Packaging is an important component across diverse industries, finding applications in medicine, pharmaceuticals, food, electronics, *etc.*<sup>17</sup> In food-related applications, packaging plays a vital role in slowing down food deterioration, enhancing food quality and safety and extending shelf life, thus reducing food losses and waste.<sup>18</sup> In this regard, packaging acts as a barrier against three main types of external influences. Firstly, it addresses chemical influences by minimizing changes caused by environmental factors like gases, moisture, or light. Secondly, it deals with biological contaminants by creating a barrier against microorganisms (pathogens and spoilage agents) and maintaining conditions that control senescence. Lastly, it addresses physical threats by protecting food from mechanical damage.<sup>19</sup>

A wide range of materials are employed in packaging preparation and manufacturing. Commonly, polymer-based composite materials, including films and nanofibers,<sup>20,21</sup> incorporate a variety of organic, inorganic, and composite nanomaterials to enhance their fundamental properties (Fig. 1).22 For example, it has been recognized that integrating nanomaterials into biopolymers enhances their mechanical and barrier properties as well as their stability under different temperature and moisture conditions.23 Furthermore, this has led to intelligent packaging that can help identify when the food has been exposed to adverse conditions, such as inadequate temperatures or elevated oxygen levels, this helps with information about food packaged quality products.<sup>24</sup> Lastly, owing to their remarkably antimicrobial properties, nanomaterials are well-suited for antimicrobial active packaging, therefore prolonging the shelf life of food products and minimizing food loss.25 Metal-based materials like silver nanoparticles, nanoforms of certain metal oxides such as copper oxide nanoparticles, titanium oxide nanoparticles, zinc oxide nanoparticles, and carbon-based materials including carbon nanotubes and graphene oxide are among the nanomaterials that have been added to food packaging as functional additions.26

#### **Processing techniques**

Polymer composites incorporating nanomaterials can be manufactured using processes similar to those employed for conventional polymer composites. This aspect makes them particularly appealing from a production point of view.<sup>27</sup> The fabrication method dictates both the concentration and dispersion of the nanofillers and nano reinforcements into the polymer.<sup>28</sup>

Solution mixing or solvent casting implies vigorously stirring or nanoparticle ultrasonication in a polymer solution before

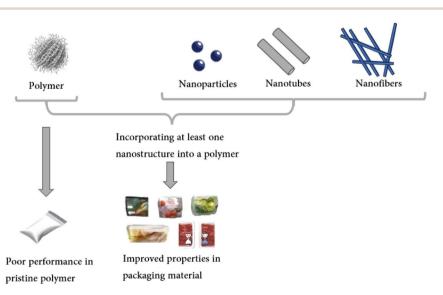


Fig. 1 Schematic representation of the overall procedure for the manufacturing of composites containing nanomaterials and enhancement of the functional properties.

casting it into a mold and subsequently evaporating the solvent. This technique allows for obtaining a homogeneous distribution of nanoparticles within the polymer while facilitating the formation of filler-rich layers.<sup>29</sup>

At the industrial scale, composite materials on nanoscale are commonly produced through extrusion or melt processing, where polymer and nanofillers are compounded in a single or twin-screw extruder. This process involves blending the components into a molten state, aided by shear and elongational stresses within the mixer. The resulting blend can then be utilized to manufacture a wide range of products such as films through processes like profile injection molding, extrusion, and blow molding.<sup>30</sup>

Electrospinning and electrospraying involve expelling (electrospinning) or spraying (electrospraying) polymer solutions by applying high electric potential at standard temperature and pressure conditions. Electrospinning provides micro and nanostructured fiber-based materials with diverse morphologies and particles in the range of nanometers to a few micrometers for electrospraying<sup>31</sup>

Sol–gel technique is widely utilized for producing nanobased coatings. A dense colloidal sol is applied to a surface *via* dipping, spraying, or spin coating methods. The resulting layers possess a thickness ranging from a few nanometres to 0.5 and 3  $\mu$ m.<sup>32</sup>

## Effect of the most used nanoparticles in food packaging

Food packaging materials are vital for preserving product quality during distribution and storage. They ideally exhibit appropriate mechanical, optical, and thermal characteristics, acting as barriers against contaminants, water vapor, oxygen, carbon dioxide, flavors, and microorganisms.33 Artificial polymers like polyethylene (PE), polypropylene (PP), polystyrene (PS), polyvinyl chloride (PVC), polyethylene terephthalate (PET), polyvinyl alcohol (PVA), and polyglycolide (PGA) are commonly utilized in food packaging owing to their thermal stability, mechanical properties, lightness, and cost-effectiveness. However, sourced from non-renewable petroleum, these polymers present potential health and environmental hazards.<sup>34</sup> Recent research focuses on developing biopolymers for food packaging. Various biodegradable polymers, sourced from plant and animal origins, include polysaccharides (agar, carrageenan, starch, pectin, inulin, chitin, and chitosan), microbial polysaccharides (xanthan, gellan, curdlan, pullulan, dextran, and bacterial cellulose), polyesters, proteins, and synthetic variants (poly(L-lactide) or poly (butylene succinate)). Some are produced through microbial fermentation, such as poly(βhydroxybutyrate) (PHB).

Unfortunately, natural polymers possess challenges due to their high gas and vapor permeability, coupled with poor resistance, limiting their broad applications.<sup>34,35</sup> One potential solution to this issue is the enhancement of their properties such as mechanical strength and gas barrier capabilities. This approach enables their effective application in food packaging while addressing environmental concerns.<sup>36</sup> Achieving this objective involves integrating nanomaterials, such as nanofillers, into biodegradable polymers to form biocomposites. These innovative materials can provide enhanced mechanical strength and act as barriers against microorganisms, moisture, and gases.<sup>37</sup>

On the other hand, nanoparticles are gaining interest due to their microbial and sensor properties. These particles show promise by directly interacting with bacterial cells, offering potential solutions.<sup>38</sup> Furthermore, the integration of nanotechnology with appropriate analytical methodologies and detection techniques proves highly valuable for evaluating the quality and safety of food.<sup>39</sup> As an example, nanosensors, made from metals and metal oxides, are integrated into 'smart packaging' for food. Enabling real-time monitoring of storage conditions, assessing freshness, providing insights into product quality, and enhancing overall safety. These nanosensors can also be used in measurement devices to evaluate factors influencing food quality and safety.<sup>40</sup>

#### Silver nanoparticles (Ag NPs)

To enhance barrier and functional properties of polymers. Several studies suggest that the addition of silver nanoparticles into biopolymers holds promise in food packaging technology by markedly enhancing packaging attributes, such as durability, barrier properties, mechanical strength and extending shelf life by reducing pathogen as summarized in Table 1.41,49 For example, Singh and Sahareen (2017)<sup>42</sup> reinforced a cellulosic material with silver nanoparticles, the resulting composite extended shelf life of vegetables by retaining its nutritional content, improving antimicrobial effectiveness, and prolonging freshness by maintaining moisture. In another study, three cellulose-based active papers-chitosan (P-CH), chitosan composite (P-CH-TiO<sub>2</sub>), and chitosan-Ag/TiO<sub>2</sub> composite (P-CH-Ag/TiO<sub>2</sub>)-showed significant yeast and mold inhibition, with P-CH-Ag/TiO<sub>2</sub> being the most effective, maintaining 79.25% inhibition after a 6 months storage period and extending kernel shelf life.43 Similarly, Shankar et al. (2021)44 found that composite films containing chitosan, essential oils, and silver nanoparticles, incorporated with gamma irradiation, significantly extended the shelf life of strawberries stored at 4 ° C. This improvement was evident in reduced weight loss and decay levels compared to control treatments. Likewise, in a study by Kavakebi et al. (2021),45 a polyvinyl alcohol coated film with silver nanoparticles significantly extended the shelf life of rainbow trout fillet, eliminating S. aureus and prolonging shelf life up to the 7th day in fish trials. Similarly, Nguyen et al. (2021)<sup>46</sup> developed a coating with polyvinyl alcohol/agar/ maltodextrin and silver nanoparticles for extending the shelf life of harvested bananas. The applied coating reduced weight loss, acidity loss, pH variations, total soluble solids, and softening during storage. Furthermore, Lee et al. (2019)47 found that adding silver nanoparticles to pullulan/pectin films improved various properties and enhanced antimicrobial activity against foodborne pathogens. Additionally, mango peel-extract and silver nanoparticles enhanced a polylactic acid (PLA) film,

Table 1 Packaging materials with silver nanoparticles in food packaging technologies

| Food packaging material               | Main finding   | Ref. |
|---------------------------------------|--|------|
| Cellulosic paper                      | The composite film had antimicrobial properties against <i>A. hydrophila</i> . Moreover, the   | 42   |
|                                       | films enhanced shelf life of tomatoes and cabbages   |      |
| Cellulose-based papers coated         | The addition of Ag NPs and $\mathrm{TiO}_2$ NPs led to an improvement of the water and oxygen  | 43   |
| with chitosan                         | barrier properties   |      |
| Chitosan incorporated with            | The composite film displayed potent antimicrobial activity against E. coli, L.                 | 44   |
| essential oils                        | monocytogenes, S. typhimurium and A. niger. Additionally, it extended the shelf life of        |      |
|                                       | strawberries by 4 days while maintaining their quality   |      |
| Polyvinyl alcohol                     | The silver/PVA composite prolonged the shelf life of salmon fillets up to the 7th day          | 45   |
|                                       | and exhibited antimicrobial properties against S. aureus                                       |      |
| Polyvinyl alcohol coated with agar    | The incorporation of Ag NPs improved the antibacterial effectiveness against E. coli           | 46   |
| and maltodextrin                      | and <i>S. aureus</i> while also enhancing the flexibility of the film. Moreover, the composite |      |
|                                       | film extended the shelf life of bananas by 5 days  |      |
| Pullulan blended with pectin          | The composite film exhibited superior physical, mechanical, optical, and barrier               | 47   |
| I I I I I I I I I I I I I I I I I I I | characteristics. The incorporation of Ag NPs improved the antimicrobial efficacy               |      |
|                                       | against S. typhimurium, E. coli and L. monocytogenes of the film                               |      |
| Polylactic acid                       | The integration of Ag NPs enhanced the mechanical strength of the film and its ability         | 48   |
| i orgiactic acta                      | to act as a barrier against water vapor and oxygen. Additionally, the composite film           | 40   |
|                                       |  |      |
|                                       | exhibited potent antibacterial properties, contributing to the extension of the shelf life     |      |
|                                       | of strawberries  |      |

improving water and oxygen transmission rates without compromising strength and stability. The film also achieved exceptional anti-oxidation and anti-ultraviolet properties.<sup>48</sup>

