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Metal oxide nanoparticles for safe active and intelligent food packaging

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20 ABSTRACT

21 *Background:* Food safety and food security remain the major concern of consumers and the
22 food industry. Bacterial contamination continues to be a crucial food safety issue. Smart
23 packaging incorporates both active and intelligent components. Intrinsic antibacterial activity,
24 oxygen and ethylene scavenging (active) and the sensing (intelligent) properties of metal oxide
25 nanoparticles are in research focus for application in smart food packaging, especially bio-
26 nanocomposite films.

27 *Scope and approach:* Metal oxide nanoparticle properties are closely linked to their morphology
28 resulting from the synthesis process. In this review, we cover current innovative synthesis
29 methods for obtaining metal oxide nanoparticles and current incorporation techniques used to
30 obtain smart (active and/or intelligent) packaging, focusing on bio-nanocomposites, commonly
31 used metal oxides and future mixed metal or doped metal oxides. Taking into account safety,
32 we focus on current legislation, and methods for risk assessment due to particle release from
33 the packaging material and a summary of cytotoxic studies of metal oxide nanoparticles on
34 human cells and the gut microbiota.

35 *Key findings and conclusions:* Antimicrobial effectiveness of metal oxide nanoparticles is
36 highly dependent on morphology as a result of the synthesis method. Solution casting and
37 electrospinning are innovative methods applied to synthesize metal oxide incorporated
38 biopolymer films for active packaging with improved mechanical and barrier properties
39 combined with active components (antimicrobial, ethylene scavenging). Metal oxides show
40 sensitivity and selectivity to most gases produced during food spoilage. In selection of metal
41 oxide for smart packaging, particle migration and cytotoxic activity are key issues requiring
42 careful and detailed characterization.

43	Table of content	
44	1. Introduction	3
45	2. Legislation	6
46	3. Synthesis and antimicrobial properties of metal oxide NPs	7
47	3.1. ZnO nanoparticles	7
48	3.2. TiO ₂ nanoparticles	8
49	3.3. Other metal oxide nanoparticles	9
50	4. Nanoparticle-biopolymer composites for active packaging	10
51	4.1. Incorporation of metal oxide NPs in packaging films	11
52	5. Nanoparticle migration from nanocomposites and food stimulants	13
53	6. Antimicrobial mechanisms of metal oxide nanoparticles	13
54	7. Antiviral activity of metal oxide nanoparticles	17
55	8. Toxicity of metal oxide nanoparticles	17
56	9. Oxygen and ethylene scavenging and moisture absorption in active packaging	20
57	10. Intelligent packaging – application of metal oxide NPs in food safety sensors	22
58	11. Conclusions	23
59		

60 1. Introduction

61 The food industry is under constant and crucial pressure to provide appetizing and safe
62 food products. To satisfy these consumer demands, the food industry regularly improves both
63 the food quality and packaging technology. Food packaging is essential in maintaining the
64 safety and quality of products from processing and manufacturing, through handling and
65 storage until it reaches the consumers. Petroleum-based plastic materials (like polyethylene
66 terephthalate, polypropylene, polystyrene) are usually used to envelop food in order to protect
67 its content from contamination and spoilage and to facilitate its transport and storage. However,
68 plastic materials cannot fully protect food from the environment and, thus, cannot completely
69 ensure product quality and safety. In addition, plastic undergoes continuous fragmentation, and
70 may create micro- and nano-plastics that have potential toxic impacts on human health. Plastic
71 pollution has increased due to the COVID-19 pandemic (Silva, et al., 2020). To improve plastic
72 inability to stop light, oxygen and other gases from penetrating and reaching the consumables

73 and causing their degradation, as well as to prolong shelf-life of food and protect human health,
74 novel materials are employed to envelop food products.

75 Starting from the beginning of the twentieth century, three main approaches have been
76 applied to improve food packaging. The first approach consists in improving plastic polymers
77 by mixing them with other materials. Doping or formation of nanoparticle-polymer composites
78 improves mechanical properties of the packaging material, which can enforce the temperature
79 and humidity resistance properties or improve oxygen barriers (Khajavi, et al., 2020).
80 Biopolymers, as ecologically sound “green” materials often suffer from degradation and
81 mechanical issues so application of these materials in food packaging can be accomplished in
82 the form of nanocomposites. The second approach aims to develop “active packaging” in which
83 particles added to the packaging material interact directly with food and protect it from UV,
84 oxygen, ethylene or microbiological contamination (Rai, et al., 2019; Vilela, et al., 2018).
85 Active packaging systems can be classified as active scavenging systems (absorbers) that
86 remove undesired elements from the product, such as moisture, carbon dioxide oxygen,
87 ethylene and odour and active releasing systems (emitters) that release into the packaging in
88 the form of antioxidants, carbon dioxide or antimicrobial compounds (Yildirim, et al., 2018).
89 Finally, the third approach develops “intelligent packaging”, which allows real-time monitoring
90 of food safety (Müller & Schmid, 2019; Rai, et al., 2019). For this, sensing elements are
91 combined with the packaging material to transform the food envelope into a miniaturized device
92 for tracking. Intelligent packaging may provide monitoring of food freshness and quality, its
93 storage condition, and, in that way, improve safety and convenience, and help to extend food
94 shelf-life. Thus, enhanced functionality of food packaging is obtained by smart packaging that
95 includes both active and intelligent components, as shown in Fig. 1.

96 Nanomaterials and nanoparticles are used in the development of all three advanced
97 packaging approaches. Adding nanomaterials including nano-metal oxides to different
98 polymers to form nanocomposites can make packaging lighter, stronger and less permeable (Y.
99 Huang, Mei, Chen, & Wang, 2018). Nanomaterials with an intrinsic antimicrobial activity
100 incorporated in active and intelligent packaging contribute to extending the shelf-life of
101 products by keeping food safe from harmful and spoilage bacteria, fungi and viruses, and by
102 providing freshness during longer storage time. Metal oxide nanoparticles (NPs) have unique
103 properties and morphology and a great potential for application in food industry NPs in
104 nanocomposite packaging can perform oxygen and ethylene scavenging and UV- blocking as
105 part of active packaging functions contributing to extending the product shelf life (Gaikwad,
106 Singh, & Lee, 2018; Gaikwad, Singh, & Negi, 2020).

107 The objective of this review is to provide an overview of the methodologies and
108 procedures carried out in earlier literature on the development of active and intelligent
109 packaging utilizing metal oxide nanoparticles. As the physicochemical properties of
110 nanoparticles and their stability in nanobiocomposites are essential for the development of
111 packaging films we describe the state-of-the art techniques for nanoparticle synthesis,
112 characterization and incorporation in polymers. Antibacterial properties of active packaging
113 containing metal oxides and current available data on the antiviral aspect is presented.
114 Antifungal and antiviral activities, also significant for food protection, are briefly mentioned.
115 To point out that the cytotoxicity of nanoparticles is the main barrier for their applications in
116 food packaging, we provide a condensed assessment of toxicity of metal oxide nanoparticles at
117 the level of cells, mucus and microbiota. It is noteworthy that new regulations, consumer
118 attitudes and acceptability, the societal involvement and impact, have been comprehensively
119 described in some recent reviews (Garcia, Shin, & Kim, 2018; Omerović, et al., 2021). Finally,
120 an overview of the current research covering the potential for utilizing metal oxide

121 nanoparticles in smart packaging for oxygen and ethylene scavenging, moisture control and in
122 food safety sensors is also given.

123 **2. Legislation**

124 The active packaging technology is defined in the European regulations as “*new types*
125 *of materials and articles designed to actively maintain or improve the condition of the food*”
126 (1935/2004/EC) and as “*deliberately incorporate components that would release or absorb*
127 *substances into or from the packaged food or the environment surrounding the food*”
128 (450/2009/EC). The intelligent packaging technology is “*designed to monitor the condition of*
129 *the food*” (1935/2004/EC). Both technologies are closely linked to the development and
130 research in nanotechnology. Although the European Food Safety Authority’s (EFSA) estimates
131 that the most common agri-food applications of nanomaterials are in active packaging (as
132 nanofillers to endow composite films) and as additives, the approval procedures for particular
133 nanoparticles are long and on a case-by-case basis. This arises mainly from the lack of validated
134 risk assessment protocols for food packaging. In other countries, especially in North America
135 and Asia Pacific, that dominate the field, the legislation bodies have provided a set of legal
136 frames for food sector applications of nanomaterial based active and intelligent packaging. The
137 commercialization of active and intelligent packaging in Europe is far behind markets in Japan,
138 USA and Australia, where these products are treated within conventional legislation for food
139 contact materials. The increasing demand of the food industry and the rise in acceptance among
140 consumers for packaging solutions based on emerging nanotechnologies is reflected by the
141 predicted revenue of about \$15 billion in 2020.

142 The ongoing global spread of a pandemic caused by SARS-CoV-2 has enhanced
143 development of active packaging that aims to prevent the transmission of the virus in order to
144 protect consumers. For this, packaging film is covered with an external active coating layer

145 based on nanoparticles or nanoparticles embedded in a polymer matrix (Imani, et al., 2020;
146 Mizielińska, Nawrotek, Stachurska, Ordon, & Bartkowiak, 2021).

147 **3. Synthesis and antimicrobial properties of metal oxide NPs**

148 Incorporation of metal oxide NPs in food packaging leads to improved mechanical,
149 thermal and barrier properties combined with excellent antimicrobial activity. The synthesis
150 method greatly influences properties of NPs including their antimicrobial and cytotoxic effects
151 (Y. Huang, et al., 2018; Stankic, Suman, Haque, & Vidic, 2016). NPs due to their small size
152 have a larger surface area per mass, thus a larger number of active surface states available for
153 reaction with foodborne pathogens. These interactions are greatly affected by the size, shape
154 and crystal structure of the NPs. Zinc oxide (ZnO) and titanium dioxide (TiO₂) are metal oxides
155 most commonly used as antimicrobial agents especially in active food packaging, but other
156 metal oxides have shown increased potential as antibacterial agents too.

157

158 *3.1. ZnO nanoparticles*

159 ZnO NPs display a large surface to volume ratio, highly crystalline structure, improved
160 mechanical properties, high thermal conductivity, and high optical absorption in the UV region
161 beneficial for interactions with bacteria. ZnO is generally recognized as a safe (GRAS) material
162 by the FDA that can be applied in the field of food and drug industry, particularly as an
163 antibacterial and antifungal agent. A broad spectrum of bacteria are sensitive to ZnO NPs (da
164 Silva, et al., 2020; Tam, et al., 2008; Vidic, et al., 2013; Zanet, et al., 2019).

165 Various methods have been used to synthesize ZnO NPs by controlling synthesis
166 parameters resulting in different ZnO particle morphologies (Fig. 2). Some examples include
167 the sol-gel method used to synthesize ZnO and Ag doped ZnO nanoparticles (Karunakaran,
168 Rajeswari, & Gomathisankar, 2011), ZnO nanorods focusing on the influence of calcination
169 temperature on structure, morphology and antimicrobial activity (Ismail, Menazea, Kabary, El-

170 Sherbiny, & Samy, 2019), co-precipitation used to obtain a flower-like morphology with high
171 antibacterial activity against *Enterococcus faecalis* and *Micrococcus luteus* in the presence of
172 visible light irradiation (Quek, Lam, Sin, & Mohamed, 2018), the ultrasonic method used to
173 synthesize ZnO NPs and investigate antibacterial activity and effect of particle size of ZnO
174 against *Escherichia coli* and *Staphylococcus aureus* (Applerot, et al., 2009), and the chemical
175 vapour based method used to synthesize ZnO, MgO and mixed ZnO-MgO NPs and investigate
176 their antibacterial efficiency to *E. coli* and *Bacillus subtilis* (Vidic, et al., 2013). Cluster-like
177 ZnO NPs were synthesized by the hydrothermal method and grown on PDA-PET substrate.
178 Growth of *Gluconobacter cerinus* was inhibited by destroying the membrane of bacterial cells,
179 while the UV protection capacity increased up to 500 fold (Cheng, et al., 2019). This method
180 was also used to prepare ZnO nanorods. Antibacterial activity against *E. coli* and *Bacillus*
181 *atrophaeus* on different substrates was investigated (Tam, et al., 2008). The hydrothermal
182 method using different stabilizing agents - polyvinyl pyrrolidone (PVP), polyvinyl alcohol
183 (PVA) and poly (α,γ , l-glutamic acid) (PGA) was used to synthesize ZnO NPs with different
184 shape and morphology (Stanković, Dimitrijević, & Uskoković, 2013). Hexagonal prismatic
185 rods (PVP), spherical (PVA) and ellipsoid (PGA) shaped particles with different sizes were
186 obtained. The highest antibacterial activity against *E. coli* and *S. aureus* was achieved
187 nanospherical ZnO particles with an average diameter around 30 nm and the largest specific
188 surface area – $25.70 \text{ m}^2\text{g}^{-1}$. Different ZnO NP morphologies were also obtained using the
189 solvothermal method. Antibacterial activity against *E. coli* and *S. aureus* was tested showing
190 that flower-like ZnO NPs had higher efficiency than rod and sphere-like shaped NPs (Talebian,
191 Amininezhad, & Doudi, 2013). ZnO has also shown exceptional antifungal properties (Q. Sun,
192 Li, & Le, 2018).

193

194 3.2. *TiO₂ nanoparticles*

195

196 TiO₂ is a well-known low cost metal oxide with high chemical stability widely used in
197 photocatalysis. As one of the most versatile compounds, TiO₂ is used in extraordinarily diverse
198 food products and technologies. However, in 2016 the EFSA highlighted the need for more
199 research on TiO₂ safety. Since this year, the EFSA no longer considers TiO₂ safe when used as
200 a food additive because they cannot rule out the genotoxicity concerns of TiO₂, nor the
201 possibility that TiO₂ after ingestion can accumulate in the body. However, TiO₂ NPs are not
202 banned from applications in the food industry. Sol-gel processing is the most common synthesis
203 method for TiO₂. TiO₂ colloids obtained using the sol-gel method combined with pectin to form
204 aerogels, have shown potential for application in food packaging (Nešić, et al., 2018). Recent
205 synthesis methods include biosynthesis (a “green” synthesis method), where TiO₂ NPs are
206 synthesized using plant extracts, showing good antibacterial activity against (Subhapiya &
207 Gomathipriya, 2018).