As antibacterial agents and food spoilage detection. Silver nanoparticles also possess a wide spectrum of antimicrobial activity to a large variety of microorganisms.<sup>50</sup> Additionally, Ag NPs also have the potential to function as detectors, identifying and responding to changes in environmental conditions, including detecting contaminants, assessing microbial quality, and monitoring gas changes.<sup>51,52</sup> Multiple research articles have evaluated the efficacy of Ag NPs integrated into food packaging to inhibit foodborne pathogens as summarized in Table 2. For example, films based on chitosan/silver nanoparticles/gold nanoparticles effectively inhibited the growth of *S. aureus*, *P. aeruginosa*, *A. niger* and *C. albicans*.<sup>53</sup> Furthermore, Patri and coworkers (2018)<sup>58</sup> developed a sensor combining silver nanoparticles with a chitosan matrix to modify graphite screenprinted electrodes. The sensor successfully measured nitrite levels in commercial milk powder samples, showing satisfactory agreement with a standard protocol. Another study reinforced pullulan films with Ag NPs and essential oils, showing strong antimicrobial activities against *Staphylococcus aureus* and *Listeria monocytogenes* in meat and poultry products.<sup>54</sup> Ghaffarlou *et al.* (2022)<sup>55</sup> compared the antimicrobial activity of Ag NPs/ pullulan and Au NPs/pullulan composites. The authors observed that Ag NPs/pullulan-based films exhibited superior

| Table 2 | Packaging | materials | with | silver | nanoparticles | in food | l packaging | techno | logies |
|---------|-----------|-----------|------|--------|---------------|---------|-------------|--------|--------|
|---------|-----------|-----------|------|--------|---------------|---------|-------------|--------|--------|

| Polymer matrices  | Nanomaterial             | Size of<br>nanomaterial (nm)  | Active against<br>bacterial species   | Possible mechanism of action   | Ref. |
|---|--------------------------|-------------------------------|---|--|------|
| Chitosan  | (a) Ag NPs<br>(b) Au NPs | (a) 70 to 100<br>(b) 20 to 30 | (a), (b) S. aureus,<br>P. aureginosa, A. niger,<br>C. albicans                        | Electrostatic attraction between the<br>negatively charged cell membrane of the<br>microorganisms and the positively<br>charged Ag NPs or Au NPs                   | 53   |
| Pullulan reinforced   | (a) Ag NPs               | (a) 100                       | (a), (b) S. aureus,   | Interference with vital cellular processes   | 54   |
| with essential oils   | (b) ZnO NPs              | (b) 110                       | L. monocytogenes,   | Disruption of DNA replication  |      |
|   |                          |                               | <i>E. coli</i> O157:H7  | Oxidative stress through the catalysis of ROS.   |      |
| Pullulan  | (a) Ag NPs<br>(b) Au NPs | (a), (b) 20 to 50             | (a), (b) P. aureginosa,<br>E. coli, S. aureus   | _  | 55   |
| Polyvinyl alcohol<br>reinforced with MMT                                | Ag NPs                   | _                             | S. typhimurium, S. aureus   | Interaction between positively charged<br>silver ions (Ag <sup>+</sup> ) and negatively charged<br>bacterial cell wall   | 56   |
| Tragacanth blended with<br>hydroxypropyl methylcellulose<br>and beeswax | Ag NPs                   | _                             | B. cereus, S. aureus,<br>S. pneumonia,<br>L. monocytogenes,<br>E. coli, S. typhimorum | Interaction between positively charged<br>silver ions (Ag <sup>+</sup> ) and negatively charged<br>phosphorous or sulfur groups of<br>macromolecules in cell walls | 57   |

antimicrobial activity against P. aeruginosa, E. coli, and S. aureus. A starch/polyvinyl alcohol film inhibited the growth of Listeria inocua, Escherichia coli, Aspergillus niger and Penicillium expansum when added silver nanoparticles. Further, Mathew et al. (2019)<sup>56</sup> developed composite films using polyvinyl alcohol/clay/silver nanoparticles (Ag NPs) for meat packaging. The films exhibited potent antibacterial activity against S. Typhimurium and S. aureus, along with improved mechanical strength, barrier properties, and water resistance. An activated biochar, polylactic acid and silver nanoparticles-based biosensor were developed using solvent casting and in situ oxidative synthesis. The resulting biosensor demonstrated enhanced sensing capabilities for detecting ammonia (NH<sub>3</sub>) in a 5-60 ppm range, suggesting its potential applications in the food and agriculture sectors.<sup>59</sup> Sodium alginate, polyvinyl alcohol, and silver nanoparticles-based sensor film showed strong reactivity to Hg<sup>2+</sup> ions in a pH range of 2.0 to 10. The sensor demonstrated a linear response to Hg<sup>2+</sup> ion concentrations from 0.9 ppb to 1200 ppb.60 A biodegradable film based on tragacanth, hydroxypropyl methylcellulose, and beeswax, fortified with silver nanoparticles. exhibited antibacterial properties against B. cereus, S. aureus, S. pneumoniae, S. Typhimurium, E. coli and L. monocytogenes.57 The authors highlighted that the resulting films exhibited a stronger antibacterial effect against Gram-negative bacteria in comparison to Gram-positive bacteria. The differing antimicrobial efficacy of Ag NPs against Gram-positive and Gram-negative bacteria can be explained through the perspective of the structure and thickness of the bacterial cell wall.61 Gram-positive bacteria possess several layers of peptidoglycan, which are thicker, usually ranging from 20 to 80 nm, in contrast to the thinner peptidoglycan layer of Gram-negative bacteria (ranging from 7 to 8 nm). This structural difference makes it challenging for Ag NPs to penetrate the cytoplasmic membrane of Gram-positive bacteria. However, due to the thinner peptidoglycan layer in Gramnegative bacteria, Ag NPs can easily penetrate and cause cell death.62

The mechanism of Ag NPs has been well established.<sup>50,63-65</sup> It is widely accepted that the positive charge of Ag NPs interacts with the negatively charged phosphorus or sulfur groups found in proteins and nucleic acids through electrostatic forces.<sup>66</sup> This interaction has the potential to deform bacterial cell walls and membranes, potentially leading to cell death. On the other hand, Ag NPs can also induce the production of reactive oxygen species (ROS) and free-radical species, such as hydrogen peroxide, superoxide anion, hydroxyl radical, hypochlorous acid, and singlet oxygen. These species can elevate oxidative stress within bacterial cells. Furthermore, they can improve the permeability characteristics of bacterial membranes, leading ultimately to cell death.<sup>67</sup> An illustration of reported antimicrobial mechanisms induced by nanoparticles is shown in Fig. 2.

Toxicity and safety concerns. According to the regulations set by the European Food Safety Authority (EFSA), the migration of silver from packaging material into foodstuffs should not exceed 0.05 mg kg<sup>-1</sup> in food and 0.05 mg L<sup>-1</sup> in water.<sup>68</sup> As outlined by the United States Environmental Protection Agency, the permissible level of silver in drinking water should not exceed  $0.10 \text{ mg L}^{-1.69}$  Although silver nanoparticles can prolong the shelf life of food products, a drawback associated with them is the potential migration of these nanoparticles into the food product, resulting in risks of toxicity.70 Silver nanoparticles may accumulate in various organs of the human body, such as the brain, kidneys, liver, and testicles.71 Moreover, elevated doses of silver nanoparticles can induce neurotoxic, hepatotoxic, and genotoxic effects. However, the possibility of silver migration from packaging systems to food reaching such levels is minimal, although the potential toxicological consequences of silver nanoparticles in food due to migration have not been extensively evaluated.72 For example, in a study conducted by Echegoyen and Nerín (2013),73 the migration of silver was assessed in three types of packaging materials: polypropylene, plastic bags, and polyolefin. The results indicated that the migration of silver fell within the limits set by European

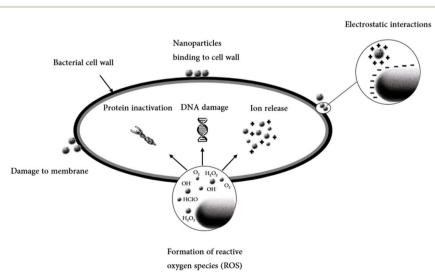


Fig. 2 Schematic of the antimicrobial mechanisms of nanoparticles in food-related applications.

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regulatory standards. Moreover, Gallocchio *et al.*  $(2016)^{74}$  conducted a study to assess the migration of silver from a food packaging containing silver nanoparticles (Ag NPs) into chicken meatballs under typical domestic storage conditions. The findings revealed that the migration was gradual. Similarly, Li *et al.*  $(2018)^{75}$  conducted research on polylactic acid film integrated with titanium dioxide and silver nanoparticles in cottage cheese. Their findings revealed that as storage time increased, the migration of silver also increased, reaching a concentration of 0.02 mg kg<sup>-1</sup>, which remained well below the standard limits. Cushen *et al.*  $(2012)^{76}$  noted that the migration rate of silver nanoparticles is influenced by the viscosity of the packaging polymer and the size of the nanoparticles. Typically, migration increases with decreasing particle size and viscosity.

#### Zinc oxide nanoparticles (ZnO NPs)

To enhance barrier and functional properties of polymers. In the past years, zinc oxide nanoparticles have attracted attention owing to their feasible properties, cost-effectiveness, and essential role in biological systems.77 ZnO nanoparticles possess the potential to improve the properties of packaging materials, like mechanical and barrier properties, and stability.78 Recently, polyvinyl alcohol and gelatin-based films incorporating ZnO and TiO2 NPs doped on 4A zeolite were developed for food packaging applications. The resulting composite doubled the shelf life of shrimp from 6 to 12 days by inhibiting bacterial growth.79 Furthermore, by incorporating ZnO NPs, a PVA and arginine chitosan blend exhibited superior mechanical properties, and water and oxygen barriers.<sup>80</sup> Jayakumar et al. (2019)<sup>81</sup> developed starch/PVA-based composite films reinforced with ZnO NPs, nutmeg oil, and jamun extract. The inclusion of ZnO NPs improved the antimicrobial features of the film as well as its water and ultraviolet barrier, and mechanical strength. Chitosan blends reinforced with ZnO NPs demonstrated superior properties such as an improvement in its antioxidant properties and bactericidal efficacy against E. coli, S. aureus,

*B.subtilis*, *P. aeruginosa*<sup>82</sup> and *L. monocytogenes*.<sup>83</sup> Further, Priyadarshi *et al.* (2017)<sup>84</sup> enhanced the mechanical properties of chitosan films (77% rise in tensile modulus and 67% increase in tensile strength) by incorporating ZnO NPs into the chitosan matrix. Additionally, polylactic acid reinforced with zinc oxide demonstrated an improvement in the firmness, phenolic content, color retention, and sensory quality of apples.<sup>85</sup> Another study incorporated 5% of ZnO NPs into polylactic acid, resulting in a reduced gas permeability as well as an improvement of its tensile properties and antimicrobial activity against *E. coli* of polylactic acid.<sup>86</sup> Examples of films and coatings containing zinc oxide nanoparticles from the available literature are documented in Table 3.

As antibacterial agents and food spoilage detection. ZnO NPs enhance the antibacterial properties of active coatings, seamlessly integrated into polymer matrices, further, they can also be used in food spoilage detection. For instance, their incorporation into chitosan-based edible films effectively inhibited E. coli growth while improving thermal stability.87 Another report developed a film based on ZnO NPs, chitosan carboxylated multiwalled carbon nanotubes and polyaniline Another report developed a film based on ZnO NPs, chitosan carboxylated multiwalled carbon nanotubes and polyaniline for detecting xanthine in fish meat during storage. The biosensor demonstrated a linear response of 0.1-100 µM.16 Hooda et al. (2018),<sup>88</sup> developed a composite strip combining chitosan, coconut fiber, and zinc oxide nanoparticles designed for polyamine sensing. The resulting composite measured polyamine levels in fruits and vegetables within a temperature range of 25 to 33 °C and an incubation time of 6 minutes, it possessed a linearity of 5.0 mM. Furthermore, Hezma et al. (2019),89 compared the effects of incorporating various concentrations of ZnO NPs in polyvinyl alcohol/chitosan blend films for food packaging applications. The authors concluded that the sample containing 10 and 15 wt% ZnO displayed the greatest thermal stability, mechanical strength, and antibacterial activity.

Table 3 Packaging materials with zinc oxide nanoparticles in food packaging technologies

| Food packaging material                     | Main finding   | Ref. |
|---|--|------|
| Polyvinyl alcohol blended                   | The addition of ZnO NPs and $TiO_2$ NPs extended the shelf life of shrimp up to 12 days and preserved the sensory characteristics of the films during storage  | 79   |
| with gelatin<br>Polyvinyl alcohol           | The incorporation of ZnO NPs improved the antibacterial efficacy against <i>S. aureus</i> and <i>E. coli</i> of the film and extended the shelf life of cherry tomatoes  | 80   |
| Starch blended with polyvinyl alcohol       | The water and UV barrier and mechanical and antimicrobial properties of starch/PVA film can be improved owing to the incorporation of ZnO NPs  | 81   |
| Chitosan and cellulose<br>acetate phthalate | Incorporating ZnO NPs enhanced the thermal stability and barrier properties of the film, extending the shelf life of black grape fruits up to 9 days   | 82   |
| Pullulan blended with chitosan              | The blend of ZnO NPs and propolis enhanced the mechanical strength of the film by 25%.<br>Additionally, there was a slight increase in the film's water vapor barrier and hydrophobicity   | 83   |
| Chitosan                                    | Chitosan film reinforced with ZnO NPs showed an enhancement of 77% and 67% in tensile modulus and tensile strength respectively. Moreover, the enhanced films exhibited a twofold increase in antimicrobial activity against <i>B. subtilis</i> and a 1.5-fold increase against <i>E. coli</i> | 84   |
| Polylactic acid                             | An improvement in water vapor permeability, elongation at break and elastic modulus of the films was observed. Additionally, the film prolonged the shelf life of fresh-cut apples for 14 days   | 85   |
| Polylactic acid                             | Adding 5 wt% of ZnO NPs enhanced the tensile properties and lowered the permeability to $O_2$ and $CO_2$ of the films. The film extended the shelf life of cherries  | 86   |

Another report revealed that the incorporation of zinc oxide nanoparticles on polylactic acid films enhanced the antibacterial efficacy against E. coli and L. monocytogenes.87 In a parallel report, the antimicrobial potential of trinary bio-composite composed of black cumin cake extract/gelatin/PVA film with ZnO NPs was tested. The resulting composite effectively inhibited the growth of three Gram-positive bacterial strains.90 A smart packaging integrated of chitosan, polyvinyl alcohol and ZnO NPs with Carissa carandas anthocyanin demonstrated improved mechanical strength, reduced moisture, and lowered water vapor permeability. Additionally, the films displayed distinct colour changes which allows the effective monitoring of fish fillet freshness.<sup>91</sup> Furthermore, Bajpai et al. (2010)<sup>92</sup> investigated the antibacterial activity of zinc oxide nanoparticles loaded on a chitosan-based edible film. The authors found that ZnO nanoparticles demonstrated fair antibacterial action against E. coli. Table 4 summarizes the antibacterial activity of different biopolymer based-materials including ZnO NPs.

The mechanism of action of ZnO NPs can be explained through the inhibition of bacteria by allowing Zn<sup>2+</sup> particles to penetrate the cell membrane, inducing oxidative stress. This stress leads to damage to lipids, carbohydrates, proteins, and DNA, ultimately disrupting cellular functions.<sup>93</sup>

Toxicity and safety concerns. ZnO nanoparticles are used as active materials in food packaging, posing potential risks to consumers upon contact. In vivo studies have shown that these nanoparticles can access organs through various pathways, including ingestion, inhalation, and parenteral routes.94 Hence, the main concern is to corroborate whether there is migration of nanoparticles from the packaging to the food or not. Should such migration occur, the subsequent focus is to investigate the impact of ingesting these nanoparticles within the body, traversing from the mouth to the gastrointestinal tract, through both in vitro and in vivo exposure tests.95 In this context, Emamifar et al. (2010)96 investigated the migration of silver and zinc oxide nanoparticles from low density polyethylene (LDPE) films into orange juice. They found that the silver ion content (0.1  $\pm$ 0.003  $\mu$ g L<sup>-1</sup>) in orange juice remained below the allowable concentration threshold (10 ppm) even after 112 days. Although zinc ion migration was higher than silver ions  $(0.68 \pm 0.002 \ \mu g \ L^{-1})$ , the levels remained within acceptable limits since ZnO is recognized as Generally Recognized as Safe (GRAS) for food applications. While these findings offer promise, further studies are imperative. These should include toxicological investigations based on data derived from migration tests to elucidate the potential actions of nanoparticles as well as released ions within the body.

#### Titanium dioxide nanoparticles (TiO<sub>2</sub> NPs)

To enhance barrier and functional properties of polymers. Titanium dioxide nanoparticles are accepted as safe materials by the Food and Drug Administration (FDA), making them significant for applications in the biomedical, food, and cosmetics sectors.97,98 Specifically, in the food packaging sector, the interaction of TiO2 NPs with film matrices enhances mechanical and gas barrier properties, and in some cases, provides a secondary function of ethylene decomposition, contributing to prolonged fruit shelf life after harvest.99-101 For example, in a study, a chitosan-based film demonstrated superior strength and enhanced barrier properties by the incorporation of TiO2 NPs, additionally, it increased the shelf life of tomatoes by delaying ripening.<sup>102</sup> Tian et al. (2019)<sup>103</sup> developed a chitosan/TiO<sub>2</sub> coating film, the resulting film demonstrated its potential to preserve Gingko biloba seeds by inhibiting mildew, delaying senescence, and preventing declines in firmness. In another report, pullulan/carboxymethyl cellulose/TiO2-NPs composites demonstrated superior antimicrobial activities against E. coli and S. aureus. Besides, it effectively prolonged the shelf life of strawberries by reducing weight loss, and maintaining the firmness, titratable acidity, and skin color.104 Polyvinyl alcohol/TiO2 NPs composite film's potential in food packaging was evidenced by extending the shelf life of Macrobrachium rosenbergii by 1-2 days105 and showing an improvement in its tensile strength and Young's modulus.<sup>106</sup> Alberton et al. (2014)<sup>107</sup> reported the fabrication of PLA/TiO<sub>2</sub> produced through melt mixing. Authors concluded that the incorporation of 1 wt% TiO2 increased PLA's tensile strength

| Table 4         Antibacterial activity of different biopolymer based-materials containing ZnO NPs |              |                              |  |   |      |  |  |
|---|--------------|------------------------------|--|---|------|--|--|
| Polymer matrices  | Nanomaterial | Size of<br>nanomaterial (nm) | Active against<br>bacterial species          | Possible mechanism of action  | Ref. |  |  |
| Chitosan blended<br>with PVA  | ZnO NPs      | 24.5                         | S. aureus, E. coli,<br>C. albicans, A. niger | The ROS (OH, O <sub>2</sub> <sup>-</sup> , H <sub>2</sub> O <sub>2</sub> ) and Zn <sup>2+</sup><br>released from ZnO react with bacterial<br>cell wall and intracellular contents of the<br>cell causing damage to nucleic acids and<br>ultimately leading to bacterial death | 89   |  |  |
| Polylactic acid   | ZnO NPs      | 50 to 100                    | E. coli, L. monocytogenes                    | Formation of reactive oxygen species  | 87   |  |  |
| Gelatin blended with<br>PVA and reinforced with<br>black cumin cake extract                       | ZnO NPs      | <100                         | M. luteus,<br>L. monocytogenes,<br>S. aureus | Permeation of Zn <sup>2+</sup> particles into the cell<br>membrane, causing oxidative stress<br>ultimately disrupting the cellular<br>functions   | 90   |  |  |
| Chitosan  | ZnO NPs      | _                            | E. coli                                      | ZnO releases ROS species which interact<br>with cell membrane causing severe  | 92   |  |  |

damage and ultimately kill the bacteria

 Table 5
 Packaging materials with titanium dioxide nanoparticles in food packaging technologies

| Food packaging material                          | Main finding   | Ref. |
|--|--|------|
| Chitosan   | The reinforced film delayed the ripening process of tomatoes and exhibited improved tensile strength, barrier properties and ethylene photodegradation ability   | 102  |
| Chitosan   | The film with $TiO_2$ and $SiO_2$ NPs improved fruit health, texture firmness, and moisture content while decreasing decay and shrinkage rates   | 103  |
| Pullulan blended with<br>carboxymethyl cellulose | Incorporation of $TiO_2$ NPs improved water vapor and UV-visible light barrier properties in the composite films. Furthermore, the films displayed strong activity against <i>E. coli</i> and <i>S. aureus</i>   | 104  |
| Polyvinyl alcohol                                | PVA reinforced with TiO <sub>2</sub> NPs exhibited strong antimicrobial activity against <i>Shewanella</i> spp., <i>Pseudomonas putida</i> and <i>Aeromonas hydrophilia</i> and extended the shelf life for 1–2 days of <i>macrobrachium rosenbergii</i> | 105  |
| Polyvinyl alcohol                                | The incorporation of $TiO_2$ NPs improved the mechanical properties of the film, although elongation at break slightly decreased   | 106  |
| Polylactic acid                                  | An improvement in the Young modulus and tensile strength of the films was observed   | 107  |
| Zein blended with chitosan                       | The addition of $0.15\%$ wt TiO <sub>2</sub> NPs increased the antibacterial properties of the film. Additionally, composite films showed better mechanical properties, thermal stability and hydrophobic property                                       | 108  |

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and Young's modulus, nevertheless, a decrease in the elongation at break was observed (from 3.56% to 3.00%). Similar results were observed by Qu *et al.* (2019)<sup>108</sup> who studied the properties of chitosan–TiO<sub>2</sub> and zein–chitosan–TiO<sub>2</sub> films. The authors observed that TiO<sub>2</sub> could induce a modification of the film matrix, particularly in chitosan–TiO<sub>2</sub> films, forming a dense structure that acts as an obstacle to water vapor diffusion through the film.<sup>109,110</sup> Examples of packaging materials incorporating titanium dioxide nanoparticles are summarized in Table 5.