208 Antimicrobial performance of TiO₂ was first investigated by Matsunaga et al.,
209 (Matsunaga, Tomoda, Nakajima, & Wake, 1985). Growth of *Lactobacillus acidophilus*,
210 *Saccharomyces cerevisiae* and *E. coli* was completely inhibited when incubated with TiO₂/Pt
211 particles during photoelectrochemical oxidation. However, TiO₂ is thermodynamically
212 unstable, tends to agglomerate and is difficult to remove from a treated solution. Since TiO₂
213 photocatalyst is only active under UV irradiation at levels dangerous for human cells, irradiation
214 in the visible regime could overcome this problem. One way is doping TiO₂ or forming
215 nanocomposites. Thus, antibacterial activity of visible-light-irradiated nitrogen- and carbon-
216 doped TiO₂ against several microbials such as *Shigella flexneri*, *Listeria monocytogenes*, *Vibrio*
217 *parahaemolyticus*, *Streptococcus pyogenes*, *S. aureus*, and *Acinetobacter baumannii*, was
218 investigated, with nitrogen doping showing better bactericidal activity against microbials
219 (Wong, et al., 2006). Nitrogen-doped mesoporous titania thin films prepared by the sol-gel
220 method using Pluronic P123 as the template resulted in a reduced band gap and improved

221 visible light induced antibacterial activity against *Bacillus amyloliquifaciens* (Soni, Dave,
222 Henderson, & Gibaud, 2013).

223 3.3. Other metal oxide nanoparticles

224
225 Other metal oxides have shown increased potential for application as antimicrobial
226 agents in food packaging, such as Cu₂O NPs, MgO NPs, Fe₃O₄ NPs, FeMnO₃ and α-Fe₂O₃ NPs
227 alone or in the form of nanocomposites. Some recent examples are shown in Table 1.
228 Nanocomposites composed of metal doped metal oxides and mixed metal oxides, such as for
229 example Ag/ZnO/CuO as small amounts have achieved high antimicrobial activity (Dehghani,
230 Peighambaroust, Peighambaroust, Hosseini, & Regenstein, 2019) or CuO/montmorillonite
231 nanocomposite incorporated in chitosan film (Nouri, Yaraki, Ghorbanpour, Agarwal, & Gupta,
232 2018).

233 Table 2 presents some successful examples of active packaging systems improved with
234 various metal oxide NPs.

235 4. Nanoparticle-biopolymer composites for active packaging

236
237 Classical food protecting films are made from polymers such as polyamide (PA),
238 polystyrene (PS), polypropylene (PP), polyethylene (PE), polyvinylchloride (PVC), and
239 polyethylene terephthalate (PET) as raw materials. These plastics have been widely used because
240 of their high accessibility, low cost and good mechanical properties (Omerović, et al., 2021).
241 However, they cannot be recycled and are not completely biodegradable. Efforts have been
242 made to replace petroleum plastics with bio-based degradable materials including
243 polysaccharides (chitosan, zein, alginate, starch, carboxymethyl cellulose), poly(α-
244 hydroxyester)s, polyhydroxybutyrates (PHB), poly(glycolic acid) (PGA), polylactic acid
245 (PLA), their co-polymers poly(lactide-co-glycolide) (PLGA), poly caprolactone (PCL), and

246 polyvinyl alcohol (PVA). However, biopolymers have drawbacks as they provide poor
247 mechanical, thermal, and barrier properties.

248 Conjugation of metal oxide NPs with biopolymers in the form of nanoparticle-
249 biopolymer composites improves the mechanical and barrier properties of biopolymers and
250 provides antimicrobial properties (Fig. 3). One form is coating the packaging film with
251 antimicrobial NPs, such as TiO₂ or ZnO coated PE films (Othman, Abd Salam, Zainal, Kadir
252 Basha, & Talib, 2014; Tankhiwale & Bajpai, 2012). PE films coated with a chitosan-ZnO
253 nanocomposite achieved a high antimicrobial activity to *Salmonella enterica*, *E. coli* and *S.*
254 *aureus* (Al-Naamani, Dobretsov, & Dutta, 2016). Metal oxide NPs can also be incorporated in
255 the polymer film. Enhanced mechanical and oxygen barrier properties were achieved with ZnO
256 incorporated in PP films that depended on the concentration and shape of ZnO NPs (Lepot, et
257 al., 2011). Low density polyethylene (LDPE) films containing ZnO NPs showed high
258 antibacterial activity to *B. subtilis* (Esmailzadeh, Sangpour, Shahraz, Hejazi, & Khaksar, 2016).

259 **Some examples of active packaging with quantitatively improved mechanical and**
260 **barrier properties are given in Table 3.**

261

262 4.1. Incorporation of metal oxide NPs in packaging films

263

264 Although the number of biodegradable materials for food packaging continuously
265 increases, there is still a lack of eco-friendly packaging biocomposite with good mechanical,
266 thermal and physical properties that can be used industrially. Methods commonly used to
267 incorporate metal oxide NPs into biocomposites include solvent casting and electrospinning.

268 The solvent (solution) casting method is a well-known technique for the preparation of
269 polymer nanocomposites. Metal oxides as nanofillers and the polymer are firstly solved in a
270 solvent (Fig. 4). The metal oxide and polymer solution is mixed to achieve homogeneous
271 dispersion. This is followed by solvent evaporation and casting resulting in the formation of a

272 metal oxide polymer nanocomposite. TiO₂ NPs incorporated in a gellan gum (biopolymer) film
273 showed good antibacterial activity against *S. aureus*, *Streptococcus*, *E. coli* and *Pseudomonas*
274 *aeruginosa* (Razali, Ismail, & Amin, 2019). Zinc oxide NPs incorporated using this technique
275 into a chitosan/carboxymethyl cellulose blend (Youssef, El-Sayed, El-Sayed, Salama, &
276 Dufresne, 2016) displayed improved mechanical and thermal properties and good antibacterial
277 activity against *S. aureus*, *P. aeruginosa*, *E. coli* and *Candida albicans*, thus increasing the shelf
278 life of the tested soft white cheese. Mixed Zn-MgO NPs incorporated in alginate film prevented
279 proliferation of *L. monocytogenes* in cold smoked salmon meat (Vizzini, Beltrame, Zanet,
280 Vidic, & Manzano, 2020). Bionanocomposite films using konjac glucomannan/chitosan (KGC)
281 with nano-ZnO and mulberry anthocyanin extract (MAE) by a modified casting method (J. Sun,
282 et al., 2020a) exhibited beside improved mechanical and thermal properties of films, good UV–
283 Vis light barrier properties and relatively high pH-sensitive properties, strong antioxidant
284 activity and good antibacterial activity against *E. coli* and *S. aureus*. ZnO NPs have also been
285 utilized in soy protein isolate films together with cinnamaldehyde showing improved oxygen
286 barrier and antifungal properties (Wu, et al., 2019). ZnO-SiO₂ infused in PVA/chitosan films
287 exhibited exceptional antimicrobial properties and extending the shelf-life of bread (Al-Tayyar,
288 Youssef, & Al-Hindi, 2020)

289 Compared to other techniques used for the preparation of polymer matrices for food
290 packaging, electrospinning is a versatile technique for fabrication of nanofibers with different
291 morphologies and structures improving mechanical and thermal but also barrier properties of
292 significance for food packaging. In this process (Fig. 4) a mixture of metal oxide and polymer
293 solution is first placed into a syringe (plastic or glass) lying horizontally or vertically on a
294 pressure and solution-flow rate controlled pump. The solution is pumped through a syringe, to
295 a metallic needle connected to the electric power supply and a droplet is formed. The
296 electrospinning process starts at a critical high voltage (10-25 kV) when the formed droplet

297 changes shape to a Taylor cone and ejects an electrically charged jet. The jet within the electric
298 field is directed toward the collector with opposite charge, leading to solvent evaporation and
299 fibre formation. Although, more complex than the solvent casting method, electrospinning is a
300 well-adapted method for industrial scale applications.

301 Different metal oxides have been incorporated into biodegradable polymer matrices,
302 though most often ZnO or TiO₂. ZnO dispersed in cellulose acetate (CA) fibrous membrane
303 was prepared by the electrospinning process and showed improved water repellent properties
304 compared to pure CA membrane and a strong antibacterial activity against *S. aureus*, *E.*
305 *coli* and *Citrobacter* (Anitha, Brabu, Thiruvadigal, Gopalakrishnan, & Natarajan, 2012).
306 Nanoparticle agglomeration was suppressed and the contact area between fibres and microbes
307 was increased. ZnO NPs incorporated into ethylcellulose/gelatin nanofibers obtained by
308 electrospinning also showed excellent surface hydrophobicity, water stability and antimicrobial
309 activity against *S. aureus* and *E.coli* (Liu, et al., 2018). Hybrid electrospun nanofibers
310 composed of ZnO NPs and rosemary essential oil incorporated zein/ κ -carrageenan showed
311 good biocompatibility, and high antibacterial and antioxidant activity (Amjadi, Almasi,
312 Ghorbani, & Ramazani, 2020b). ZnO/GO nanocomposites incorporated into gelatin fibres by
313 a side-by-side electrospinning technique showed high antibacterial activity and complete
314 degradation within 7 days (H. Li, et al., 2020). High surface area electrospun zein-TiO₂
315 nanofibers improved the storage life of cherry tomatoes by absorbing ethylene (Böhmer-Maas,
316 Fonseca, Otero, da Rosa Zavareze, & Zambiasi, 2020) Electrospun zein/sodium alginate
317 nanofibers loaded with TiO₂ NPs and betanin showed good antioxidant and antibacterial
318 activity against *E. coli* and *S. aureus* (Amjadi, Almasi, Ghorbani, & Ramazani, 2020a).

319 **5. Nanoparticle migration from nanocomposites and food stimulants**

320 The antibacterial efficiency of NPs imbedded into a packaging film is usually inferior
321 of that used for film production. Cierech et al., have shown that the concentration of released
322 ZnO NPs from a nanocomposite was several times lower than the concentration of the
323 nanoparticle in the film (Cierech, et al., 2019). This parameter has to be evaluated for packaging
324 films. Migration of nanoparticles into enveloped food is a diffusion process when low molecular
325 mass particles initially incorporated in the package are released into the contained product or
326 into the space around. The release is usually experimentally measured using food stimulants
327 instead of particular food matrices. In 1985, the EC promulgated a list of food simulants that
328 can be used to test migration of constituents of plastic materials and particles intended to come
329 into contact with foodstuffs (EC, 1985). Among food simulants 95% (v/v) aqueous ethanol and
330 3% (w/v) aqueous acetic acid are frequently used. To estimate release, packaging films are cut
331 into pieces, weighed and immersed in a simulant solution. The solution is kept at a given
332 temperature (for instance, room or refrigerated temperatures) and the amount of released NPs
333 is measured regularly during the defined period of time. Such studies enable correlation of the
334 migration kinetics of NPs or their ions from the film and their antibacterial, oxygen and ethylene
335 scavenging and moisture absorption activities.

336 The migration of metal oxide NPs to food simulants takes several steps. For instance, in
337 the case of ZnO, the first step was shown to be Zn^{2+} dissociation from ZnO and diffusion
338 through the film (Espitia, et al., 2012; Petchwattana, Covavisaruch, Wibooranawong, &
339 Naknaen, 2016). Zn^{2+} ions then leave the film surface and enter into the food simulant. This
340 process of mass transferring from the film surface to the food continues until the
341 thermodynamic equilibrium is reached. Practical application of active packaging depends
342 strongly on the possibility to achieve the release of active compounds in a controlled manner.
343 Controlled release can be obtained through the design of nanoparticle-biopolymer composites,

344 method of NPs incorporation, choice of NPs shape, size, polarity, and weight, utilization of two
345 or more active compounds in the same packaging film or addition of cross-linking agents into
346 the film (Appendini & Hotchkiss, 2002). The main challenge in designing the nanobiopolymer
347 system is slowing the migration rate of active compounds to obtain prolonged activity of the
348 packaging film. Techniques utilized for the design of controlled release in active food
349 packaging have been review recently (Almasi, Jahanbakhsh Oskouie, & Saleh, 2020).

350 **6. Oxygen and ethylene scavenging and moisture absorption in active packaging**

351

352 In many cases food deterioration is caused by oxygen, ethylene or excess of moisture.
353 Active packaging systems incorporating metal oxide nanoparticles offer an advantage of
354 actively contributing to reducing food waste, by scavenging oxygen and ethylene and/or by
355 moisture absorption.

356 The presence of oxygen in packaging has a detrimental influence on shelf-life and
357 quality of packaged food, as it leads to oxidation of the product and proliferation of bacteria,
358 moulds and insects (Yildirim, et al., 2018). Iron based scavengers are most common where the
359 oxygen scavenging mechanism is triggered by moisture resulting in irreversible oxidation of
360 iron into a stable ferric oxide trihydrate complex (Gaikwad, et al., 2018). Sachets have been
361 proved effective, but the future lies in incorporation of the oxygen scavenging component into
362 packaging films, such as coated LDPE/PET films modified with $\text{FeO}(\text{OH})\cdot x\text{H}_2\text{O}$, Fe_2O_3 and
363 ascorbic acid (Wołosiak-Hnat, et al., 2019) or moisture-activated nanostructures with a Zn/ZnO
364 core-shell structure (Gomes, Ferreira, & Carvalho, 2017) or a nanocomposite based on ethylene
365 acetate containing ZnO/Fe+montmorillonite nanoparticles (Eskandarabadi, et al., 2019).
366 Another way for oxygen scavenging is UV light activation, with research focusing on TiO_2
367 bionanocomposite films (Fathi, Almasi, & Pirouzifard, 2019).

368 Ethylene (C_2H_4) is a plant growth regulator that influences/accelerates ripening and
369 senescence (Gaikwad, et al., 2020; Wei, Seidi, Zhang, Jin, & Xiao, 2020; Yildirim, et al., 2018).