As antibacterial agents and food spoilage detection.  $TiO_2$  nanoparticles are commonly used as additives in food for their non-toxic, photostable, and antibacterial properties. They are extensively studied for their ability to enhance functional properties and inhibit microbial growth in food, making them cost-effective and highly demanded in the field, further, they are

integrated into biosensors due to their remarkable stability, photocatalytic performance, and biocompatibility.<sup>111,112</sup> Table 6 summarizes the application of TiO<sub>2</sub> NPs in improving the antimicrobial properties of different biopolymers. For example, Li et al. (2016)<sup>113</sup> observed that chitosan-TiO<sub>2</sub> composites exhibited increased antibacterial efficacy against Xanthomonas oryzae pv. Another report found that chitosan/TiO<sub>2</sub>/Ag NPs composites reduced Escherichia coli by 6 logs after 24 hours and showed a minimum inhibitory concentration (MIC) value of 0.38 mg ml<sup>-1</sup> during refrigerated fruit storage.<sup>114</sup> A dual-layer antibacterial chromogenic material based on chitosan, hydroxyethyl cellulose, and mulberry anthocyanins, and TiO<sub>2</sub> NPs was designed to measure litchi fruit freshness. The resulting material showed antibacterial properties against E. coli and S. aureus and changed colors as the quality of the litchi decreased.<sup>118</sup> Another study documented that incorporating

Table 6 Antibacterial activity of different biopolymer based-materials containing TiO<sub>2</sub> NPs

|                               |   | ~! 0                         |  |   |      |
|-------------------------------|---|------------------------------|--|---|------|
| Polymer matrices              | Nanomaterial                            | Size of<br>nanomaterial (nm) | Active against bacterial species   | Possible mechanism of action  | Ref. |
| Chitosan                      | $TiO_2$ NPs                             | 21                           | S. aureus, E. coli, S. Typhimurium,<br>Pseudomonas aeruginosa, Aspergillus,<br>Penicillium | Photocatalytic reaction and generation of ROS under exposure of UV light  | 102  |
| Chitosan                      | TiO <sub>2</sub> NPs                    | 5                            | Xanthomonas oryzae strains   | Release of toxic metal ions<br>Generation of hydroxyl radicals and other<br>ROS under radiation with UV light                                   | 113  |
| Chitosan                      | (a) Ag NPs<br>(b) TiO <sub>2</sub> NPs  | (a), (b) <100                | E. coli  | _   | 114  |
| Polylactic acid               | TiO <sub>2</sub> NPs                    | 10 to 20                     | E. coli, S. aureus   | Generation of hydrogen peroxide,<br>hydroxyl radicals and superoxide anions<br>under UV light that ultimately contacts<br>and kill the microbes | 115  |
| Polylactic acid               | (a) ZnO NPs<br>(b) TiO <sub>2</sub> NPs | (a) 10 to 30<br>(b) 18       | (a), (b) L. monocytogenes, E. coli   | Zn <sup>2+</sup> release into the medium leads to<br>direct physical attack on bacterial cell<br>walls <i>via</i> electrostatic interactions    | 116  |
| Cellulose blended<br>with PVA | TiO <sub>2</sub> NPs                    | 0.32 to 20                   | Bacillus cereus, E. coli   | Electromagnetic attraction between microorganism and metal oxides   | 117  |

TiO<sub>2</sub> significantly enhances the antimicrobial properties of PLA films, as seen in inhibition zone results, measuring 4.86  $\pm$ 0.50 mm for *E. coli* and 4.63  $\pm$  0.45 mm for *S. aureus*.<sup>115</sup> Tajdari et al. (2020)<sup>116</sup> developed a film based on ZnO NPs/TiO<sub>2</sub> NPs/ polylactic acid. In comparison to neat PLA, the resulting composite exhibited greater antimicrobial action against L. monocytogenes and E. coli. In another study, the antimicrobial potential of cellulose/PVA/TiO2 NPs-based composite films was tested. The films effectively suppressed the growth of pathogens including Bacillus cereus and Escherichia coli.117 Likewise, Jiang et al. (2023),<sup>119</sup> developed a pH-responsive smart film using alginate, polyvinyl alcohol, purple garlic peel extract, and titanium dioxide nanoparticles to visually monitor beef freshness. During the storage of beef, the developed film exhibited noticeable color changes, effectively indicating its freshness (blue) and deterioration (yellow-green). Similarly, a composite film based on polylactic acid/TiO2 NPs/lycopene effectively monitored the oxidative changes of packaged margarine during storage, changing color from dark orange to pale yellow.<sup>120</sup> Additionally, the antimicrobial effectiveness of binary biocomposite film based on chitosan and TiO<sub>2</sub> NPs was tested. The biocomposite inhibited the growth of different pathogens including E. coli and S. aureus, as well as fungi (Aspergillus and Penicillium). The authors emphasized that the films demonstrated greater efficacy against Gram-positive bacteria compared to Gram-negative bacteria, possibly due to variances in cell wall structure, physiology, metabolism, or surface charge of bacterial cells.102

The possible action mode of  $TiO_2$  has been established. It mainly includes the release of toxic metal ions causing damage to cell membranes upon direct contact with nanoparticles. This leads to the inactivation and death of bacteria by oxidizing the polyunsaturated phospholipids within the cell membrane. Additionally, it facilitates the degradation of toxic compounds expelled by bacteria through the generation of hydroxyl radicals (OH) and other reactive oxygen species (ROS) when exposed to UV light. The antimicrobial effectiveness of TiO<sub>2</sub> NPs is related to their size as well as their high surface-to-volume ratio.<sup>121</sup>

Safety and toxicity concerns. Since 2002, the United States Food and Drug Administration (FDA) has formally approved the utilization of titanium dioxide in food additives, with a restriction that the added quantity should not surpass 1% of the total food mass. Similarly, in the European Union (EU), titanium dioxide is authorized as a food additive (listed as E 171) at quantum satis, indicating that no maximum level is specified.122 Nevertheless, it is relevant to ascertain both the occurrence and extent of nanoparticle migration from packaging materials when in contact with food, as well as the repercussions of their ingestion on the gastrointestinal tract and other organs. In this scenario, Lin and colleagues (2014)123 examined the migration of titanium from LDPE-TiO2 nanocomposites into food simulants (acetic acid and ethanol). Their findings revealed that the highest amount of migrated titanium was 12.1  $\mu$ g kg<sup>-1</sup>, observed after exposure to 3% acetic acid at 100 °C for 8 hours. In a separate investigation, migration tests of polyvinyl alcoholchitosan-TiO2 composites revealed that only a minimum quantity of titanium migrated (3.87  $\times$  10<sup>-3</sup>% for film treated at 200 MPa) into olive oil after 11 hours, with none detected in water, ethanol, or acetic acid.<sup>124</sup> Moreover, Li *et al.* (2018)<sup>125</sup> recently assessed the migration of titanium from PLA-based composites, demonstrating that similar to synthetic composites, the migrated nanomaterial amounted to a small quantity within the safe range.

#### Copper oxide nanoparticles (CuO NPs)

To enhance barrier and functional properties of polymers. Copper oxide nanoparticles are in high demand due to their biological potential. Research on the application of CuO nanoparticles in food packaging is limited but often emphasizes its capacity to modify oxygen and water barrier properties, optical characteristics, and confer antimicrobial effects, including bactericidal activity against both Gram-positive and Gram-negative bacteria, particularly in nonbiodegradable plastics and a few biopolymers.<sup>126</sup> Previously, the fabrication of chitosan films together with CuO nanoparticles was reported to effectively enhance the polymer's properties. For example, Kalia et al. (2021)<sup>127</sup> found that ZnO and CuO NPs supplementation improved chitosan characteristics by decreasing moisture content, water holding capacity, and solubility of the films. Besides, it extended the shelf life of guava fruits by one week. Another report reinforced chitosan films with montmorillonite/ CuO NPs, the resulting composites demonstrated superior mechanical strength and antibacterial properties without affecting film transparency or water solubility.<sup>128</sup> Additionally, CuO NPs could be integrated into polyvinyl alcohol-based blends to improve their properties. For example, Youssef et al. (2020),<sup>129</sup> developed carboxymethyl cellulose, polyvinyl alcohol and CuO-based composites. The resulting composites effectively extended the shelf life of cheese by reducing bacterial count, slowing moisture loss, and increasing hardness during storage. Likewise, PVA/CuO NPs-based films showed an improvement in their tensile modulus (4.5 GPa) in comparison to neat PVA (0.9 GPa).<sup>69</sup> Furthermore, Francis et al. (2022)<sup>130</sup> improved water barrier properties of PVA/starch/glycerol (PSG) composites for food packaging by adding CuO and ZnO. The resulting films showed increased hydrophobicity, reducing water absorptivity by 51.49% and solubility by 60% compared to PSG film. Recently, a polylactic acid/zinc oxide/copper oxide composite film was developed to study its potential in the food packaging sector. The resulting composite showed improved antioxidant and antimicrobial properties and could be employed to extend the shelf life of orange juice.131 Table 7 summarizes the main applications of CuO nanoparticles in different biopolymers.

As antibacterial agents and food spoilage detection. CuO NPs are also widely employed in food packaging due to their potent antimicrobial properties, effectively inhibiting the growth of bacteria, viruses, and fungi. For example, Revathi *et al.* (2019)<sup>133</sup> indicated that chitosan/CuO NPs/neem seed biocomposite exhibited remarkably antimicrobial activity against *S. aureus*. Further, a CuO NPs/cellulose/chitosan nanofibers composite showed remarkably antimicrobial activity against *E. coli*, *P. aeruginosa*, and *L. monocytogenes*.<sup>21</sup> Fathi *et al.* 

Table 7 Packaging materials with copper oxide nanoparticles in food packaging technologies

| Food packaging material                               | Main finding  | Ref. |
|---|---|------|
| Chitosan  | Incorporation of CuO and $TiO_2$ NPs improved the antimicrobial potential of composite films.<br>The films exhibited great transparency and better physical characteristics | 127  |
| Chitosan  | The incorporation of MMT-CuO NPs increased the tensile strength and elongation at break, but reduced the water vapor permeability and oxygen permeability of the films      | 128  |
| Carboxymethyl cellulose                               | Incorporating 0.9 wt% CuO NPs improved the water vapor permeability, mechanical properties,   | 129  |
| blended with polyvinyl alcohol                        | and antimicrobial efficacy of the coating material  |      |
| Polyvinyl alcohol blended<br>with starch and glycerol | The mechanical properties, thermal stability, water resistance, and UV barrier properties of the films were enhanced by incorporating CuO and ZnO nanoparticles             | 130  |
| Polylactic acid modified with polyaniline             | The antioxidant and antimicrobial characteristics of the film were enhanced due to the addition of CuO and ZnO NPs  | 131  |
| Polyvinyl alcohol                                     | The composite film exhibited reinforced mechanical, dielectric properties and antibacterial properties  | 132  |

(2022)<sup>134</sup> developed biobased films with carboxymethyl chitosan, saffron petal anthocyanin, and copper oxide nanoparticles. The films exhibited potent antimicrobial activity, changed color in different pH environments, and were effective for real-time monitoring of lamb meat freshness. Table 8 summarizes the antimicrobial activity of biopolymer-based materials incorporating CuO NPs.

The antimicrobial activity of CuO NPs is commonly attributed to various mechanisms. Firstly, CuO NPs attach to the cell membrane, interacting with bacterial lipid membranes. This interaction alters membrane permeability, obstructing nutrient intake and ultimately affecting bacterial viability.<sup>135</sup> Also, the release of copper ions and the subsequent formation of copperpeptide complexes disrupt the integrity of the bacterial membrane is another mechanism widely accepted.<sup>136</sup> Finally, CuO NPs could catalyze the generation of reactive oxygen species (ROS), significantly enhancing their production, and ultimately resulting in cell death.<sup>137</sup>

**Safety and toxicity concerns.** The toxicological effects of employing CuO nanoparticles on human health and the environment are primarily dependent on their physicochemical characteristics.<sup>138</sup> Until today, there's scarce information related to the toxicity of copper oxide nanoparticles in food-based applications, therefore, given the repercussions of excessive CuO NP utilization, it is imperative to intensify efforts to comprehend their adverse effects, particularly their migration into food products, and to establish regulatory measures aimed at mitigating human exposure to these nanoparticles.

#### Carbon nanotubes (CNTs)

To enhance barrier and functional properties of polymers. Single-walled and multi-walled carbon nanotubes have been thoroughly examined for their physicochemical, mechanical, and antimicrobial properties, making them potential additives in packaging. Blending them with synthetic or biopolymers enhances flexibility, thermal stability, mechanical strength, and provides effective barriers against gases and moisture. This modification improves food preservation, shielding it from physical, chemical, and biological deterioration and facilitating transportation and storage.139,140 In this context, Wen et al. (2022),141 observed that PVA films with MWCNTs/ZnO had the potential to suppress natural microorganism growth in chicken meat for at least 36 hours under refrigerated storage. Similarly, Khachatryan et al. (2023)142 improved a chitosan/alginate blend by adding carbon nanostructures. The resulting composite demonstrated enhanced mechanical strength, solubility, water absorption, and UV radiation protection with a 14% reduction in solubility. Another report found that polyvinyl alcohol/ multiwall carbon nanotubes/ZnO NPs composite films effectively extended the shelf life of stored vegetables by reducing water loss.143 Likewise, the association of carbon nanotubes and

| Table 8 | Antimicrobial effic | cacv of diverse | biopolymer- | <ul> <li>based materials</li> </ul> | incorporating | CuO na | anoparticles |
|---------|---------------------|-----------------|-------------|-------------------------------------|---------------|--------|--------------|

| •   |              |                              |   |   |      |
|---|--------------|------------------------------|---|---|------|
| Polymer matrices                                      | Nanomaterial | Size of nanomaterial<br>(nm) | Active against<br>bacterial species                 | Possible mechanism of action  | Ref. |
| Bacterial cellulose and chitosan nanofibers           | CuO NPs      | 48                           | E. coli, P. aeruginosa,<br>L. monocytogenes         | Formation of reactive oxygen species  | 21   |
| Chitosan and neem                                     | CuO NPs      | 22                           | S. aureus, E. coli, K.<br>aerogenes, S.<br>pyogenes | Adsorption of Cu <sup>2+</sup> ions to<br>the surface of the bacterial<br>and damage the cell<br>membrane | 133  |
| Carboxymethyl chitosan blended with petal anthocyanin | CuO NPs      | _                            | Staphylococcus<br>aureus, E. coli                   | _   | 134  |

Table 9 Packaging materials with carbon nanotubes in food packaging technologies

| Food packaging material         | Main finding  | Ref. |
|---------------------------------|---|------|
| Polyvinyl alcohol               | PVA reinforced with MWCNTs–ZnO exhibited enhanced thermal stability, water vapor transmission rate, hydrophobicity and antibacterial activity | 141  |
| Sodium alginate and<br>chitosan | Mechanical properties of the composite films were improved by the addition of CNTs and GO.  | 142  |
| PHBV                            | Crystallization temperature, crystallinity, storage modulus and dielectric properties of the films were enhanced by the incorporation of CNTs | 143  |
| Polylactic acid                 | Crystallization rate, barrier, mechanical, antibacterial and antifungal properties of the films were improved by the addition of MWCNTs       | 144  |
| Polylactic acid                 | PLA reinforced with fMWCNTs exhibited better mechanical properties and Young modulus  | 145  |

PLA blends have demonstrated potential for food packaging applications. For example, Yakduomi *et al.* (2022)<sup>144</sup> enhanced PLA film's barrier properties, mechanical strength (increment of Young's Modulus by 815%), antibacterial and antifungal activities by incorporating polydopamine-wrapped carbon nanotubes and TiO<sub>2</sub> NPs. Another study reinforced PLA films with functionalized carbon nanotubes (fMWCNT), revealing a remarkable improvement in Young's Modulus (up to 50%) and a 20% increase in crystallinity, compared to neat PLA.<sup>145</sup> Table 9 summarizes the effects of carbon nanotubes on food packaging materials.

As antibacterial agents and food spoilage detection. Furthermore, CNTs can be integrated into biopolymers improving its antimicrobial properties as illustrated in Table 10.150 For example, Cui et al. (2020)146 demonstrated that a film containing polylactic acid/poly(ɛ-caprolactone)/carbon nanotubes/cinnamaldehyde exhibited a sustained cinnamaldehyde release and prolonged its antibacterial effects on S. aureus and E. coli for 21 days, surpassing the film without CNTs by 7 days. Further, the antibacterial properties and thermomechanical features of polylactic acid are significantly enhanced by the incorporation of Ag NPs and CNTs.147 Additionally, Goodwin et al. (2015)148 explored the influence of CNTs on polyvinyl alcohol. The bacterial viability against P. aureginosa demonstrated a gradual decrease with escalating concentrations of CNTs. In another study, a lignin/polyvinyl alcohol/ lignin-decorated thin-walled carbon nanotubes composite

films exhibited increased breaking stress and modulus, along with enhanced antimicrobial properties against *S. aureus*, compared to neat lignin/PVA films.<sup>149</sup> Further, Rezaei *et al.* (2018),<sup>151</sup> immobilized amino-linked lysozyme aptamers in a reduced graphene oxide/multiwalled carbon nanotubes/ chitosan/synthesized carbon quantum dot-based composite using glutaraldehyde linker. The resulting composite success-fully detected lysozyme protein demonstrating high sensitivity, reproducibility, specificity, and rapid response.

The mechanism of action of CNTs relies on their interaction with microorganisms, which disrupts cellular membranes, metabolic processes, and morphology.<sup>152</sup> Research has revealed that the bacteriostatic properties of CNTs arises from their direct contact with microorganisms, causing damage to their cell membranes and subsequent bacterial cell death. Scanning electron microscopy (SEM) observations have revealed morphological alterations in microorganisms following incubation with CNTs, indicative of compromised cellular integrity. The bacteriostatic attributes of CNTs are increasingly acknowledged and attributed to their high surface-to-volume ratio and substantial inner volume.<sup>153</sup> Fig. 3 shows the schematic mechanism of antimicrobial activity of some carbonbased nanomaterials such as carbon nanotubes and graphene oxide sheets.

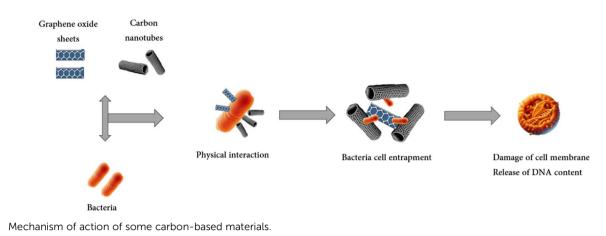
**Safety and toxicity concerns.** To date, despite the promising properties of CNTs-based composites, their practical use in food packaging remains severely restricted due to significant health

| Polymer matrices                               | Nanomaterial           | Size of nanomaterial (nm)   | Active against<br>bacterial species | Possible mechanism of action  | Ref. |
|--|------------------------|---|-------------------------------------|---|------|
| Polylactic acid reinforced<br>with PCL and CIN | CNTs                   | Diameter: 3–5<br>Outer diameter: 8–15<br>Length: 0.05                 | S. aureus, E. coli                  | _   | 146  |
| Polylactic acid                                | (a) Ag NPs<br>(b) CNTs | (a), (b) Diameter: 60 to 100,<br>length: 0.015                        | S. haemolyticus                     | _   | 147  |
| Polyvinyl alcohol                              | CNTs                   | Diameter: 15 to 5<br>Length: 0.005 to 20                              | P. aureginosa                       | Membrane lipid disruption or protein<br>binding due to CNT-microorganism<br>contact | 148  |
| Polyvinyl alcohol                              | MWCNTs                 | Diameter: 7 to 10<br>Length: 0.100 to 0.300<br>Length: 0.100 to 0.300 | S. aureus                           | Harmonious effect of MWCNTs through penetration cell                                | 149  |

Table 10 Antimicrobial effectiveness of diverse bionolymer-based materials containing carbon nanotubes

#### Review

Fia. 3



concerns. These concerns are mainly related to both the inherent toxicity of CNTs and their potential migration from composite materials.<sup>154</sup> Primarily, owing to their unique nanoscale dimensions, CNTs possess the capability to breach biological barriers within the human body, engaging with cells at a molecular level. This interaction can lead to detrimental impacts on various bodily systems, including the lungs, skin, kidneys, and nervous system.<sup>155</sup> In this context, Bott et al. (2014)<sup>156,157</sup> developed an investigation into the migration behavior of two variants of carbon nanotubes. The assessment involved incorporating these nanomaterials into low-density polyethylene (LDPE) and polystyrene (PS), followed by exposure to various food simulants. These simulants included a 3% acetic acid solution and 95% ethanol, maintained at 60 °C for extended contact periods, as well as an isooctane solution at 40 °C under rapid extraction conditions. Based on both experimental findings and theoretical analysis, it can be concluded that carbon black particles, upon integration into LDPE or PS, do not exhibit migration out of the matrix into food. Once these nanoparticles are fully immobilized, their diffusion remains consistently below the detection limit of any currently available sensitive method. The authors suggest that this conclusion can be extrapolated to other food-contact plastics where carbon black particles are fully embedded. Furthermore, effective reductions in CNT release from their composites have been documented through CNT functionalization<sup>158</sup> or irradiation treatment.159 Nevertheless, a comprehensive understanding of the migration characteristics of CNTs is imperative and necessitates extensive studies. Such information is essential to guide their practical applications.