370 In packed food ethylene accelerates chlorophyll degradation rates especially in leafy products
371 and causes excessive softening of fruit leading to shortening of product shelf life (Yildirim, et
372 al., 2018). In active packaging scavengers with catalytic roles are incorporated in
373 bionanocomposite films (Wei, et al., 2020). When exposed to UV or visible light the
374 photocatalytic component in the active packaging degrades ethylene to H₂O and CO₂.
375 Application of metal oxides, as photocatalytic ethylene scavengers in bionanocomposite films
376 has included TiO₂ with chitosan (Kaewklin, Siripatrawan, Suwanagul, & Lee, 2018) and TiO₂-
377 zein nanofibers (Böhmer-Maas, et al., 2020) both used to preserve and prolong the shelf-life of
378 tomatoes. Nanocomposites with TiO₂ such as Bi₂WO₆-TiO₂ incorporated into starch films can
379 perform catalytic degradation of ethylene in the visible light region (Wang, Wang, Ye, & Song,
380 2019). A degradation rate of 12.47% achieved for a film containing 4 wt.% BT. Another
381 approach is to focus on other metal oxides with photocatalytic properties in the visible light
382 region. Graphene oxide (GO) added to Bi₂WO₆ (GBW) reduced the band gap of Bi₂WO₆ and
383 was combined with starch in a nanocomposite film (J. Xie, Huang, Wang, Ye, & Song, 2020).
384 The highest reaction rate constant (9.91×10^{-4}) was achieved with 0.5% GO addition.
385 Nanocomposites of monoclinic WO₃ (band gap between 2.5 and 2.8 eV) enhanced with Pt
386 loaded on zeolite (ZSM-5) have shown good potential for ethylene removal (Kim, Jeong, &
387 Kim, 2019). The catalytic mechanism of these granules on ethylene was adsorption, migration
388 and decomposition with hydroxyl radicals due to WO₃-Pt migrating into the micropores of the
389 ZSM-5 matrix.

390 Excess moisture is not good in high water activity food such as meat and poultry
391 (Gaikwad, Singh, & Aji, 2019). Physical absorption is the working mechanism of moisture
392 absorbers that are mostly applied in the form of sachets and pads. Calcium oxide is the only
393 metal oxide used for these applications (Gaikwad, et al., 2019). Metal oxide NPs in active
394 packaging can prevent moisture or other gases entering the packed food acting as a packaging

395 barrier against water and increasing the film tensile strength (Khajavi, et al., 2020). Addition of
396 Mg doped ZnO quantum dots to zein films achieved a better barrier with a more cohesive
397 polymer network and reduced intermolecular space between chains (Schmitz, de Albuquerque,
398 Alberton, Riegel-Vidotti, & Zimmermann, 2020).

399

400 **7. Antimicrobial mechanisms of metal oxide nanoparticles**

401 Prior to their integration into a packaging film, nanoscaled engineering materials and
402 particles are tested for their ability to inhibit proliferation of microorganisms in pure cultures.
403 The methods used to estimate antimicrobial efficiency include disk diffusion, broth dilution,
404 agar dilution, and the microtiter plate-based method (Auger, et al., 2019; Auger, et al., 2018;
405 Stankic, et al., 2016; Vasiljevic, et al., 2020; Vidic, et al., 2013). The broth dilution method is
406 most commonly used as it enables determination of the minimum inhibitory concentration
407 (MIC) through culture turbidity and the minimum bactericidal concentration (MBC) through
408 plating of serial dilutions and viable colony counts. The microtiter plate-based method
409 performed on a 96-well plate is a modification of the broth dilution method. Multiple tests are
410 easily performed due to miniaturization. The agar diffusion method has been standardized as
411 an official method for detecting bacteriostatic activity in an indirect way. Monitoring of the
412 optical density at the wavelength of 600 nm of the bacterial culture in the presence and absence
413 of NPs enables determination of growth curves and estimation of the growth inhibition. Other
414 methods including modified standard procedures methods are also used such as the
415 conductometric assay, SEM, urease inhibition assay, flow cytometry viability assay
416 (Sirelkhatim, et al., 2015). Finally, molecular methods like those based on polymer chain
417 reaction (PCR) and enzyme-linked immunosorbent assay (ELISA) can be used to determine the
418 antibacterial effect of NPs (Manzano, Viezzi, Mazerat, Marks, & Vidic, 2018; Vidic, Manzano,
419 Chang, & Jaffrezic-Renault, 2017; Vidic, et al., 2019; Vizzini, et al., 2020).

420 Application of nanomaterials showing good antibacterial efficiency *in vitro* in food
421 packaging needs additional validation because the food structure and composition may
422 influence NP antibacterial activity. Although inorganic NPs are less sensitive to temperature
423 and pH variations than organic bactericidal compounds, the molecules and ions in the food
424 matrices and the food microbial flora may inhibit their activity. The exact mechanism how
425 metal oxide NPs prevent bacterial proliferation in foods is still under investigation. However,
426 several mechanisms have been suggested including the generation of reactive oxidative species
427 (ROS), with or without light radiation, release of antimicrobial metal ions, and mechanical
428 damaging upon NPs binding to microorganisms (Stankic, et al., 2016). In addition, small NPs
429 (< 10 nm diameter) penetrate bacterial cells, and subsequently may release toxic ions or
430 generate ROS intracellularly. Fig. 2 illustrates some of the described antimicrobial mechanisms.
431 Some authors described that multiple mechanisms took place. ZnO NPs were shown to directly
432 interact with *Campylobacter jejuni* cells, destabilize the membrane and penetrate the bacterial
433 cell where they induced oxidative stress (Y. Xie, He, Irwin, Jin, & Shi, 2011).

434 ZnO and TiO₂ NPs have been shown to produce a large quantity of ROS upon UV
435 radiation. For instance, one hour illumination of TiO₂ NPs completely irradiated *E. coli* due to
436 the formation of H₂O₂. During photocatalysis, electron-hole pairs are formed on TiO₂ after
437 nanoparticle absorbed energy larger than their energy band gap. Holes react with water
438 molecules on the surface of TiO₂ and generate surface active oxygen species, such as hydroxyl
439 radicals ($\cdot\text{OH}$), superoxide radicals ($\text{O}_2^{\cdot-}$) or hydrogen peroxide (H₂O₂). These active species
440 react with a microbial, destroy its structure and at the end kill it (Stankic, et al., 2016). Similarly,
441 nano-ZnO upon radiation forms ROS due to positively charged holes and defects at the surface
442 that react with surrounding water molecules. The holes separate H₂O₂ in OH⁻ and H⁺ and form
443 O₂⁻ from dissolved oxygen, which in turn can react with H⁺ and form a hydroperoxyl radical
444 (HO₂^{*}). It produces hydrogen peroxide anions, which subsequently react with H⁺ and produce

445 H₂O₂. All mentioned ROS can damage and eradicate bacterial cells. A higher concentration and
446 smaller size of NPs provide higher production of ROS and, thus, increased antibacterial
447 efficiency.

448 A moderate release of metal ions from CuO, FeMnO₃, ZnO, or TiO₂ NPs was shown to
449 be tolerated by a variety of microorganisms (Auger, et al., 2019; Stankic, et al., 2016;
450 Vasiljevic, et al., 2020). Bacterial cells can finely tune import and efflux of metal ions,
451 maintaining metal homeostasis (Randazzo, et al., 2020). However, tuning is possible to some
452 extent and high concentrations of metal ions released from NPs cause bacterial death. The
453 tolerance of various microorganisms to particular NPs can be explained by their capacity for
454 metal ion homeostasis. The solubility of metal and metal oxide particles, and the release of ions
455 into solution depend on particle concentration, time and medium (Vasiljevic, et al., 2020; Vidic,
456 et al., 2014).

457 Other modes of action of metal and metal oxide particles on bacterial cells have been
458 proposed because transcriptomic and proteomic analyses have indicated that nanoparticles
459 inhibit enzymes, inactivate proteins and perturb the bacterial metabolism and bioenergetics.
460 Moreover, metal oxide NPs modify the expression of proteins involved in bacterial information
461 processing, protection from oxidative stress, cell envelope dynamics and cell division (Auger,
462 et al., 2019; Auger, et al., 2018; Zanet, et al., 2019).

463 Finally the activity of incorporated NPs in packaging films is determined using a
464 standard ASTM E2180-01 method designed for evaluation of antimicrobial agents in polymeric
465 materials. The method can indicate the antimicrobial activity of polymer films containing NPs
466 in a plastic matrix or in a coating layer by quantifying differences in antimicrobial activity
467 between untreated plastics or polymers and those with bound or incorporated antimicrobial
468 agents. It can be also applied to compare the numbers of pathogen survivors on NP-treated and

469 control hydrophobic surfaces. The official ISO method 22196:2011 is used for measurements
470 of antibacterial activity on plastics and other non-porous surfaces. Such measurements are
471 needed because active NPs in the polymer matrix are only those that migrate from film to
472 products or those on the film surface that are in contact with the food product, as explained
473 above.

474 **8. Antiviral activity of metal oxide nanoparticles**

475 Transmission of viruses via contaminated surfaces is one of the important routes for
476 their spreading. The antiviral activity of some metal oxide NPs has motivated research into the
477 development of consumer protective packaging. For instance, CuO, ZnO, TiO₂ and La_xMnO₃
478 have shown a virucidal activity towards enveloped viruses, such as Influenza A virus, yellow
479 fever virus, respiratory virus, and non-enveloped viruses, such as rhinovirus-2 (Imani, et al.,
480 2020). Since surfaces coated with NPs showed higher virucidal effectiveness against enveloped
481 viruses than non-enveloped it was suggested that the main mechanism involved ROS
482 generation. ROS efficiently damaged the outer lipid envelope but has a lesser effect on protein
483 capsid (Imani, et al., 2020).

484 Another proposed mechanism is that metal oxide NPs prevent virus entry into the human
485 cells (El-Megharbel, Alsawat, Al-Salmi, & Hamza, 2021). Recently, ZnO NPs were shown to
486 target the ACE2 receptor of SARS-CoV-2 which is a key protein enabling virus entry into host
487 cells (Hamdi, et al., 2021).

488 **9. Toxicity of metal oxide nanoparticles**

489 Humans may be exposed to nanoparticle dissolute from food packaging films either
490 directly through food or indirectly by ingestion of inhaled particles. It is, thus, very important
491 to test potential cytotoxicity of nano-enforcers used in active packaging. Cytotoxicity of NPs

492 has most commonly been evaluated by measuring cell viability after cell exposure to
493 nanoparticles in a buffer or in a cell culture medium. Metal oxide NPs have been shown to
494 reduce cell viability, induce membrane lipid peroxidation and damage DNA in various
495 mammalian cell lines (Sahu & Hayes, 2017; Vidic, et al., 2013). The cytotoxic pattern varies
496 for different metal oxides and cell types and is dose- and time-dependent. In general, smaller
497 nanoparticles are more active and can be internalized by cells faster than larger ones.
498 Cytotoxicity is also dependent on the medium used to suspend them. Thus, cytotoxicity
499 drastically decreases in a cell medium supplemented with serum compared to buffer or serum-
500 free medium (Vidic, et al., 2014). Small NPs may aggregate into entities of different sizes and
501 shapes, depending on the medium, resulting in a modified surface and reactivity (Stankic, et al.,
502 2016). Biocompatibility of NPs is largely determined by their surface. Ingested nanoparticles
503 could both stimulate and/or suppress immune responses depending on their surface chemistry
504 (Dobrovolskaia, Germolec, & Weaver, 2009).

505 The cytotoxicity of ZnO NPs on human immune cells was correlated with the
506 intracellular solubility of nanoparticles into Zn^{2+} -ions. Different anions significantly affect
507 nanoparticle suspension stability, and release of metal ions from NPs. The pro-oxidative and
508 pro-inflammatory effects of TiO_2 and ZnO NPs were lowered using a medium containing some
509 anions such as chloride and phosphate (Ng, et al., 2013). When exposed to Mg doped ZnO (Mg-
510 *n*ZnO) NPs murine macrophages mainly rested unchanged but some cells indicated signs of
511 necrosis as observed using electron microscopy (Fig. 5A). Healthy macrophages displayed
512 pseudopodia to cell debris suggesting phagocytosis of damaged cells. Cytotoxicity was shown
513 to be concentration-dependent, because macrophages were able to neutralize the toxic effect of
514 Mg-*n*ZnO NPs at concentrations lower than 1 mg/ml while higher concentrations disturbed
515 membranes in macrophages and induced cell death (Auger, et al., 2019).

516 The importance of considering the interrelationship between NPs, mucus and the gut
517 microbiota was recently underlined by EFSA's report on the assessment of risks associated with
518 human exposure to nanoparticles used in the food industry (Hardy, et al., 2018). Exposure to
519 large numbers of ingested NPs, persistent enough to survive gastrointestinal processing, has
520 become regular for many populations. The surface area of the gastrointestinal tract (GIT)
521 provides a large zone for interaction with ingested NPs. NPs can move through the intestinal
522 barrier in a multistep route involving diffusion through the mucus layer, contact with
523 enterocytes or Microfold cells, and via paracellular transport or cellular entry (da Silva, et al.,
524 2020). It is likely that NPs accumulate in specialized intestinal cells at the base of large
525 lymphoid follicles (Peyer's patches) and that a degree of absorption goes beyond this, from
526 lymphatics to blood circulation to tissues. Gene-sequencing analysis of the 16S rRNA of the
527 gut bacteria showed that NPs can readily influenced the composition and richness of the
528 bacterial community. In a healthy human gut, most commensal bacteria belong to phyla
529 Firmicutes and Bacteroides playing critical roles in digestion, immunological functions of the
530 GIT including immune system maturation, maintaining intestinal permeability, and protection
531 against pathogens. Alteration of the intestinal microbiota (called dysbiosis) (Fig. 5B), in its
532 ecology (microbial population) and/or metabolic functions (production of bacterial metabolites)
533 is known to promote a number of chronic digestive and metabolic disorders. Several studies
534 suggest that NPs, including Ag, TiO₂, and ZnO impact the microbiota, characterized by an
535 alteration of the Firmicutes/Bacteroidetes ratio, depletion of *Lactobacillus* strains and an
536 increase in the abundance of Proteobacteria (Lamas, Breyner, & Houdeau, 2020). Indeed, NPs
537 detrimental effects may resemble the microbiome shifts in inflammatory bowel disease,
538 colorectal cancer or obesity where gut dysbiosis play a key pathogenic role. Moreover, recent
539 evidence indicates that disturbance of the microbiota-gut-brain axis induced by ZnO NPs may
540 result in neurobehavioral impairment by affecting gut microbiota (Chen, et al., 2020).

541 Published studies on cytotoxicity of metal oxide NPs are limited. Moreover, these
542 studies have used different cell models, various media, cells, applied different methods for
543 nanomaterial characterization, and different experimental conditions for cytotoxicity testing.
544 Therefore, data from these studies is difficult to interpret and the mechanism of toxicity of metal
545 oxide NPs is currently unknown. Extensive development of active packaging indicates that the
546 test methods need to be standardized and validated, positive and negative controls need to be
547 identified and cytotoxicity data need to be harmonized. Indeed, insufficient information is
548 available concerning the safety risk of NPs present in consumer products.

549 **10. Intelligent packaging – application of metal oxide NPs in food safety sensors**

550 The food industry regularly performs microbiological and chemical tests of the products
551 during production and before distribution. However, in most cases, there is no such control
552 when food items arrive to the market. Intelligent packaging does not interact with food, but
553 monitors the condition of the packaged product and informs on food quality degradation using
554 indicators (labels) and sensors, and enables traceability with unique codes and tags such as bar
555 codes, RFID tags, smart tags or NFC codes (Müller & Schmid, 2019; Rai, et al., 2019).
556 Environmental conditions monitored inside or outside the packaging include time temperature,
557 freshness and gas leakage indicators and relative humidity sensors. Freshness indicators,
558 usually colour changing labels on the container/package, show the change in pH or
559 characteristic gases released during food spoilage monitored by sensors inside the packaging
560 (Fuertes, et al., 2016). Recent research has also focused on multifunctional pH dependent colour
561 changing intelligent packaging composed of a biodegradable polymer (chitosan, starch etc.),
562 metal oxide (ZnO, TiO₂) and pH sensitive component (phenolic compounds such as
563 anthocyanin extracted from apple pomace, black plum peel or butterfly pea flowers (Lan, et al.,
564 2021; Mary, et al., 2020; Zhang, et al., 2019). UV activated oxygen indicators commonly use
565 TiO₂ nanoparticles (Wen, et al., 2019). Progress in affordable printed and flexible electronics

566 and the development of advanced bionanocomposite materials has resulted in many advances
567 in intelligent packaging. Wireless passive RFID tags can monitor different food spoilage
568 indicators (Raju, Bridges, & Bhadra, 2020), Metal oxides have been extensively investigated
569 and applied as sensing materials for a wide range of different gases including CO₂, NH₃, H₂S,
570 H₂O and also dimethylamine and trimethylamine released during food spoilage. Recent
571 research includes development of a Ni-SnO₂ sensor using a simple sol-gel spin coating method
572 for the detection of ethylene in apple fruit quality monitoring (Beniwal, 2019). Manganese
573 oxide nanoarchitectures with Au/Ag NPs also showed ethylene sensing potential (Bigiani, et
574 al., 2020). Niobium doping of TiO₂ nanotubes resulted in good selectivity and ability to detect
575 low concentrations (5-50 ppm) of dimethylamine (Galstyan, et al., 2020). Gelatin based
576 nanocomposite films incorporating ZnO NPs showed good potential as a relative humidity
577 sensing layer at room temperature in food packaging (Pereira, Picciani, Calado, & Tonon,
578 2020). **Table 4 shows some recent examples of intelligent food packaging utilizing metal oxide**
579 **NPs.**

580 **11. Conclusions**

581 Effective utilization of metal oxide nanoparticles in smart packaging using biopolymers
582 has been demonstrated through a review of recent research. Besides improving film properties,
583 such as tensile strength and water barrier, packaging with metal oxides has shown improved
584 antimicrobial (antibacterial, antifungal and antiviral), barrier, UV blocking, oxygen and
585 ethylene scavenging and moisture absorption potential. An added benefit of using metal oxides
586 in smart packaging is incorporation in food safety sensors as part of the intelligent packaging
587 component for providing information on the product to consumers and promotion of consumer
588 confidence in consumer safety, while to the distributors it could bring increased sales and waste
589 reduction.

590 The food industry is constantly developing new packaging films, and smart packaging
591 based on nanoparticles has been gaining in popularity over the last years due to multiple benefits
592 as illustrated in Fig. 6. The possibility to efficiently disperse and incorporate metal oxide NPs
593 within a packaging substrate provides active packaging film with increased efficacy. Currently,
594 the most commercially important categories of active packaging are oxygen scavengers and
595 moisture absorbers, followed by ethylene scavengers, CO₂ emitters and scavengers, and
596 temperature control packaging. All of them are expected to be used more in the future because
597 they enable shelf life extension, prevention of recalls costs, and brand reputation damage.

598 The most prevalent nano-sized antimicrobial metal oxides in active packaging are ZnO
599 and TiO₂ NPs. One of the main concerns regarding use of metal oxide NPs in smart packaging
600 is their safety, so migration from the packaging and cytotoxicity present key issues for their
601 future utilization in smart packaging. A recent safety assessment of titanium dioxide as a food
602 additive has deemed it unsafe emphasizing the significance of this aspect when evaluating the
603 application of any metal oxide in the food industry thus opening the door to further research of
604 the suitability other metal oxide NPs for this purpose. In addition, the green synthesis route
605 represents a potential solution to improve metal oxide NPs' safety and biocompatibility.
606 Finally, the migration tests of NPs from packaging to food or simulants have to be involved in
607 safety assessment. By adapting parameters such as type and composition of film or coating
608 material, pH, and film/coating thickness, the migration of NPs can be controlled to minimize
609 the risk of nanoparticle toxicity.

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616 **Table 1**

617 Some examples of synthesis and antibacterial application of other metal oxides

Nanoparticle	Size (nm)	Synthesis method	Pathogen	Reference
Cu ₂ O	400	One-step reduction	<i>S. aureus</i> , <i>E. coli</i>	(Yan, et al., 2021)
Cu ₂ O	150	Sol-gel	<i>E. coli</i>	(Ma, Guo, Guo, & Ge, 2015)
Cu ₂ O	36-450	In-situ mediated solution	<i>E. coli</i>	(Deng, et al., 2014)
Fe ₂ O ₃	45, 70	Green hydrothermal	<i>E. coli</i> , <i>S. aureus</i> , <i>Vibrio fisheri</i>	(Vihodceva, et al., 2021)
Fe ₃ O ₄	5-20	Modified co-precipitation	<i>E. coli</i>	(Gabrielyan, Hakobyan, Hovhannisyan, & Trchounian, 2019)
Fe ₃ O ₄	6-9	Low temperature solution route	<i>E. coli</i> , <i>P. aeruginosa</i> , <i>L. monocytogenes</i>	(Al-Shabib, et al., 2018)
MgO	50	Green synthesis	<i>E. coli</i>	(Khan, et al., 2020)
MgO	50	Combustion	<i>E. coli</i> , <i>B. subtilis</i>	(Vidic, et al., 2013)
Zn-MgO	5-100	Chemical vapour	<i>B. subtilis</i> , <i>S. aureus</i> , <i>Salmonella enterica</i> , <i>E. coli</i> , <i>Saccharomyces cerevisiae</i>	(Zanet, et al., 2019)
FeMnO ₃	200-1000	Sol gel	<i>B. subtilis</i>	(Vasiljevic, et al., 2020)

618

619 **Table 2.**

620 Some recent examples of antibacterial packaging films containing metal oxide NPs

Nanoparticle	Size	Food	Film	Pathogen	method	reference
SiO ₂	15 nm	Soybean oil	Chitosin	<i>E. coli</i> , <i>S. typhimurium</i> , <i>S. aureus</i> , <i>L. monocytogenes</i>	Disk	(Bi, et al., 2020)
ZnO	10-30 nm	White brined chees	Chitosan	<i>E. coli</i> O157:H7	plating	(Al-Nabulsi, et al., 2020)
ZnO	50	RTE poultry meat	Alginate	<i>S. typhimurium</i> , <i>S. aureus</i>	plate count	(Akbar & Anal, 2014)
ZnO	23–62	Chicken fillet; cheese	Chitosan	<i>E. coli</i> , <i>S. aureus</i> , <i>P. aeruginosa</i>	disk	(Amjadi, et al., 2019)
ZnO	<25 nm	Bread	Chitosan, cellulose	yeasts/fungi/ molds	culturing	(Noshirvani, Ghanbarzadeh, Mokarram, & Hashemi, 2017)
ZnO		Chicken meat	Cellulose, polypyrrole	<i>E. coli</i>	culturing	(Pirsa & Shamus, 2019)
ZnO		Chicken meat	Cellulose	<i>Campylobacter</i>	Culturing, sequencing	(Hakeem, et al., 2020)
Ag/ZnO		Chicken meat	LDPE ¹	<i>E. coli</i> , <i>P. aeruginosa</i> , <i>L. monocytogenes</i>	plate count	(Panea, Ripoll, González, Fernández-Cuello, & Albertí, 2014)

Zn-MgO	5-10 nm	Smoke salmon meat	Alginate	<i>L. monocytogenes</i>	qPCR, plate count	(Vizzini, et al., 2020)
ZnO/TiO ₂		Shrimp	PVA ⁵ /gelatin	<i>S. aureus</i> , <i>E. coli</i> O157H7, <i>L. monocytogenes</i>	count	(Azizi-Lalabadi, Ehsani, Ghanbarzadeh, & Divband, 2020)
ZnO	10-30 nm	Chicken meat	Gelatin	<i>S. aureus</i> , <i>Pseudomonas fluorescens</i>	Disk	(Ahmadi, Ahmadi, & Ehsani, 2020)
ZnO	130-200 nm	Food stimuli	SCP ⁴	<i>E. coli</i>	Zone inhibition	(Tankhiwale & Bajpai, 2012)
ZnO	35-45 nm	Food stimuli	Chitosan+PE	<i>E. coli</i> , <i>S. enterica</i> , <i>S. aureus</i>	culturing	(Al-Naamani, et al., 2016)
ZnO	50 nm	Food stimuli	LDPE ¹	<i>B. subtilis</i> , <i>E. aerogenes</i>	Plate count	(Esmailzadeh, et al., 2016)
ZnO	8 nm	Soft white cheese	Chitosan + CMP ⁴	<i>S. aureus</i> , <i>E. coli</i> , <i>P. aeruginosa</i>	Plate count	(Youssef, et al., 2016)
ZnO	30 nm	Food stimuli	Chitosan	<i>S. aureus</i> , <i>E. coli</i>	Disk	(J. Sun, et al., 2020a)
ZnO	30 nm	Food stimuli	Ethyl cellulose	<i>S. aureus</i> , <i>E. coli</i>	culturing	(Liu, et al., 2018)
ZnO	30 nm	Food stimuli	Zein	<i>S. aureus</i> , <i>E. coli</i>	Disk	(Amjadi, et al., 2020b)
ZnO	<20 nm	Spinach	Olive flounder bone gelatin	<i>L. monocytogenes</i>	Disk	(Beak, Kim, & Song, 2017)
TiO ₂		fresh pear	LDPE ¹	<i>P. aeruginosa</i> , <i>R. mucilaginosa</i>	plate count	(Bodaghi, et al., 2013)
TiO ₂	<100 nm	food stimuli	PLA ³	<i>E. coli</i> , <i>L. monocytogenes</i>		(W. Li, et al., 2017)
TiO ₂	25 nm	Lettuce	LDPE ¹	<i>E. coli</i>	Plate count	(Othman, et al., 2014)
TiO ₂		Lamb meat	Whey protein isolate /cellulose nanofibre / rosemary essential oil	<i>L. monocytogenes</i> , <i>E. coli</i> O157:H7, <i>S. aureus</i>	Micro dilution method	(Sani, Ehsani, & Hashemi, 2017)
CuO	191 nm	Food stimuli	PHBV ⁵	<i>S. enteria</i> , <i>L. monocytogenes</i>	Plate count	(Castro Mayorga, Fabra Rovira, Cabedo Mas, Sánchez Moragas, & Lagarón Cabello, 2018)
CuO	<50 nm	Pepper	Microcrystalline cellulose, sodium alginate	<i>Salmonella</i> spp., <i>Listeria</i> spp.	Plating	(Saravanakumar, Sathiyaseelan, Mariadoss, Xiaowen, & Wang, 2020)
ZnO-SiO ₂	25-100 nm	Bread	PVA/Chitosan	<i>S. aureus</i> , <i>E. coli</i>	Plate count	(Al-Tayyar, et al., 2020)
Cu ₂ O	400 nm	Cherry tomato	PVA-chitosan	<i>S. aureus</i> , <i>E. coli</i>	Plate count	(Yan, et al., 2021)

621 ¹LPDE, Low-Density Polyethylene; LLDPE, linear low density polyethylene; ²SEM, scanning electron
 622 microscopy; ³PLA, poly(lactic acid); ⁴Carboxymethyl cellulose; ⁵PVA, polyvinyl alcohol.

623

624 **Table 3.**

625 **Some examples of packaging films containing metal oxide NPs with quantitatively improved**
 626 **mechanical and barrier properties.**

627

Nanoparticles	Biopolymer	Barrier properties	Mechanical properties	References
ZnO-SiO ₂	Chitosan-PVA	With increased content of metal oxide NPs, WVTR ¹ decreased from 980.86 to 500.60 g/(m ² day)	With increased content of metal oxide NPs, TS ² increased from 7.45 MPa up to 37.5 MPa	(Al-Tayyar, et al., 2020)
ZnO	Soy protein	OP ³ values were decreased by 33.8 %, with addition of NPs	TS ² and EAB ⁴ were raised up to 2.11 MPa and 164.0%, with addition of NPs, respectively	(Wu, et al., 2019)
CuO	Montmorillonite	WVP ⁵ was significantly reduced after incorporation of nanocomposite	TS ² was improved 59% after incorporation of NPs	(Nouri, et al., 2018)
TiO ₂	Chitosan	WVTR ¹ was decreased from 26 to 19 g m ⁻² d ⁻¹ with addition of NPs	An increase of TS ² from 10 to 16 MPa and decrease of EAB ⁴ from 57 to 53 %, after addition of NPs to biopolymer	(Kaewklin, et al., 2018)
ZnO	Chitosan/ Carboxymethyl cellulose	Final contact angle values increased after addition of NPs	At higher level of NPs, TS ² was increased from 6.8 to 12.6 MPa	(Youssef, et al., 2016)
GO-Bi ₂ WO ₆	Starch	WPR ⁶ was improved (4.98 × 10 ⁻⁷ g/(m ² ·h·Pa) after addition of Bi ₂ WO ₆	TS ² gradually increased with higher content of NPs from 11.06 to 23.19 MPa	(J. Xie, et al., 2020)
Bi ₂ WO ₆ -TiO ₂	Starch		With increased NPs, TS ² increased while EAB ⁴ decreased	(Wang, et al., 2019)
ZnO	Glucomanan/ Chitosan	WVP ⁵ reduced from 2.61 (g mm/m ² ·day.kPa) to 1.82 (g mm/m ² ·day.kPa)	Optimum concentration of NPs improved TS ² and EAB ⁴ (52 MPa and 12.81 ± 0.42%, respectively)	(J. Sun, et al., 2020b)
ZnO	Alginate		At lower level of ZnO NPs, TS ² increased from 2.35 to 4.75 MPa, while EAB ⁴ decreased from 602 to 131 %	(Akbar & Anal, 2014)
ZnO	Ethyl cellulose/Gelatine	WCA ⁷ was increased with higher levels of ZnO NPs	Optimum concentration of NPs improved values of TS ² and EAB ⁴	(Liu, et al., 2018)
ZnO	Starch	WCA ⁷ exhibited higher value with the addition of ZnO NPs	Optimum concentration of NPs improved values of TS ² from 5.65 MPa to 10.29 MPa, and decreased	(Abdullah, et al., 2020)

			EAB ⁴ from 43.71% to 16.84%	
ZnO	Gelatin/starch	The WVP ⁵ values decreased and melting temperature increased after addition of NPs	At higher level of NPs, TS ² was increased from 23 to 50 MPa, while EAB ⁴ decreased	(Lee, Said, & Sarbon, 2020)
ZnO	Gelatin/chitosan	Addition of NPs increased WVP ⁵ values	The incorporation of NPs increased TS ² from 0.20 to 0.22 MPa and decreased the EAB ⁴	(Ahmad & Sarbon, 2021)

628 ¹WVTR, water vapor transmission rate; ²TS, tensile strength; ³OP, oxygen permeability; ⁴EAB, elongation
629 at break; ⁵WVP, water vapor permeability; ⁶WVR, water vapour resistance; ⁷WCA, water contact angle.