#### Graphene oxide (GO)

To enhance barrier and functional properties of polymers. Graphene oxide stands out as a noteworthy graphene-based material (GBM), garnering considerable attention owing to its expansive surface area, biocompatibility, as well as its antimicrobial and antioxidant properties.<sup>157</sup> Earlier research has demonstrated the effectiveness of graphene oxide in improving preservation capabilities of composites and overall barrier properties, enhancing their physicochemical and biological properties as exemplified in Table 11.166 In this context, F. Han Lyn et al. (2021)157 reinforced chitosan with 2.0% GO and the resulting composite possessed reduced water vapor and oxygen permeability by around 43% and 55%, respectively, demonstrating its potential as an antioxidant material for food packaging. Further, the incorporation of graphene oxide and  $TiO_2$ NPs in chitosan films showed a reduction in moisture loss, inhibition of polyphenol oxidase (PPO) activity, additionally, it enhanced antioxidant enzyme activity of the film, especially superoxide dismutase (SOD).160 Vilvert et al. (2022)161 evaluated chitosan/graphene oxide composites on the postharvest preservation of 'Palmer' mangoes during cold storage. The resulting composites delayed mango ripening, preserved appearance, firmness and nutritional attributes. Furthermore, the composites decreased weight loss, reduced respiration rate, and minimized both the incidence and severity of anthracnose in mangoes during storage. Other reports evidenced the effects on polyvinyl alcohol-based films upon the addition of graphene oxide materials. For example, Loryuenyong et al. (2015)<sup>162</sup> enhanced mechanical and barrier properties of polyvinyl alcohol by incorporating 2.0 wt% GO. Further, bananas wrapped in the resulting composite showed a slower ripening process than those without packaging or packaged in neat PVA. Furthermore, a PVA/Ag NPs/GO/tragacanth gum composite exhibited improved strength, thermal stability, barrier properties and effectively inhibited bacteria growth in raw beef for at least 7 days in refrigerator.<sup>163</sup> Additionally, Arfat et al. (2018)<sup>164</sup> developed a clove essential oil/graphene oxide nanosheets/ polylactide composites for food packaging applications. The study revealed improved antibacterial activity against Staphylococcus aureus and Escherichia coli. Similarly, Kim et al. (2020)<sup>165</sup> used graphene oxide and carbon nanotubes (GOCNT), as a co-filler in PLA composite films. A 75% improvement in tensile strength, 140% rise in Young's Modulus and 67% reduction in oxygen transmission was observed in comparison to neat PLA films.

As antimicrobial agents and food spoilage detection. Additionally, graphene oxide possesses remarkably antimicrobial properties attributed to its extensive surface area and unique thermal, electrical, and physicomechanical properties.<sup>167</sup> In this context, several research suggests that the introduction of GO in Table 11 Packaging materials with graphene oxide in food packaging technologies

| Food packaging material            | Main finding   | Ref. |
|------------------------------------|--|------|
| Chitosan                           | The resulting film exhibited significantly lower vapor permeability oxygen permeability, water solubility and light transmittance                              | 157  |
| Chitosan                           | Antimicrobial effects against <i>B. subtilis</i> and <i>A. niger</i> of the film were enhanced by the incorporation of GO and $TiO_2$ NPs                      | 160  |
| Chitosan                           | The packaging material slowed down the ripening process of mangoes, resulting in reduced respiration rate, weight loss, and incidence and severity of diseases | 161  |
| Polyvinyl alcohol                  | The tensile strength, elastic modulus, and failure stain of the films were markedly enhanced by incorporating 0.3 and 2.0 wt% of graphene oxide                | 162  |
| PVA blended with<br>tragacanth gum | The resulting films effectively preserved raw beef samples by inhibiting the growth of natural beef bacteria for a minimum of 7 days                           | 163  |
| Polylactide doped with<br>clove EO | The addition of GO enhanced the optical and anti-UV properties of the films  | 164  |
| Polylactic acid                    | Polylactic acid reinforced with GO–CNTs exhibited a 75% increase in tensile strength and a 130% increase in Young's modulus                                    | 165  |

biopolymers can remarkably enhance its antimicrobial properties as shown in Table 12. As an example, a report suggested that antibacterial activity against *E. coli* and *B. subtilis* of chitosan films were higher when graphene oxide was incorporated.<sup>168</sup> Further, Khawaja *et al.* (2018)<sup>169</sup> compared the antimicrobial efficacy of different composites containing

graphene oxide, chitosan and/or AgNPs. The resulting composites demonstrated notable antibacterial activity against several bacterial strains and the authors concluded that the order of antibacterial effectiveness was GO/CS/Ag > GO/Ag > GO/ CS > GO. A highly sensitive humidity-sensing material based on GO/folic acid/chitosan/polyvinyl alcohol was developed by

 Table 12
 Antimicrobial effectiveness of diverse biopolymer-based materials containing graphene oxide

| Polymer matrices                         | Nanomaterial   | Size of nanomaterial (nm)                             | Active against<br>bacterial species   | Possible mechanism of action  | Ref. |
|--|--|---|---|---|------|
| Chitosan                                 | (a) Graphene oxide<br>(b) ZnO NPs  | _   | S. aureus, E. coli  | Active superoxide ions<br>generated on the surface of the<br>oxide reacts with the peptide<br>linkages in the cell wall of<br>bacteria and thus disrupt   | 168  |
| Chitosan                                 | (a) ZnO NPs<br>(b) Graphene oxide  | _   | E. coli, K. pneumonia,<br>S. aureus, S. mutans,<br>Salmonella, P.<br>aureginosa | Ions of nanomaterials<br>deactivate cellular enzymes,<br>DNA and proteins by reacting<br>with electron-donating groups<br>interfering with respiratory<br>sequence and leading to cell<br>death | 169  |
| Polylactic acid                          | (a) ZnO NPs<br>(b) Graphene oxide  | (a), (b) 1–5 nm<br>thickness, 4–8<br>number of layers | E. coli, B. cereus,<br>S. cerevisiae  | _   | 170  |
| Polylactic acid                          | (a) ZnO NPs<br>(b) Graphene oxide  | _   | S. aureus, E. coli  | Inactivation of cell due to<br>direct contact between ZnO<br>and bacteria. Adhesion of GO<br>sheets to the surface cells,<br>covering them and inhibiting<br>cell proliferation                 | 171  |
| Polyvinyl alcohol                        | (a) Cu <sub>2</sub> O NPs<br>(b) Reduced graphene<br>oxide<br>(a) TiO <sub>2</sub> NPs | _   | P. aureginosa, S. aureus,<br>S. oralis, E. coli                                 | Generation of reactive oxygen<br>species due to light irradiaton  | 172  |
| Polyvinyl alcohol                        | (a) Ag NPs<br>(b) Graphene oxide   | _   | S. aureus, E. coli  | Chemical oxidation based on<br>the oxidation of cellular<br>components by GO sheets   | 173  |
| Polyvinyl alcohol<br>blended with starch | (a) Ag NPs<br>(b) Graphene oxide<br>(b) Graphene oxide                                 | _   | S. aureus, E. coli  | _ ` `   | 174  |

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Moustafa et al. (2023).<sup>170</sup> The sensor showed rapid response and recovery times (2.6 s/3.5 s), making it promising for quick and accurate humidity detection in intelligent food packaging. Also, the inhibition rate of polylactic acid films against E. coli, B. cereus, S. cerevisiae<sup>171</sup> and S. aureus<sup>172</sup> have been reported to be increased by the incorporation of GO and ZnO NPs. Dhanasekar et al. (2018)<sup>173</sup> highlighted the remarkable bacteriostatic properties of a polyvinyl alcohol film infused with graphene oxide, coupled with either Cu<sub>2</sub>O or TiO<sub>2</sub>. This innovative film exhibited significant effectiveness against bacterial strains such as S. aureus, Streptococcus oralis, E. coli, and P. aeruginosa when exposed to UV light. Another report stated that the addition of GO and Ag NPs conferred antibacterial activity against S. aureus and E. coli to polyvinyl alcohol films.<sup>174</sup> Usman et al. (2016),<sup>175</sup> compared the antimicrobial effectiveness of different composites based on polyvinyl alcohol, graphene oxide, starch and Ag NPs. The authors observed that composite films showed antibacterial activity, with rankings in ascending order: PVA/GO, PVA/Ag, PVA/GO/Ag, and PVA-GO/Ag/Starch. In another report, a dual-purpose sensor based on polylactic acid and graphene oxide successfully detected biogenic amines in food spoilage, providing increased color intensity with analyte concentration and sensitive quantification at low limits of detection (LOD), specifically 0.07 pM for putrescine and 0.02 pM for cadaverine.176

The mechanism by which GO nanoparticles inhibit bacterial growth can be explained through (a) physical interactions between the bacterial cell and the nanoparticles. This interaction manifests through direct contact with the basal planes or sharp edges of the graphene material, or through the envelopment of bacteria with nanosheet; (b) physical demolition and chemical oxidation of the cell membrane and cell wall of microorganisms, achieved by the generation of reactive oxygen species (ROS), culminating in microbial death and a subsequent reduction in microbial resistance.<sup>173</sup>

Safety and toxicity concerns. Graphene and its derivatives exhibit remarkable properties, including excellent dispersibility and stability in human physiological environments, rendering them highly promising for diverse applications. Nevertheless, investigations into the toxicity of graphene derivatives in human biological organisms have yielded inconclusive results. For example, in a study by Yang et al. (2013),<sup>177</sup> biodistribution and toxicological analyses of nanographene oxide were conducted in mice through oral and intraperitoneal administration routes. The researchers observed that the graphene derivatives were not adsorbed by the organs but were readily excreted. However, they emphasized that toxicity would be dependent upon factors such as surface coating, size, and routes of administration. Furthermore, in a study by Liu et al. (2012),<sup>178</sup> the impact of size and dose on the biodistribution of graphene oxide (GO) in mice was investigated. Their findings indicated that GO particles ranging between 1 and 5 µm accumulated in the lungs, while those sized between 110 and 500 nm accumulated in the liver. Consequently, they concluded that graphene oxide may not be suitable for human use. In contrast, Nguyen et al. (2015)179 demonstrated the low toxicity of graphene oxide against specific intestinal bacteria. Their study

revealed that cells remained unaffected across all tested concentrations of graphene oxide for 24 hours, with no observed dose-dependent cytotoxicity. Additionally, Manikandan *et al.* (2020)<sup>180</sup> concluded that PHB/graphene nanocomposites exhibit a negligible cytotoxic effect. Considering these findings collectively, the safety assessment of graphene derivatives remains in its early stages, highlighting the need for further research efforts.