630 **Table 4.**

631 Some examples of intelligent packaging films utilizing metal oxide NPs.

Nanoparticle	Intelligent packaging function	Reference
TiO ₂	UV activated visible colorimetric oxygen indicator using Ag-loaded TiO ₂ nanotubes/methylene blue and hydroxyethylcellulose and glycerol	(Wen, et al., 2019)
Graphene oxide -TiO ₂	Self-adhesive UV activated colorimetric oxygen detection using graphene oxide TiO ₂ and methylene blue	(Son, et al., 2015)
TiO ₂	UV activated water based colorimetric oxygen indicator comprising a redox dye (methylene blue), colloidal semiconductor (TiO ₂) and a sacrificial electron donor (tartaric acid) ink-jet printed on polyester film	(Lawrie, Mills, & Hazafy, 2013)
IrO _x	Wireless pH sensor for monitoring pH level changes in fish meat using an IrO _x sensing electrode, sensitivity -49.7 mV/pH	(W.-D. Huang, et al., 2011)
ZnO	Starch-PVA composite films with incorporated ZnO nanoparticles, capable of color change in response to pH variation (acidic, neutral, alkaline)	(Jayakumar, et al., 2019)
TiO ₂	Starch films incorporating anthocyanins from butterfly pea flowers and TiO ₂ nanoparticles, showed noticeable color change in the pH range 1-12, tested on prawn storage	(Mary, et al., 2020)
TiO ₂	Chitosan films incorporating apple polyphenols and TiO ₂ nanoparticles, showed noticeable pH responsive color changing properties in the pH range 3-13, tested on monitoring salmon meat	(Lan, et al., 2021)
TiO ₂	Chitosan films incorporating anthocyanin from black plum peel extract and TiO ₂ nanoparticles, pH sensitive in the pH range 2-13	(Zhang, et al., 2019)
ZnO	Bacterial-cellulose-polypyrrole-ZnO nanoparticle films used for monitoring chicken thigh meat, change of electrical resistance can be linked with storage time and temperature, rate of microbial growth, sensory properties and pH	(Pirsa & Shamus, 2019)
ZnO	Gelatin films incorporating ZnO nanoparticles and glycerol used for monitoring relative humidity change at room temperature through change in electrical impedance	(Pereira, et al., 2020)
MnO ₂	Chemical vapor deposition of MnO ₂ co-sputtered with Ag and Au, used for monitoring fruit ripening	(Bigiani, et al., 2020)

	through detection of change in ethylene concentration	
Ni-SnO ₂	Thin film Ni-SnO ₂ sensor used for ethylene detection in apple fruit	(Beniwal, 2019)
Nb-TiO ₂	Radio-frequency deposited niobium doped titanium dioxide nanotubes were used for dimethylamine detection and monitoring seafood quality	(Galstyan, et al., 2020)

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634

635 **Figure legends:**

636 **Figure 1.**

637 Classification of smart packaging and its functions in the improvement of food quality.

638 **Figure 2.**

639 Schematic presentation of antibacterial mechanisms of ZnO NPs with different morphology:
640 (a) teraped NPs, that mainly generate H₂O₂ and release Zn²⁺-ions in aqueous solution, adapted
641 with permission from (Xu, et al., 2013); (b) flower NPs, shown to generate various ROS upon
642 visible light illumination, that injure bacterial cells by causing an oxidative stress, cell content
643 leakage or by damaging nucleic acid and proteins, adapted with permission from (Quek, et al.,
644 2018); (c) ZnO nanoparticle assembly were shown to be highly efficient antimicrobial agent
645 towards Gram-positive and Gram-negative bacteria, under different conditions. Adapted with
646 permission from (Joe, et al., 2017).

647 **Figure 3.**

648 Schematic representation of the preparation of smart food packaging using metal oxide NPs as
649 coating or incorporated in a biodegradable polymer and its application in the inhibition of
650 microorganisms, UV light protection, barrier, oxygen and ethylene scavenging and sensing.

651 **Figure 4.**

652 Schematic representation of biopolymer – metal oxide film synthesis using solvent casting (a)
653 and electrospinning (b) methods. Adapted in part with permission from (Liu, et al., 2018;
654 Razali, et al., 2019).

655 **Figure 5.**

656 (A) Representative thin section electron micrographs of macrophage cells incubated with
657 0.1 mg/ml Mg-nZnO for 24 h m, mitochondria; er, endoplasmic reticulum; mv, microvilli;
658 MVB, Multi Vesicular Body; red rectangle points autophagy. Adapted with permission from
659 (Auger, et al., 2019). (B) Potential impact of NP ingestion on the crosstalk between the
660 microbiota and the immune system. Adapted with permission from (Lamas, et al., 2020).

661 **Figure 6.**

662 List of improved packaging functions obtained utilizing metal oxide NPs.

663 **References**

- 664 Abdullah, A. H. D., Putri, O. D., Fikriyyah, A. K., Nissa, R. C., Hidayat, S., Septiyanto, R. F., Karina, M., &
665 Satoto, R. (2020). Harnessing the excellent mechanical, barrier and antimicrobial properties of
666 zinc oxide (ZnO) to improve the performance of starch-based bioplastic. *Polymer-Plastics*
667 *Technology and Materials*, *59*, 1259-1267.
- 668 Ahmad, A. A., & Sarbon, N. M. (2021). A comparative study: Physical, mechanical and antibacterial
669 properties of bio-composite gelatin films as influenced by chitosan and zinc oxide
670 nanoparticles incorporation. *Food Bioscience*, 101250.
- 671 Ahmadi, A., Ahmadi, P., & Ehsani, A. (2020). Development of an active packaging system containing
672 zinc oxide nanoparticles for the extension of chicken fillet shelf life. *Food Science & Nutrition*,
673 *8*, 5461-5473.
- 674 Akbar, A., & Anal, A. K. (2014). Zinc oxide nanoparticles loaded active packaging, a challenge study
675 against *Salmonella typhimurium* and *Staphylococcus aureus* in ready-to-eat poultry meat.
676 *Food Control*, *38*, 88-95.
- 677 Al-Naamani, L., Dobretsov, S., & Dutta, J. (2016). Chitosan-zinc oxide nanoparticle composite coating
678 for active food packaging applications. *Innovative Food Science & Emerging Technologies*, *38*,
679 231-237.
- 680 Al-Nabulsi, A., Osaili, T., Sawalha, A., Olaimat, A. N., Albiss, B. A., Mehayar, G., Ayyash, M., & Holley, R.
681 (2020). Antimicrobial activity of chitosan coating containing ZnO nanoparticles against *E. coli*
682 O157: H7 on the surface of white brined cheese. *International journal of food microbiology*,
683 *334*, 108838.
- 684 Al-Shabib, N. A., Husain, F. M., Ahmed, F., Khan, R. A., Khan, M. S., Ansari, F. A., Alam, M. Z., Ahmed,
685 M. A., Khan, M. S., & Baig, M. H. (2018). Low temperature synthesis of superparamagnetic iron
686 oxide (Fe₃O₄) nanoparticles and their ROS mediated inhibition of biofilm formed by food-
687 associated bacteria. *Frontiers in microbiology*, *9*, 2567.
- 688 Al-Tayyar, N. A., Youssef, A. M., & Al-Hindi, R. R. (2020). Antimicrobial packaging efficiency of ZnO-SiO₂
689 nanocomposites infused into PVA/CS film for enhancing the shelf life of food products. *Food*
690 *Packaging and Shelf Life*, *25*, 100523.
- 691 Almasi, H., Jahanbakhsh Oskouie, M., & Saleh, A. (2020). A review on techniques utilized for design of
692 controlled release food active packaging. *Critical reviews in food science and nutrition*, 1-21.

693 Amjadi, S., Almasi, H., Ghorbani, M., & Ramazani, S. (2020a). Preparation and characterization of
694 TiO₂NPs and betanin loaded zein/sodium alginate nanofibers. *Food Packaging and Shelf Life*,
695 24, 100504.

696 Amjadi, S., Almasi, H., Ghorbani, M., & Ramazani, S. (2020b). Reinforced ZnONPs/rosemary essential
697 oil-incorporated zein electrospun nanofibers by κ-carrageenan. *Carbohydrate Polymers*, 232,
698 115800.

699 Amjadi, S., Emaminia, S., Nazari, M., Davudian, S. H., Roufegarinejad, L., & Hamishehkar, H. (2019).
700 Application of reinforced ZnO nanoparticle-incorporated gelatin bionanocomposite film with
701 chitosan nanofiber for packaging of chicken fillet and cheese as food models. *Food and*
702 *Bioprocess Technology*, 12, 1205-1219.

703 Anitha, S., Brabu, B., Thiruvadigal, D. J., Gopalakrishnan, C., & Natarajan, T. (2012). Optical, bactericidal
704 and water repellent properties of electrospun nano-composite membranes of cellulose
705 acetate and ZnO. *Carbohydrate Polymers*, 87, 1065-1072.

706 Appendini, P., & Hotchkiss, J. H. (2002). Review of antimicrobial food packaging. *Innovative Food*
707 *Science & Emerging Technologies*, 3, 113-126.

708 Applerot, G., Lipovsky, A., Dror, R., Perkas, N., Nitzan, Y., Lubart, R., & Gedanken, A. (2009). Enhanced
709 antibacterial activity of nanocrystalline ZnO due to increased ROS-mediated cell injury.
710 *Advanced Functional Materials*, 19, 842-852.

711 Auger, S., Henry, C., Péchaux, C., Lejal, N., Zanet, V., Nikolic, M. V., Manzano, M., & Vidic, J. (2019).
712 Exploring the impact of Mg-doped ZnO nanoparticles on a model soil microorganism *Bacillus*
713 *subtilis*. *Ecotoxicology and environmental safety*, 182, 109421.

714 Auger, S., Henry, C., Péchoux, C., Suman, S., Lejal, N., Bertho, N., Larcher, T., Stankic, S., & Vidic, J.
715 (2018). Exploring multiple effects of Zn 0.15 Mg 0.85 O nanoparticles on *Bacillus subtilis* and
716 macrophages. *Scientific reports*, 8, 1-14.

717 Azizi-Lalabadi, M., Ehsani, A., Ghanbarzadeh, B., & Divband, B. (2020). Polyvinyl alcohol/gelatin
718 nanocomposite containing ZnO, TiO₂ or ZnO/TiO₂ nanoparticles doped on 4A zeolite:
719 Microbial and sensory qualities of packaged white shrimp during refrigeration. *International*
720 *journal of food microbiology*, 312, 108375.

721 Beak, S., Kim, H., & Song, K. B. (2017). Characterization of an olive flounder bone gelatin-Zinc oxide
722 nanocomposite film and evaluation of its potential application in spinach packaging. *Journal of*
723 *food science*, 82, 2643-2649.

724 Beniwal, A. (2019). Apple fruit quality monitoring at room temperature using sol-gel spin coated Ni-
725 SnO₂ thin film sensor. *Journal of Food Measurement and Characterization*, 13, 857-863.

726 Bi, F., Zhang, X., Liu, J., Yong, H., Gao, L., & Liu, J. (2020). Development of antioxidant and antimicrobial
727 packaging films based on chitosan, D-α-tocopheryl polyethylene glycol 1000 succinate and
728 silicon dioxide nanoparticles. *Food Packaging and Shelf Life*, 24, 100503.

729 Bigiani, L., Zappa, D., Comini, E., Maccato, C., Gasparotto, A., & Barreca, D. (2020). Manganese Oxide
730 Nanoarchitectures as Chemosensitive Gas Sensors to Monitor Fruit Ripening. *Journal of*
731 *nanoscience and nanotechnology*, 20, 3025-3030.

732 Bodaghi, H., Mostofi, Y., Oromiehie, A., Zamani, Z., Ghanbarzadeh, B., Costa, C., Conte, A., & Del Nobile,
733 M. A. (2013). Evaluation of the photocatalytic antimicrobial effects of a TiO₂ nanocomposite
734 food packaging film by in vitro and in vivo tests. *LWT-Food Science and Technology*, 50, 702-
735 706.

736 Böhmer-Maas, B. W., Fonseca, L. M., Otero, D. M., da Rosa Zavareze, E., & Zambiazzi, R. C. (2020).
737 Photocatalytic zein-TiO₂ nanofibers as ethylene absorbers for storage of cherry tomatoes.
738 *Food Packaging and Shelf Life*, 24, 100508.

739 Castro Mayorga, J. L., Fabra Rovira, M. J., Cabedo Mas, L., Sánchez Moragas, G., & Lagarón Cabello, J.
740 M. (2018). Antimicrobial nanocomposites and electrospun coatings based on poly (3-
741 hydroxybutyrate-co-3-hydroxyvalerate) and copper oxide nanoparticles for active packaging
742 and coating applications. *Journal of Applied Polymer Science*, 135, 45673.

- 743 Chen, J., Zhang, S., Chen, C., Jiang, X., Qiu, J., Qiu, Y., Zhang, Y., Wang, T., Qin, X., & Zou, Z. (2020).
744 Crosstalk of gut microbiota and serum/hippocampus metabolites in neurobehavioral
745 impairments induced by zinc oxide nanoparticles. *Nanoscale*, *12*, 21429-21439.
- 746 Cheng, D., He, M., Li, W., Wu, J., Ran, J., Cai, G., & Wang, X. (2019). Hydrothermal growing of cluster-
747 like ZnO nanoparticles without crystal seeding on PET films via dopamine anchor. *Applied*
748 *Surface Science*, *467*, 534-542.
- 749 Cierech, M., Wojnarowicz, J., Kolenda, A., Krawczyk-Balska, A., Prochwicz, E., Woźniak, B., Łojkowski,
750 W., & Mierzwińska-Nastalska, E. (2019). Zinc Oxide Nanoparticles cytotoxicity and release from
751 newly formed PMMA–ZnO nanocomposites designed for denture bases. *Nanomaterials*, *9*,
752 1318.
- 753 da Silva, A. B., Minitier, M., Thom, W., Hewitt, R. E., Wills, J., Jugdaohsingh, R., & Powell, J. J. (2020).
754 Gastrointestinal absorption and toxicity of nanoparticles and microparticles: Myth, reality and
755 pitfalls explored through titanium dioxide. *Current Opinion in Toxicology*.
- 756 Dehghani, S., Peighambaroust, S. H., Peighambaroust, S. J., Hosseini, S. V., & Regenstein, J. M.
757 (2019). Improved mechanical and antibacterial properties of active LDPE films prepared with
758 combination of Ag, ZnO and CuO nanoparticles. *Food Packaging and Shelf Life*, *22*, 100391.
- 759 Deng, Y., Zhao, J., Li, Q., Xu, X., Lin, H., & Li, Y. (2014). A generic in situ seed-mediated size-control
760 method in the case of cuprous oxide nanocubes and their antibacterial activities.
761 *CrystEngComm*, *16*, 5184-5188.
- 762 Dobrovolskaia, M. A., Germolec, D. R., & Weaver, J. L. (2009). Evaluation of nanoparticle
763 immunotoxicity. *Nature Nanotechnology*, *4*, 411-414.
- 764 EC. (1985). Council Directive 85/572/EEC of 19 December 1985. Laying down the list of simulants to be
765 used for testing migration of constituents of plastic materials and articles intended to come
766 into contact with foodstuffs. *Official Journal of the European Communities*, *327*, 14-21.
- 767 El-Megharbel, S. M., Alsawat, M., Al-Salmi, F. A., & Hamza, R. Z. (2021). Utilizing of (Zinc Oxide Nano-
768 Spray) for Disinfection against “SARS-CoV-2” and Testing Its Biological Effectiveness on Some
769 Biochemical Parameters during (COVID-19 Pandemic)—“ ZnO Nanoparticles Have Antiviral
770 Activity against (SARS-CoV-2)”. *Coatings*, *11*, 388.
- 771 Eskandarabadi, S. M., Mahmoudian, M., Farah, K. R., Abdali, A., Nozad, E., & Enayati, M. (2019). Active
772 intelligent packaging film based on ethylene vinyl acetate nanocomposite containing extracted
773 anthocyanin, rosemary extract and ZnO/Fe-MMT nanoparticles. *Food Packaging and Shelf Life*,
774 *22*, 100389.
- 775 Esmailzadeh, H., Sangpour, P., Shahraz, F., Hejazi, J., & Khaksar, R. (2016). Effect of nanocomposite
776 packaging containing ZnO on growth of *Bacillus subtilis* and *Enterobacter aerogenes*. *Materials*
777 *Science and Engineering: C*, *58*, 1058-1063.
- 778 Espitia, P. J. P., Soares, N. d. F. F., dos Reis Coimbra, J. S., de Andrade, N. J., Cruz, R. S., & Medeiros, E.
779 A. A. (2012). Zinc oxide nanoparticles: synthesis, antimicrobial activity and food packaging
780 applications. *Food and Bioprocess Technology*, *5*, 1447-1464.
- 781 Fathi, N., Almasi, H., & Pirouzifard, M. K. (2019). Sesame protein isolate based bionanocomposite films
782 incorporated with TiO₂ nanoparticles: Study on morphological, physical and photocatalytic
783 properties. *Polymer Testing*, *77*, 105919.
- 784 Fuertes, G., Soto, I., Carrasco, R., Vargas, M., Sabattin, J., & Lagos, C. (2016). Intelligent packaging
785 systems: sensors and nanosensors to monitor food quality and safety. *Journal of Sensors*, *2016*.
- 786 Gabrielyan, L., Hakobyan, L., Hovhannisyan, A., & Trchounian, A. (2019). Effects of iron oxide (Fe₃O₄)
787 nanoparticles on *Escherichia coli* antibiotic-resistant strains. *Journal of applied microbiology*,
788 *126*, 1108-1116.
- 789 Gaikwad, K. K., Singh, S., & Ajji, A. (2019). Moisture absorbers for food packaging applications.
790 *Environmental Chemistry Letters*, *17*, 609-628.
- 791 Gaikwad, K. K., Singh, S., & Lee, Y. S. (2018). Oxygen scavenging films in food packaging. *Environmental*
792 *Chemistry Letters*, *16*, 523-538.
- 793 Gaikwad, K. K., Singh, S., & Negi, Y. S. (2020). Ethylene scavengers for active packaging of fresh food
794 produce. *Environmental Chemistry Letters*, 1-16.

795 Galstyan, V., Ponzoni, A., Kholmanov, I., Natile, M. M., Comini, E., & Sberveglieri, G. (2020). Highly
796 sensitive and selective detection of dimethylamine through Nb-doping of TiO₂ nanotubes for
797 potential use in seafood quality control. *Sensors and Actuators B: Chemical*, *303*, 127217.

798 Garcia, C. V., Shin, G. H., & Kim, J. T. (2018). Metal oxide-based nanocomposites in food packaging:
799 Applications, migration, and regulations. *Trends in food science & technology*, *82*, 21-31.

800 Gomes, B., Ferreira, P., & Carvalho, S. (2017). Zinc nanostructures for oxygen scavenging. *Nanoscale*,
801 *9*, 5254-5262.

802 Hakeem, M. J., Feng, J., Nilghaz, A., Ma, L., Seah, H. C., Konkell, M. E., & Lu, X. (2020). Active Packaging
803 of Immobilized Zinc Oxide Nanoparticles Controls *Campylobacter jejuni* in Raw Chicken Meat.
804 *Applied and environmental microbiology*, *86*.

805 Hamdi, M., Abdel-Bar, H. M., Elmowafy, E., El-Khouly, A., Mansour, M., & Awad, G. A. (2021).
806 Investigating the Internalization and COVID-19 Antiviral Computational Analysis of Optimized
807 Nanoscale Zinc Oxide. *ACS omega*, *6*, 6848-6860.

808 Hardy, A., Benford, D., Halldorsson, T., Jeger, M. J., Knutsen, H. K., More, S., Naegeli, H., Noteborn, H.,
809 Ockleford, C., & Ricci, A. (2018). Guidance on risk assessment of the application of nanoscience
810 and nanotechnologies in the food and feed chain: Part 1, human and animal health. *EFSA*
811 *Journal*, *16*.

812 Huang, W.-D., Deb, S., Seo, Y.-S., Rao, S., Chiao, M., & Chiao, J. (2011). A passive radio-frequency pH-
813 sensing tag for wireless food-quality monitoring. *IEEE Sensors Journal*, *12*, 487-495.

814 Huang, Y., Mei, L., Chen, X., & Wang, Q. (2018). Recent developments in food packaging based on
815 nanomaterials. *Nanomaterials*, *8*, 830.

816 Imani, S. M., Ladouceur, L., Marshall, T., Maclachlan, R., Soleymani, L., & Didar, T. F. (2020).
817 Antimicrobial Nanomaterials and Coatings: Current Mechanisms and Future Perspectives to
818 Control the Spread of Viruses Including SARS-CoV-2. *ACS nano*, *14*, 12341-12369.

819 Ismail, A., Menazea, A., Kabary, H. A., El-Sherbiny, A., & Samy, A. (2019). The influence of calcination
820 temperature on structural and antimicrobial characteristics of zinc oxide nanoparticles
821 synthesized by Sol–Gel method. *Journal of Molecular Structure*, *1196*, 332-337.

822 Jayakumar, A., Heera, K., Sumi, T., Joseph, M., Mathew, S., Praveen, G., Nair, I. C., & Radhakrishnan, E.
823 (2019). Starch-PVA composite films with zinc-oxide nanoparticles and phytochemicals as
824 intelligent pH sensing wraps for food packaging application. *International journal of biological*
825 *macromolecules*, *136*, 395-403.

826 Joe, A., Park, S.-H., Shim, K.-D., Kim, D.-J., Jhee, K.-H., Lee, H.-W., Heo, C.-H., Kim, H.-M., & Jang, E.-S.
827 (2017). Antibacterial mechanism of ZnO nanoparticles under dark conditions. *Journal of*
828 *industrial and engineering chemistry*, *45*, 430-439.

829 Kaewklin, P., Siripatrawan, U., Suwanagul, A., & Lee, Y. S. (2018). Active packaging from chitosan-
830 titanium dioxide nanocomposite film for prolonging storage life of tomato fruit. *International*
831 *journal of biological macromolecules*, *112*, 523-529.

832 Karunakaran, C., Rajeswari, V., & Gomathisankar, P. (2011). Enhanced photocatalytic and antibacterial
833 activities of sol–gel synthesized ZnO and Ag-ZnO. *Materials Science in Semiconductor*
834 *Processing*, *14*, 133-138.

835 Khajavi, M. Z., Ebrahimi, A., Yousefi, M., Ahmadi, S., Farhoodi, M., Alizadeh, A. M., & Taslikh, M. (2020).
836 Strategies for producing improved oxygen barrier materials appropriate for the food packaging
837 sector. *Food Engineering Reviews*, *12*, 346-363.

838 Khan, M. I., Akhtar, M. N., Ashraf, N., Najeeb, J., Munir, H., Awan, T. I., Tahir, M. B., & Kabli, M. R.
839 (2020). Green synthesis of magnesium oxide nanoparticles using *Dalbergia sissoo* extract for
840 photocatalytic activity and antibacterial efficacy. *Applied Nanoscience*, *10*, 2351-2364.

841 Kim, S., Jeong, G. H., & Kim, S.-W. (2019). Ethylene Gas Decomposition Using ZSM-5/WO₃-Pt-Nanorod
842 Composites for Fruit Freshness. *ACS Sustainable Chemistry & Engineering*, *7*, 11250-11257.

843 Lamas, B., Breyner, N. M., & Houdeau, E. (2020). Impacts of foodborne inorganic nanoparticles on the
844 gut microbiota-immune axis: potential consequences for host health. *Particle and Fibre*
845 *Toxicology*, *17*, 1-22.

846 Lan, W., Wang, S., Zhang, Z., Liang, X., Liu, X., & Zhang, J. (2021). Development of red apple pomace
847 extract/chitosan-based films reinforced by TiO₂ nanoparticles as a multifunctional packaging
848 material. *International journal of biological macromolecules*, *168*, 105-115.

849 Lawrie, K., Mills, A., & Hazafy, D. (2013). Simple inkjet-printed, UV-activated oxygen indicator. *Sensors
850 and Actuators B: Chemical*, *176*, 1154-1159.

851 Lee, S., Said, N., & Sarbon, N. (2020). The effects of zinc oxide nanoparticles on the physical, mechanical
852 and antimicrobial properties of chicken skin gelatin/tapioca starch composite films in food
853 packaging. *Journal of food science and technology*, 1-9.

854 Lepot, N., Van Bael, M., Van den Rul, H., D'haen, J., Peeters, R., Franco, D., & Mullens, J. (2011).
855 Influence of incorporation of ZnO nanoparticles and biaxial orientation on mechanical and
856 oxygen barrier properties of polypropylene films for food packaging applications. *Journal of
857 Applied Polymer Science*, *120*, 1616-1623.

858 Li, H., Chen, Y., Lu, W., Xu, Y., Guo, Y., & Yang, G. (2020). Preparation of Electrospun Gelatin Mat with
859 Incorporated Zinc Oxide/Graphene Oxide and Its Antibacterial Activity. *Molecules*, *25*, 1043.

860 Li, W., Zhang, C., Chi, H., Li, L., Lan, T., Han, P., Chen, H., & Qin, Y. (2017). Development of antimicrobial
861 packaging film made from poly (lactic acid) incorporating titanium dioxide and silver
862 nanoparticles. *Molecules*, *22*, 1170.

863 Liu, Y., Li, Y., Deng, L., Zou, L., Feng, F., & Zhang, H. (2018). Hydrophobic ethylcellulose/gelatin
864 nanofibers containing zinc oxide nanoparticles for antimicrobial packaging. *Journal of
865 agricultural and food chemistry*, *66*, 9498-9506.

866 Ma, J., Guo, S., Guo, X., & Ge, H. (2015). Preparation, characterization and antibacterial activity of core-
867 shell Cu₂O@ Ag composites. *Surface and Coatings Technology*, *272*, 268-272.

868 Manzano, M., Viezzi, S., Mazerat, S., Marks, R. S., & Vidic, J. (2018). Rapid and label-free
869 electrochemical DNA biosensor for detecting hepatitis A virus. *Biosensors and Bioelectronics*,
870 *100*, 89-95.

871 Mary, S. K., Koshy, R. R., Daniel, J., Koshy, J. T., Pothan, L. A., & Thomas, S. (2020). Development of
872 starch based intelligent films by incorporating anthocyanins of butterfly pea flower and TiO₂
873 and their applicability as freshness sensors for prawns during storage. *RSC Advances*, *10*,
874 39822-39830.

875 Matsunaga, T., Tomoda, R., Nakajima, T., & Wake, H. (1985). Photoelectrochemical sterilization of
876 microbial cells by semiconductor powders. *FEMS microbiology letters*, *29*, 211-214.

877 Mizielińska, M., Nawrotek, P., Stachurska, X., Ordon, M., & Bartkowiak, A. (2021). Packaging Covered
878 with Antiviral and Antibacterial Coatings Based on ZnO Nanoparticles Supplemented with
879 Geraniol and Carvacrol. *International Journal of Molecular Sciences*, *22*, 1717.