#### Cellulose nanocrystals

To enhance barrier and functional properties of polymers. Cellulose stands as the most extensively distributed and prevalent polysaccharide in nature<sup>181</sup>. Nanocellulose refers to cellulose structured at nanoscale dimension.182 This can include cellulose nanofibers (CNF), cellulose nanocrystals (CNC), or bacterial nanocellulose.183 Recently, CNCs have been utilized to reinforce packaging materials, the notable improvements are mainly attributed to the interactions between CNCs and the polymer matrix as summarized in Table 13.190 Different kind of polymers have been used as the matrixes. For example, A. Anžlovar et al. (2018)<sup>184</sup> demonstrated that acetic anhydridemodified CNCs can act as reinforcement in linear low-density polyethylene (LLDPE) composites. The authors found an improvement in the compatibility between CNCs and the matrix, resulting in a 90% increase in the breaking strain of the composite. However, the introduction of CNCs influenced the crystallinity of LLDPE, which consequently restricted the reinforcing effect. Similarly, Perumal et al. (2018)185 produced CNCs from rice straw via acid hydrolysis and incorporated them into PVA/chitosan composite films for reinforcement. FTIR analysis indicated significant electrostatic interactions and hydrogen bonding between CNCs and PVA/chitosan, leading to a 130% enhancement in tensile strength. Additionally, the resulting composites also exhibited superior barrier properties. Furthermore, El Achaby et al. (2017)<sup>186</sup> formulated a composite film using CNCs, PVA, and carboxymethyl cellulose (CMC) through solvent casting. They observed an 82% increase in tensile strength for the optimized product, coupled with an 81% reduction in water vapor permeability. Remarkably, the film retained approximately 90% optical transparency. Moreover, Yadav et al. (2019)187 demonstrated that CNC into ĸcarrageenan/glycerol films reduced water vapor permeability by 52%. Another study found that the addition of 5% of CNC into chitosan-based films enhanced by 26% and 27% in mechanical properties and water vapor permeability, respectively.188 Additionally, a chitosan-CNC composite film was fabricated through covalent linkage, using CNC isolated from eucalyptus wood pulp. The resulting film exhibited a substantial enhancement in mechanical properties (150%).189

As antimicrobial agents. To date, several semicrystalline polymers, including polycaprolactone, polyamide, and polylactic acid, have been reinforced through the addition of CNC. However, CNC lacks intrinsic antibacterial properties, restricting its application in functional packaging. Furthermore, most studies have predominantly investigated the mechanical behavior of CNC in polymer matrices, with limited research on Table 13 Packaging materials containing cellulose nanocrystals in food packaging technologies

| Food packaging material                                      | Main finding  | Ref. |
|--|---|------|
| Low density poly(ethylene)                                   | The addition of acetic anhydride-modified CNCs increased composites' stiffness and strain at  | 184  |
| Polyvinyl alcohol blended<br>with chitosan                   | break by 20% and up to 90%, respectively. Further, Young modulus increased by $\sim$ 45% Composite films increased tensile strength (98.16 MPa) and thermal stability   | 185  |
| Polyvinyl alcohol blended<br>with carboxymethyl<br>cellulose | The tensile modulus and strength were markedly enhanced (141% and 83%, respectively) by the addition of 5 wt% CNC. Additionally, water vapor permeability was reduced by 87% while composites maintained the same transparency level                                      | 186  |
| k-carrageenan  | Incorporation of CNCs increased the tensile strength and elongation at break of films (from $38.33 \pm 3.79$ MPa to $52.73 \pm 0.70$ MPa and from $21.50 \pm 3.72\%$ to $28.27 \pm 2.39\%$ , respectively). Additionally, water vapor permeability of the films decreased | 187  |
| Chitosan   | Improvement of 26% in films' tensile strength was achieved by the addition of 5% (w/w) CNCs. In addition, water vapor permeability of the composite decreased by 27%  | 188  |
| Chitosan   | Chitosan films reinforced with functionalized cellulose nanocrystals demonstrated a remarkably improvement in tensile strength (up to 150%), while achieving a considerable decrease in hydrophilicity  | 189  |

modifying the functional properties of CNC composites. In this context, Meng et al. (2023)<sup>191</sup> enhanced the antibacterial properties of polyvinyl alcohol by incorporating quaternized cellulose nanocrystals as nanofillers. The composite film achieved 100% bactericidal efficiency against E. coli and S. aureus. Moreover, Huang et al. (2023)<sup>192</sup> used methacrylamide, cetyltrimethylammonium bromide, and zinc oxide to modify CNCs, and investigated their effect in polylactic acid films. S. aureus and E. coli were effectively inhibited, and the shelf life of packaged pork samples was effectively extended from 3 days to 10 days. Likewise, Leite et al. (2020)<sup>193</sup> explored the antimicrobial activity of gelatin films incorporating rosin-grafted cellulose nanocrystals. Authors highlighted that E. coli and S. aureus growth were effectively inhibited by using this composite. Additionally, Costa et al. (2021)<sup>194</sup> developed chitosan/cellulose nanocrystals films via solvent casting method. The films were designed as active pads in order to extend the shelf life and

maintain the quality of meat. Overall results showed and effective supress effect on the growth of *Pseudomonas* and Enterobacteriaceae bacteria during the initial storage period. In another study, a remarkably inhibitory effect against *L. monocytogenes* was observed in corn starch/chitosan-based films when a concentration of 0.5% CNCs was added.<sup>195</sup> The various applications of cellulose nanocrystals as antimicrobial agents in different polymers are summarized in Table 14.

**Safety and toxicity concerns.** Manufacturing of CNCs offers excellent properties that make them promise for food-related applications. However, being a nanoscale derivative, CNCs still possess unknown properties that could potentially expose humans and the environment to unforeseen risks.<sup>190</sup> Recent evaluations have focused on the health and safety aspects of CNCs. It was suggested that studying the gastrointestinal processing of CNCs was important to assess the associated safety concerns. In this context, Koshani and Madadlou (2018),<sup>196</sup>

Table 14 Antimicrobial effectiveness of diverse biopolymer-based materials containing cellulose nanocrystals

| Polymer matrices                   | Nanomaterial                          | Size of nanomaterial<br>(nm)                    | Active against<br>bacterial species | Possible mechanism of action   | Ref. |
|------------------------------------|---------------------------------------|---|-------------------------------------|--|------|
| Polyvinyl alcohol                  | Quaternized cellulose<br>nanocrystals | $150 \pm 20~ m nm$ length $6 \pm 1~ m nm$ width | S. aureus, E. coli                  | _  | 191  |
| Polylactic acid                    | Modified CNCs                         | _   | S. aureus, E. coli                  |  | 192  |
| Gelatin                            | Rosing-grafted CNCs                   | _   | S. aureus, E. coli                  | Increased permeability and<br>leakage of cytoplasm due to<br>the interaction of rosing<br>grafted CNCs with the<br>phospholipid cell membrane            | 193  |
| Chitosan                           | CNCs                                  | ~75 nm diameter                                 | S. aureus, E. coli,<br>C. albicans  | Cell membrane damage due to<br>direct contact with rodlike<br>CNCs particles making<br>microbial cells susceptible to<br>protonated chitosan             | 194  |
| Corn starch mixed<br>with chitosan | CNCs                                  | _   | L.<br>monocytogenes,<br>S. aureus   | Damage to the structural<br>integrity of the cell membrane<br>due to the interaction of<br>nanoparticles and bacteria <i>via</i><br>electrostatic forces | 195  |

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highlighted that CNCs are indigestible and could interact with the gut microbiome in the distal ileum and colon. These interactions might influence microbiome metabolism, though the implications of these effects remain uncertain in terms of whether they are beneficial or harmful. Likewise, Ni et al. (2012)<sup>197</sup> evaluated the cytotoxicity of cellulose nanowhiskers using L929, while Dong et al. (2012)198 assessed cytotoxicity with nine different cell lines of CNC. Both studies concluded that CNCs demonstrated low cytotoxicity potential. In recent years, cellulose has been classified as a GRAS substance by the FDA. However, as of now, there is no common regulation for nanocellulose, particularly for CNC, in the EU. In 2018, the European Food Safety Authority (EFSA) published guidance on assessing the safety of nanoscience and nanotechnology applications.<sup>199</sup> This guidance outlines strategies for characterizing risks and analysing uncertainties, aiming to offer suggestions for future CNC research.

#### Lipid nanoparticles

To enhance barrier and functional properties of polymers. The concept of lipid nanoparticles is related to utilizing lipids derived from various sources such as animal and vegetable fats, waxes, fatty acids, and acylglycerols, engineered into nanoscale dimensions.<sup>200</sup> Recent studies have demonstrated that lipid nanostructured materials possess several beneficial properties that can be effectively used to enhance the properties of food packaging. In this context, research findings indicate that the incorporation of solid-lipid nanoparticles (SLNs) into xanthan gum remarkably improves several properties such as mechanical strength, thermal stability and water vapor permeability of the films.<sup>201</sup> Similarly, M. L. Zambrano-Zaragoza et al. (2013)<sup>202</sup> developed an edible coating by incorporating SLNs into xanthan gum in order to extend shelf life of guava fruits. Overall results showed a reduced weight loss, lower respiration rates and minimal change in greenish color of guava fruits when stored under refrigeration conditions for 30 days. Moreover, addition of candeuba wax SLNs into xanthan gum enhanced the mechanical strength of films by improving tensile strength, elongation and elastic modulus. The resulting system also extended the shelf life of tomatoes (12 °C for 26 days) by maintaining its firmness and controlling parameters such as pH, acidity, soluble solids, colour changes and antioxidant properties.<sup>203</sup> Moreover, incorporating solid-lipid nanoparticles (SLNs) into protein (β-lactoglobulin)-based edible films demonstrated a significant reduction in water vapor permeability while enabling control over mass transfer.<sup>204</sup> Similar results were obtained when beeswax-based solid-lipid nanoparticles were incorporated into xanthan gum for food packaging applications. The developed coating effectively reduced weight loss and decaying rate, preserved firmness and minimized colour changes, which in overall aided in enhancing the shelf life of strawberries during refrigerated storage at 4 °C for up to 21 days.<sup>205</sup> The diverse applications of nanostructured lipid in food packaging systems are summarized in Table 15.

As antimicrobial agents. Various lipid-based nanostructures including liposomes, solid lipid nanoparticles, nanostructured lipid carriers, and nanoemulsions have been acknowledged for their role in enhancing the preservation of food packaging by improving the antimicrobial activity and acting as effective carriers for releasing natural antimicrobial agents.111 The various applications of lipid nanoparticles to different food packaging systems are summarized in Table 16. For example, an agar-based edible film incorporating nanoliposomes loaded with medicinal plant extract (Artemisia annua oil) and chitosan can effectively preserve cherry tomatoes by inhibiting E. coli O157:H7.206 Furthermore, nanoemulsion-based edible coating loaded with citrus essential oil and chitosan nanoparticles was developed for seafood packaging purposes. The resulting system effectively extended the shelf life of silvery pomfret from 12 to 16 days by preventing lipid oxidation and inhibiting microorganisms' growth.207 Similarly, L. Salvia-Trujillo et al. (2015)<sup>208</sup> developed a sodium alginate-based antimicrobial edible coating incorporating lemongrass essential oil nanoemulsion in order to preserve fresh-cut apples. The system effectively inhibits the growth of Escherichia coli, while maintaining firmness, reducing respiration rate and browning, and improving overall quality attributes. Similarly, the incorporation of oleic acid nanoemulsion (OAN) loaded with natural antimicrobials (lactic acid, nisin and lauric alginate) into starch-based coatings significantly inhibited Brochothrix thermosphacta, Listeria monocytogenes Scott A, and Micrococcus luteus. Additionally, the OAN offered stable suspension and high optical clarity in the coating.209

**Safety and toxicity concerns.** The widespread adoption of lipid nanoparticles for food-related applications faces

 Table 15
 Packaging materials containing lipid nanoparticles in food packaging technologies

| Food packaging material                 | Main finding   | Ref. |
|---|--|------|
| Xanthan gum                             | Improvement of flexibility and strength of the films was achieved by the addition of 60–75 g $L^{-1}$ solid lipid nanoparticles                                | 201  |
| Xanthan gum                             | Addition of solid lipid nanoparticles improved shelf life of guava fruit by showing lowest range of weight loss and delaying the maturation process            | 202  |
| Xanthan gum                             | Composite films exhibited improved barrier properties  | 203  |
| Proteins                                | Incorporation of solid lipid nanoparticles led to a remarkably decrease in water vapor<br>permeability of the film   | 204  |
| Xanthan gum mixed with propylene glycol | The composite films exhibited appropriated properties (decreased decay rates, less fungal growth and weight loss) in order to enhance strawberries' shelf life | 205  |