880 Müller, P., & Schmid, M. (2019). Intelligent packaging in the food sector: A brief overview. *Foods*, *8*,
881 16.

882 Nešić, A., Gordić, M., Davidović, S., Radovanović, Ž., Nedeljković, J., Smirnova, I., & Gurikov, P. (2018).
883 Pectin-based nanocomposite aerogels for potential insulated food packaging application.
884 *Carbohydrate Polymers*, *195*, 128-135.

885 Ng, A. M. C., Chan, C. M. N., Guo, M. Y., Leung, Y. H., Djurišić, A. B., Hu, X., Chan, W. K., Leung, F. C. C.,
886 & Tong, S. Y. (2013). Antibacterial and photocatalytic activity of TiO₂ and ZnO nanomaterials
887 in phosphate buffer and saline solution. *Applied microbiology and biotechnology*, *97*, 5565-
888 5573.

889 Noshirvani, N., Ghanbarzadeh, B., Mokarram, R. R., & Hashemi, M. (2017). Novel active packaging
890 based on carboxymethyl cellulose-chitosan-ZnO NPs nanocomposite for increasing the shelf
891 life of bread. *Food Packaging and Shelf Life*, *11*, 106-114.

892 Nouri, A., Yarak, M. T., Ghorbanpour, M., Agarwal, S., & Gupta, V. K. (2018). Enhanced Antibacterial
893 effect of chitosan film using Montmorillonite/CuO nanocomposite. *International journal of
894 biological macromolecules*, *109*, 1219-1231.

895 Omerović, N., Džisalov, M., Živojević, K., Mladenović, M., Vunduk, J., Milenković, I., Knežević, N. Ž.,
896 Gadžanski, I., & Vidić, J. (2021). Antimicrobial nanoparticles and biodegradable polymer

897 composites for active food packaging applications. *Comprehensive Reviews in Food Science and*
898 *Food Safety*.

899 Othman, S. H., Abd Salam, N. R., Zainal, N., Kadir Basha, R., & Talib, R. A. (2014). Antimicrobial activity
900 of TiO₂ nanoparticle-coated film for potential food packaging applications. *International*
901 *Journal of Photoenergy*, 2014.

902 Panea, B., Ripoll, G., González, J., Fernández-Cuello, Á., & Albertí, P. (2014). Effect of nanocomposite
903 packaging containing different proportions of ZnO and Ag on chicken breast meat quality.
904 *Journal of Food Engineering*, 123, 104-112.

905 Pereira, P. F., Picciani, P. H., Calado, V., & Tonon, R. (2020). Gelatin-Based Nanobiocomposite Films as
906 Sensitive Layers for Monitoring Relative Humidity in Food Packaging. *Food and Bioprocess*
907 *Technology*.

908 Petchwattana, N., Covavisaruch, S., Wibooranawong, S., & Naknaen, P. (2016). Antimicrobial food
909 packaging prepared from poly (butylene succinate) and zinc oxide. *Measurement*, 93, 442-448.

910 Pirsá, S., & Shamusí, T. (2019). Intelligent and active packaging of chicken thigh meat by conducting
911 nano structure cellulose-polypyrrole-ZnO film. *Materials Science and Engineering: C*, 102, 798-
912 809.

913 Quek, J.-A., Lam, S.-M., Sin, J.-C., & Mohamed, A. R. (2018). Visible light responsive flower-like ZnO in
914 photocatalytic antibacterial mechanism towards *Enterococcus faecalis* and *Micrococcus*
915 *luteus*. *Journal of Photochemistry and Photobiology B: Biology*, 187, 66-75.

916 Rai, M., Ingle, A. P., Gupta, I., Pandit, R., Paralikar, P., Gade, A., Chaud, M. V., & dos Santos, C. A. (2019).
917 Smart nanopackaging for the enhancement of food shelf life. *Environmental Chemistry Letters*,
918 17, 277-290.

919 Raju, R., Bridges, G. E., & Bhadra, S. (2020). Wireless Passive Sensors for Food Quality Monitoring:
920 Improving the Safety of Food Products. *IEEE Antennas and Propagation Magazine*, 62, 76-89.

921 Randazzo, P., Anba-Mondoloni, J., Aubert-Frambourg, A., Guillot, A., Pechoux, C., Vidic, J., & Auger, S.
922 (2020). *Bacillus subtilis* regulators MntR and Zur participate in redox cycling, antibiotic
923 sensitivity, and cell wall plasticity. *Journal of Bacteriology*, 202.

924 Razali, M. H., Ismail, N. A., & Amin, K. A. M. (2019). Fabrication and Characterization of Antibacterial
925 Titanium Dioxide Nanorods Incorporating Gellan Gum Films. *J Pure Appl Microbiol*, 13, 1909-
926 1916.

927 Sahu, S. C., & Hayes, A. W. (2017). Toxicity of nanomaterials found in human environment: a literature
928 review. *Toxicology Research and Application*, 1, 2397847317726352.

929 Sani, M. A., Ehsani, A., & Hashemi, M. (2017). Whey protein isolate/cellulose nanofibre/TiO₂
930 nanoparticle/rosemary essential oil nanocomposite film: Its effect on microbial and sensory
931 quality of lamb meat and growth of common foodborne pathogenic bacteria during
932 refrigeration. *International journal of food microbiology*, 251, 8-14.

933 Saravanakumar, K., Sathiyaseelan, A., Mariadoss, A. V. A., Xiaowen, H., & Wang, M.-H. (2020). Physical
934 and bioactivities of biopolymeric films incorporated with cellulose, sodium alginate and copper
935 oxide nanoparticles for food packaging application. *International journal of biological*
936 *macromolecules*.

937 Schmitz, F., de Albuquerque, M. B. S., Alberton, M. D., Riegel-Vidotti, I. C., & Zimmermann, L. M. (2020).
938 Zein films with ZnO and ZnO: Mg quantum dots as functional nanofillers: New nanocomposites
939 for food package with UV-blocker and antimicrobial properties. *Polymer Testing*, 91, 106709.

940 Silva, A. L. P., Prata, J. C., Walker, T. R., Duarte, A. C., Ouyang, W., Barcelò, D., & Rocha-Santos, T. (2020).
941 Increased plastic pollution due to COVID-19 pandemic: Challenges and recommendations.
942 *Chemical Engineering Journal*, 126683.

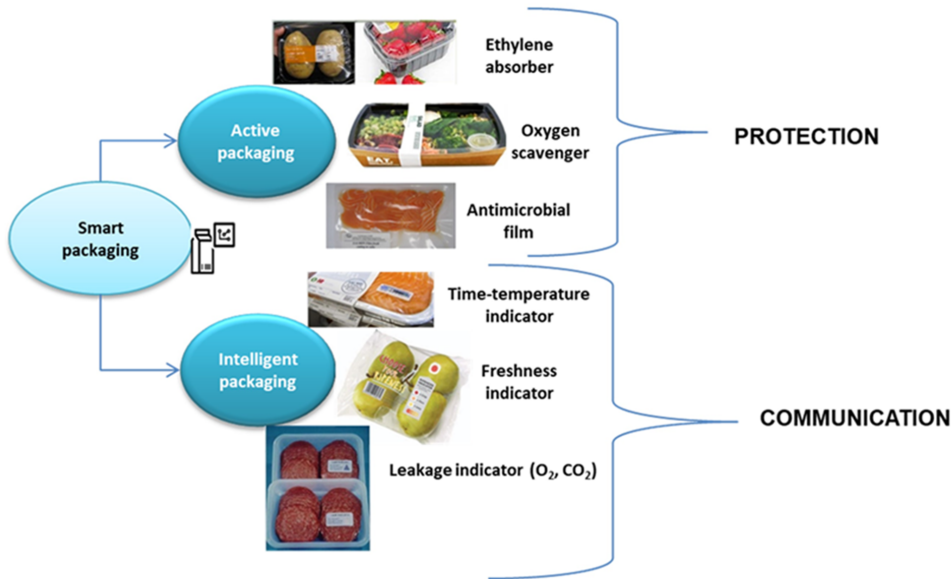
943 Sirelkhatim, A., Mahmud, S., Seeni, A., Kaus, N. H. M., Ann, L. C., Bakhori, S. K. M., Hasan, H., &
944 Mohamad, D. (2015). Review on zinc oxide nanoparticles: antibacterial activity and toxicity
945 mechanism. *Nano-micro letters*, 7, 219-242.

946 Son, E. J., Lee, J. S., Lee, M., Vu, C. H. T., Lee, H., Won, K., & Park, C. B. (2015). Self-adhesive graphene
947 oxide-wrapped TiO₂ nanoparticles for UV-activated colorimetric oxygen detection. *Sensors*
948 *and Actuators B: Chemical*, 213, 322-328.

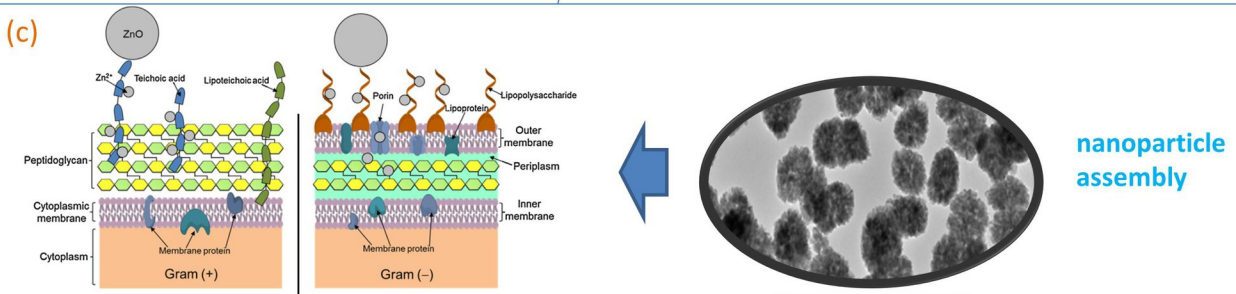
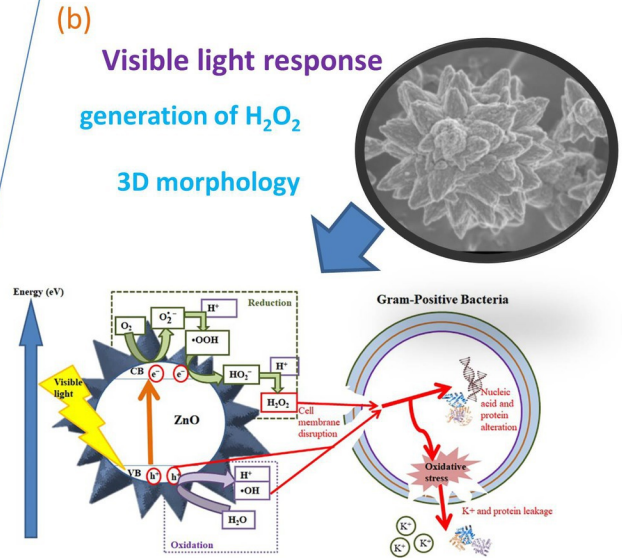
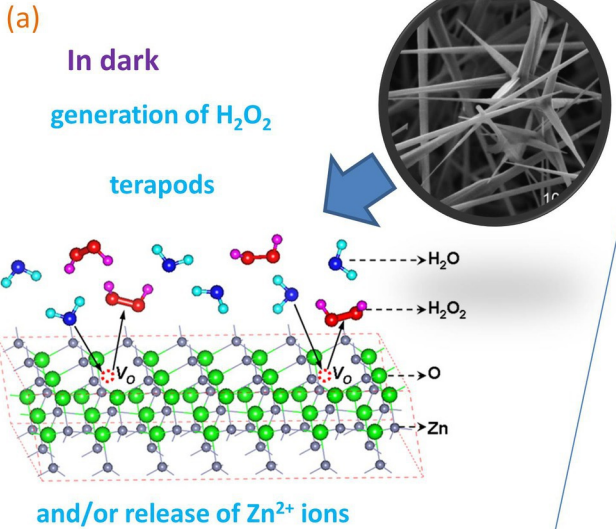
- 949 Soni, S., Dave, G., Henderson, M., & Gibaud, A. (2013). Visible light induced cell damage of Gram
950 positive bacteria by N-doped TiO₂ mesoporous thin films. *Thin solid films*, 531, 559-565.
- 951 Stankic, S., Suman, S., Haque, F., & Vidic, J. (2016). Pure and multi metal oxide nanoparticles: synthesis,
952 antibacterial and cytotoxic properties. *Journal of nanobiotechnology*, 14, 1-20.
- 953 Stanković, A., Dimitrijević, S., & Uskoković, D. (2013). Influence of size scale and morphology on
954 antibacterial properties of ZnO powders hydrothermally synthesized using different surface
955 stabilizing agents. *Colloids and Surfaces B: Biointerfaces*, 102, 21-28.
- 956 Subhapiya, S., & Gomathipriya, P. (2018). Green synthesis of titanium dioxide (TiO₂) nanoparticles by
957 Trigonella foenum-graecum extract and its antimicrobial properties. *Microbial pathogenesis*,
958 116, 215-220.
- 959 Sun, J., Jiang, H., Wu, H., Tong, C., Pang, J., & Wu, C. (2020a). Multifunctional bionanocomposite films
960 based on konjac glucomannan/chitosan with nano-ZnO and mulberry anthocyanin extract for
961 active food packaging. *Food hydrocolloids*, 105942.
- 962 Sun, J., Jiang, H., Wu, H., Tong, C., Pang, J., & Wu, C. (2020b). Multifunctional bionanocomposite films
963 based on konjac glucomannan/chitosan with nano-ZnO and mulberry anthocyanin extract for
964 active food packaging. *Food hydrocolloids*, 107, 105942.
- 965 Sun, Q., Li, J., & Le, T. (2018). Zinc oxide nanoparticle as a novel class of antifungal agents: current
966 advances and future perspectives. *Journal of agricultural and food chemistry*, 66, 11209-
967 11220.
- 968 Talebian, N., Amininezhad, S. M., & Doudi, M. (2013). Controllable synthesis of ZnO nanoparticles and
969 their morphology-dependent antibacterial and optical properties. *Journal of Photochemistry
970 and Photobiology B: Biology*, 120, 66-73.
- 971 Tam, K., Djurišić, A., Chan, C., Xi, Y., Tse, C., Leung, Y., Chan, W., Leung, F., & Au, D. (2008). Antibacterial
972 activity of ZnO nanorods prepared by a hydrothermal method. *Thin solid films*, 516, 6167-6174.
- 973 Tankhiwale, R., & Bajpai, S. (2012). Preparation, characterization and antibacterial applications of ZnO-
974 nanoparticles coated polyethylene films for food packaging. *Colloids and Surfaces B:
975 Biointerfaces*, 90, 16-20.
- 976 Vasiljevic, Z. Z., Dojcinovic, M. P., Krstic, J. B., Ribic, V., Tadic, N. B., Ognjanovic, M., Auger, S., Vidic, J.,
977 & Nikolic, M. V. (2020). Synthesis and antibacterial activity of iron manganite (FeMnO₃)
978 particles against the environmental bacterium *Bacillus subtilis*. *RSC Advances*, 10, 13879-
979 13888.
- 980 Vidic, J., Haque, F., Guigner, J. M., Vidy, A., Chevalier, C., & Stankic, S. (2014). Effects of water and cell
981 culture media on the physicochemical properties of ZnMgO nanoparticles and their toxicity
982 toward mammalian cells. *Langmuir*, 30, 11366-11374.
- 983 Vidic, J., Manzano, M., Chang, C.-M., & Jaffrezic-Renault, N. (2017). Advanced biosensors for detection
984 of pathogens related to livestock and poultry. *Veterinary research*, 48, 1-22.
- 985 Vidic, J., Stankic, S., Haque, F., Ciric, D., Le Goffic, R., Vidy, A., Jupille, J., & Delmas, B. (2013). Selective
986 antibacterial effects of mixed ZnMgO nanoparticles. *Journal of Nanoparticle Research*, 15,
987 1595.
- 988 Vidic, J., Vizzini, P., Manzano, M., Kavanaugh, D., Ramarao, N., Zivkovic, M., Radonic, V., Knezevic, N.,
989 Giouroudi, I., & Gadjanski, I. (2019). Point-of-need DNA testing for detection of foodborne
990 pathogenic bacteria. *Sensors*, 19, 1100.
- 991 Vihodceva, S., Šutka, A., Sihtmäe, M., Rosenberg, M., Otsus, M., Kurvet, I., Smits, K., Bikse, L., Kahru,
992 A., & Kasemets, K. (2021). Antibacterial Activity of Positively and Negatively Charged Hematite
993 (α -Fe₂O₃) Nanoparticles to *Escherichia coli*, *Staphylococcus aureus* and *Vibrio fischeri*.
994 *Nanomaterials*, 11, 652.
- 995 Vilela, C., Kurek, M., Hayouka, Z., Röcker, B., Yildirim, S., Antunes, M. D. C., Nilsen-Nygaard, J.,
996 Pettersen, M. K., & Freire, C. S. (2018). A concise guide to active agents for active food
997 packaging. *Trends in food science & technology*, 80, 212-222.
- 998 Vizzini, P., Beltrame, E., Zanet, V., Vidic, J., & Manzano, M. (2020). Development and Evaluation of
999 qPCR Detection Method and Zn-MgO/Alginate Active Packaging for Controlling *Listeria*
1000 *monocytogenes* Contamination in Cold-Smoked Salmon. *Foods*, 9, 1353.

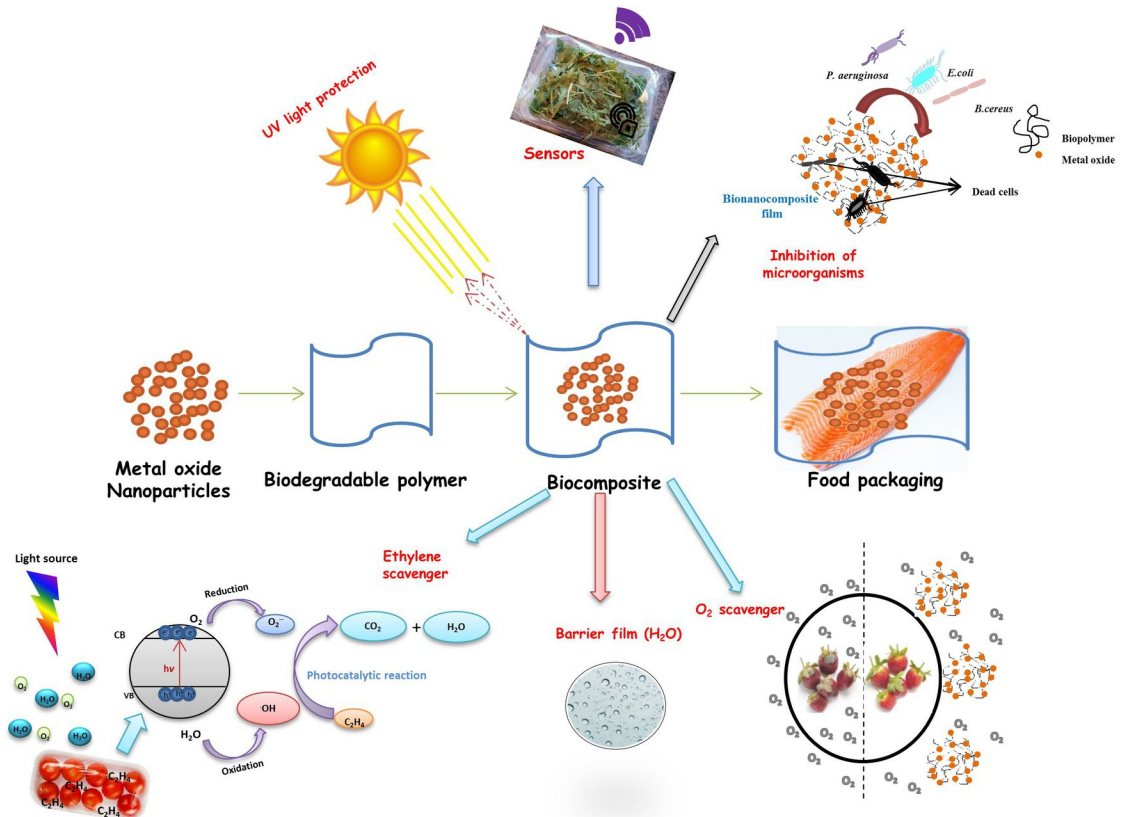
- 1001 Wang, H., Wang, L., Ye, S., & Song, X. (2019). Construction of Bi₂WO₆-TiO₂/starch nanocomposite
1002 films for visible-light catalytic degradation of ethylene. *Food hydrocolloids*, *88*, 92-100.
- 1003 Wei, H., Seidi, F., Zhang, T., Jin, Y., & Xiao, H. (2020). Ethylene scavengers for the preservation of fruits
1004 and vegetables: A review. *Food chemistry*, 127750.
- 1005 Wen, J., Huang, S., Jia, L., Ding, F., Li, H., Chen, L., & Liu, X. (2019). Visible Colorimetric Oxygen Indicator
1006 Based on Ag-Loaded TiO₂ Nanotubes for Quick Response and Real-Time Monitoring of the
1007 Integrity of Modified Atmosphere Packaging. *Advanced Materials Technologies*, *4*, 1900121.
- 1008 Wołosiak-Hnat, A., Zych, K., Mężyńska, M., Kifonidis, A., Dajworski, M., Lisiecki, S., & Bartkowiak, A.
1009 (2019). LDPE/PET laminated films modified with FeO (OH)× H₂O, Fe₂O₃, and ascorbic acid to
1010 develop oxygen scavenging system for food packaging. *Packaging Technology and Science*, *32*,
1011 457-469.
- 1012 Wong, M.-S., Chu, W.-C., Sun, D.-S., Huang, H.-S., Chen, J.-H., Tsai, P.-J., Lin, N.-T., Yu, M.-S., Hsu, S.-F.,
1013 & Wang, S.-L. (2006). Visible-light-induced bactericidal activity of a nitrogen-doped titanium
1014 photocatalyst against human pathogens. *Applied and environmental microbiology*, *72*, 6111-
1015 6116.
- 1016 Wu, J., Sun, Q., Huang, H., Duan, Y., Xiao, G., & Le, T. (2019). Enhanced physico-mechanical, barrier and
1017 antifungal properties of soy protein isolate film by incorporating both plant-sourced
1018 cinnamaldehyde and facile synthesized zinc oxide nanosheets. *Colloids and Surfaces B:
1019 Biointerfaces*, *180*, 31-38.
- 1020 Xie, J., Huang, L., Wang, R., Ye, S., & Song, X. (2020). Novel visible light-responsive graphene
1021 oxide/Bi₂WO₆/starch composite membrane for efficient degradation of ethylene.
1022 *Carbohydrate Polymers*, *246*, 116640.
- 1023 Xie, Y., He, Y., Irwin, P. L., Jin, T., & Shi, X. (2011). Antibacterial activity and mechanism of action of zinc
1024 oxide nanoparticles against *Campylobacter jejuni*. *Applied and environmental microbiology*,
1025 *77*, 2325-2331.
- 1026 Xu, X., Chen, D., Yi, Z., Jiang, M., Wang, L., Zhou, Z., Fan, X., Wang, Y., & Hui, D. (2013). Antimicrobial
1027 mechanism based on H₂O₂ generation at oxygen vacancies in ZnO crystals. *Langmuir*, *29*,
1028 5573-5580.
- 1029 Yan, J., Li, M., Wang, H., Lian, X., Fan, Y., Xie, Z., Niu, B., & Li, W. (2021). Preparation and property
1030 studies of chitosan-PVA biodegradable antibacterial multilayer films doped with Cu₂O and
1031 nano-chitosan composites. *Food Control*, *126*, 108049.
- 1032 Yildirim, S., Röcker, B., Pettersen, M. K., Nilsen-Nygaard, J., Ayhan, Z., Rutkaite, R., Radusin, T.,
1033 Suminska, P., Marcos, B., & Coma, V. (2018). Active packaging applications for food.
1034 *Comprehensive Reviews in Food Science and Food Safety*, *17*, 165-199.
- 1035 Youssef, A. M., El-Sayed, S. M., El-Sayed, H. S., Salama, H. H., & Dufresne, A. (2016). Enhancement of
1036 Egyptian soft white cheese shelf life using a novel chitosan/carboxymethyl cellulose/zinc oxide
1037 bionanocomposite film. *Carbohydrate Polymers*, *151*, 9-19.
- 1038 Zanet, V., Vidic, J., Auger, S., Vizzini, P., Lippe, G., Iacumin, L., Comi, G., & Manzano, M. (2019). Activity
1039 evaluation of pure and doped zinc oxide nanoparticles against bacterial pathogens and
1040 *Saccharomyces cerevisiae*. *Journal of applied microbiology*, *127*, 1391-1402.
- 1041 Zhang, X., Liu, Y., Yong, H., Qin, Y., Liu, J., & Liu, J. (2019). Development of multifunctional food
1042 packaging films based on chitosan, TiO₂ nanoparticles and anthocyanin-rich black plum peel
1043 extract. *Food hydrocolloids*, *94*, 80-92.

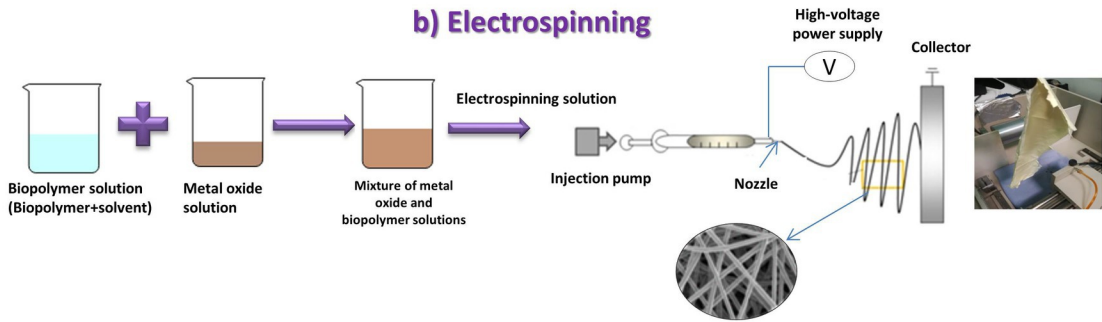
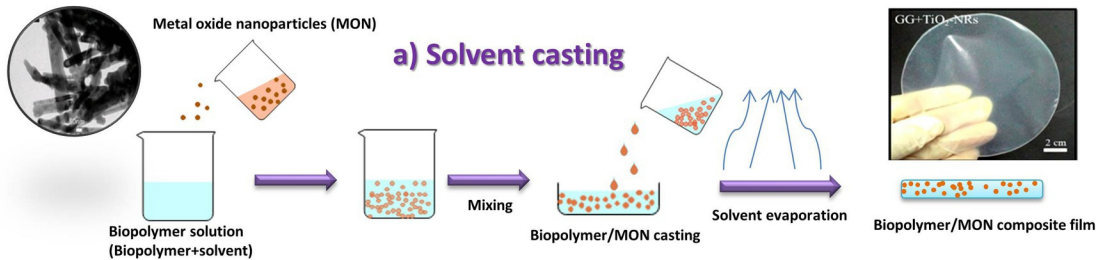
1044



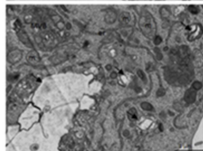
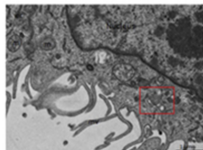
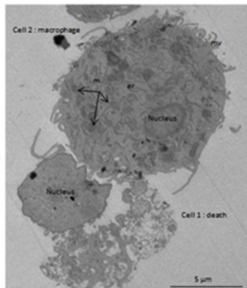
Antimicrobial mechanisms of ZnO



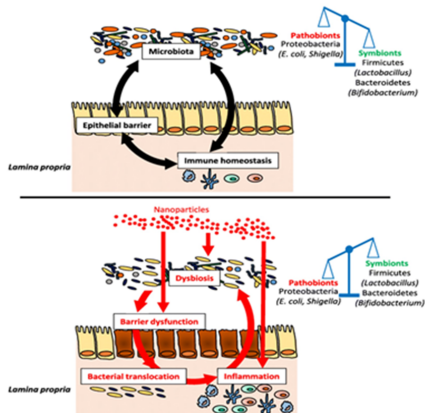




A



B





Materials with improved performances

Packaging film with enforced mechanical and barrier properties

Biodegradable packaging film

Active packaging for prolonged shelf-life

Intelligent packaging to inform on food quality degradation and enable traceability