 Table 16
 Applications of lipid-based nanostructures in food packaging systems

| Types of<br>nanolipid | Desing of packaging material content                      | Types of packaging | Food products          | Properties  | Ref. |
|-----------------------|---|--------------------|------------------------|---|------|
| Nanoliposome          | Agar/ <i>Artemisia annua</i><br>oil/chitosan              | Edible film        | Cherry tomato          | Cellular leakage and alterations in cell<br>membrane permeability resulting from<br>the release of large molecular substances                     | 206  |
| Nanoemulsion          | Citrus essential oil/<br>chitosan nanoparticles           | Edible coating     | Silvery pomfret        | Inhibited microbial proliferation and<br>decreased oxidation of proteins and<br>lipids  | 207  |
| Nanoemuslion          | Sodium alginate/<br>lemongrass<br>essential oil/tween 80  | Edible coating     | Fresh-cut apple        | Extended the shelf life of apples by<br>exhibiting antimicrobial properties,<br>lowering respiration rates, and<br>decreasing ethylene production | 208  |
| Nanoemulsion          | Starch/oleic acid/lactic<br>acid/nisin/lauric<br>alginate | Edible coating     | Fresh-cut<br>pineapple | Suppresses microbial growth while<br>reducing the respiration rate and<br>mitigating changes in color   | 209  |

limitations due to insufficient understanding and undisclosed properties regarding safety. There are concerns about potential toxicity related to prolonged storage times, which could adversely impact human health. Furthermore, the potential toxicity of these nanoparticles depends on factors such as particle size, bioavailability, biocompatibility, and the amount used. Therefore, the incorporation of lipid nanoparticles into food systems should adhere to specified limits as described by standard bodies or regulatory agencies. Metal and inorganic nanoparticles are non-digestible and can potentially be absorbed directly into epithelial cells, where they may accumulate, be metabolized, or transported through the bloodstream. If these particles are transported from epithelial cells, they can circulate throughout the body, leading to metabolic reactions, excretion, and potential accumulation in specific tissues. However, unlike metal and inorganic NPs, lipid nanoparticles have not been observed to undergo direct absorption in the gastrointestinal tract to date.<sup>210</sup> However, there is a possibility of encountering similar occurrences when non-digestible oils are employed for encapsulating bioactives in the production of lipid nanoparticles. Additionally, particle aggregation may occur due to factors such as size, shape, charge, composition, and interfacial chemistry. The presence of lipid nanoparticles in the mouth, stomach, and small intestine could disrupt normal gastrointestinal tract functions due to their smaller size, extensive surface area, and elevated surface energy. This could potentially lead to toxicity concerns, as their behaviour differs significantly from that of microlipids.<sup>211,212</sup> Furthermore, the inclusion of organic solvents and certain components such as surfactants could pose potential toxicity risks, as these substances are necessary during the production of nanostructured lipids. However, most of the organic solvent typically evaporates during drying, although minimum amounts may remain in the final product. Therefore, it is important to understand the potential toxic effects of the chemicals employed in nanostructured lipids fabrication before their application. Nevertheless, based on the aforementioned discussion, further research on different forms of nanolipids is required to

comprehensively explore all aspects of these nanomaterials and their potential impact on human health when consumed through food and beverages.

## Regulations of nanomaterials in food packaging

Guidelines from regulatory bodies offer secure routes for manufacturers, importers, and consumers to safeguard food products' safety in the market.213 However, globally, the absence of established regulations for nanotechnology applications persists due to the scarcity of comprehensive and dependable fundamental research concerning the safety assessment and migration properties of nanomaterials from packaging into the food system.24 In certain countries, nanomaterials are permitted for use in Food Contact Materials (FCMs), whereas in others, their usage is prohibited due to concerns regarding potential toxicity as illustrated in Table 17.214 The Food and Drug Administration (FDA) oversees the use of nanomaterials in food packaging within the United States. Manufacturers of nanomaterials must secure pre-market approval from the FDA, either through a Food Additive Petition (FAP) or the Food Contact Notification (FCN) system. However, substances deemed Generally Recognized as Safe (GRAS) are exempt from this premarket authorization requirement. Additionally, if an organization publishes a scientific risk assessment of its product in a peer-reviewed scientific journal, it may market the product without prior FDA approval.<sup>219</sup> The regulation of packaging materials including nanomaterials in Europe falls under the review of the European Union, governed by regulation EC 1935/2004. This regulation permits their use in food packaging as long as they do not pose a risk to human health, as outlined in Article 3. Furthermore, according to Article 23 of regulation EC 10/2011, packages containing nanoparticles must undergo evaluation before entering the market, in accordance with the Novel Food Regulation EC 258/97. Additionally, the regulation of nanomaterials, even if previously authorized in bulk form, is necessary under EEC 89/109. In cases where non-authorized

| Table 17 | Applications and regulations of selected nanomaterials used in food packaging |  |
|----------|---|--|
|----------|---|--|

| Nanomaterial         | Applications   | Current<br>status                  | Used in                              | Commercially available products   | Note  | Ref.           |
|----------------------|--|------------------------------------|--------------------------------------|---|---|----------------|
| Ag                   | Utilized as<br>preservatives,<br>antimicrobials,<br>antibiotics, and<br>antistatic agents                | FCS<br>inventory <sup>a</sup>      | Reusable<br>food<br>containers       | Nano-silver baby milk<br>bottle<br>Silver-nano noble one-<br>touch mug cup<br>Fresh food containers (OSO<br>Fresh®)<br>Nano-silver NS-315 water<br>bottle<br>Nano-silver salad bowl<br>FresherLonger™ Miracle<br>Food Storage<br>FresherLonger™ Plastic<br>Storage Bags | FCN no. 1235. (<4 ppm<br>by weight of silver as an<br>antimicrobial agent<br>blended into polymers) | 214 and<br>215 |
| TiO <sub>2</sub>     | It is utilized as a color additive   | Not subject<br>to<br>certification |                                      | 0 0   | Less than 1% by weight of the food  | 216            |
| ZnO                  | Utilized as an additive<br>for UV filtering,<br>antimicrobial purposes,<br>and as a fungistatic<br>agent | GRA <sup>b</sup>                   | Plastic<br>glasses,<br>plastic films | Nano Plastic Wrap<br>(SongSing Nano<br>Technology Co., Ltd.<br>Taiwan)  | Authorized under EC<br>regulation 10/2011<br>(based on conventional<br>particle size)               | 217            |
| CuO                  | Used as a nutritional dietary supplement   |                                    |                                      |   | Approved for use in animal feed   |                |
| CNT and GO<br>sheets | Food packaging   |                                    | Films, bottles<br>for packaging      |   | There is no conclusive<br>information available<br>for the U.S at this time                         | 218            |

substances are utilized, a maximum migration limit of 0.01 mg  $\rm kg^{-1}$  must be ensured through a functional barrier, as specified in Article 14, EC 450/2009.^220

## Limitations and challenges of nanomaterials in food packaging

Numerous challenges must be addressed before nanotechnology can revolutionize product development and processes in food-related applications. The main challenge is the creation of edible delivery systems through cost-effective processing techniques, ensuring formulations that are both effective and safe for human consumption.<sup>221</sup> Ensuring food safety involves addressing concerns about nanoparticles leaching and migrating from packaging materials into food products. Nanomaterials, whether added directly or indirectly, can sometimes be isolated due to migration from other sources.<sup>222</sup> At the nanoscale, materials exhibit distinct behaviors, and our current understanding of analyzing these phenomena remains limited. A comprehensive understanding of the functional aspects and toxicity of nanomaterials at the nanoscale will significantly enhance the practical applications and safety standards of nanotechnology. The potential risks, toxicity issues, and environmental concerns associated with nanoparticles must be acknowledged. Nanoparticles can pass the biological barriers and permeate various tissues and organs. Moreover, the synthesis of nanoparticles through diverse chemical methods

can produce harmful non-eco-friendly by-products that lead to significant environmental pollution.<sup>223</sup> Hence, it is relevant to establish a comprehensive risk assessment program, regulatory frameworks, and biosecurity measures, and address public concerns before manufacturing, packaging, and consuming nano-based food products. Additionally, both *in vitro* and *in vivo* studies on nanoparticle interactions with living organisms are essential before commercial application, especially in the production of antibacterial nanoparticles that are environmentally friendly.<sup>224</sup>

## The trend of research in food packaging

The evolution of food packaging has been driven by continual adaptations to meet the evolving demands of the food industry. Today, the significance of food packaging rivals that of the contents it safeguards, primarily by extending shelf life and reducing waste during transportation, storage, and distribution. However, the growing demand for packaging, predominantly produced from materials that pose potential environmental hazards, underscores a critical opportunity for research into eco-friendly alternatives.

Transitioning to environmentally sustainable packaging materials presents challenges, foremost among them being the need to meet current industry standards and demands. Key considerations include economic viability, ecological sustainability, and the ability to uphold essential physical and chemical properties that prolong product freshness and quality. Moreover, modern packaging should incorporate interactive and intelligent features to inform consumers about product freshness and quality, while also being aesthetically pleasing and potentially offering added consumer benefits through active ingredients.

In response to these demands, recent studies in nanotechnology have focused on developing composite materials based on biopolymers. These materials are enhanced with nanoparticles and micro/nanostructures in precise combinations to impart the requisite physicochemical and biological properties demanded by the food industry. Such research represents a fraction of ongoing efforts aimed at transitioning towards advanced, environmentally friendly packaging solutions.

### Conclusions

The increasing focus on health, nutrition, and food safety, along with growing global food demand, has fueled interest in exploring nanotechnology for enhancing food quantity and quality. Metal nanoparticles like silver (Ag), zinc oxide (ZnO), titanium dioxide (TiO<sub>2</sub>), copper oxide (CuO), and nanomaterials such as carbon nanotubes and graphene oxide are widely used in food preservation. Integrating them into various polymer matrices, including biopolymers, enhances properties and functionality, making nanotechnology invaluable in the food industry. Hence, incorporating metal-based nanoparticles into functional food packaging enhances biological properties, including antioxidant and antimicrobial activities. It also improves the mechanical, physical, barrier, and optical characteristics of the material, ensuring food safety, preserving nutritional value, and extending shelf life. Furthermore, nanotechnology enables real-time monitoring during production, allowing for the development of smart packaging systems for continuous monitoring of food quality and safety throughout the supply chain. Indeed, while nanomaterials hold promise in the food sector, it's essential to assess both their benefits and risks. Addressing biosafety concerns and establishing regulatory frameworks present challenges that require thorough research. Ensuring safety and regulatory compliance is important for the successful integration of these materials into the food packaging industry.

### Data availability

This study constitutes a scientific review and does not include original experimental data or other unpublished information. The images included in this manuscript are original creations, while the tables were compiled from cited references. Consequently, this manuscript does not contain supplementary electronic materials.

### Author contributions

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### Conflicts of interest

The authors declare no competing interests.

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