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Silver nanoparticles (AgNPs) as antimicrobials in marine shrimp farming: A review

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ABSTRACT

Shrimp aquaculture is a growing food producing industry which historically has faced the economic consequences of diverse epidemics. Silver nanoparticles (AgNPs) offer a novel and innovative alternative to traditional drugs (i.e. antibiotics) to cope with infectious diseases in human medicine and veterinary, due their application flexibility and broad spectrum activity against microbes. Herein, we summarize the research advances and fundamentals in the use of AgNPs as prophylactics and therapeutic agents against bacteria and viruses affecting cultured shrimp. We also discuss the major concerns about the toxicity and biosecurity of these nanomaterials for shrimp and other marine organisms, as well as the major challenges and perspectives for a feasible large-scale administration and applications of AgNPs as antimicrobials in shrimp farming.

1. Introduction

Aquaculture is a food production industry that nowadays is expanding fast worldwide (Kobayashi et al., 2015). In 2018, the global aquaculture harvested 114.5 million tons with an estimated commercial value of 236.6 billion (USD) (FAO, 2020a). Shrimp breeding represents about 64 % of total production in shrimp industry (FAO, 2020b), which is dominated by two marine species, the whiteleg shrimp *Litopenaeus vannamei* and the giant tiger shrimp *Penaeus monodon* (Benzie, 2009). Aquaculture of marine shrimp has been developing since 1970s mainly in countries of Asia and America, where occurred a transition from the utilization of rustic extensive methods to the culture in intensive technified systems, which allow a high biomass production in a shorter time (Thornber et al., 2020). Despite these progresses in aquaculture technology, the growth in global production of cultured shrimp has been rather erratic over time, mainly due the occurrence of episodic epidemics that caused massive mortalities in farms during the last three decades (Flegel, 2019).

Historically, one of the major concerns in shrimp aquaculture has been the incidence and prevalence of infections with white spot syndrome virus (WSSV) that can cause high mortalities up to 100 % of population in just 7–10 days (Sánchez-Martínez et al., 2007). An extensively adopted strategy to prevent diseases produced by WSSV and other viruses has been the rearing of domesticated, specific pathogen free (SPF) shrimp stocks (Flegel, 2019). However, shrimp can host other pathogens causative of epidemics (Table 1) (Gomez-Gil et al., 2001), among which viruses generate around 60 % disease-associated losses in aquaculture, followed by bacteria with 20 %, and the rest corresponding to fungi and parasites (Stentiford et al., 2012). Moreover, most of the disease outbreaks in farms occur due poor practices in culture management and scarce biosecurity settings to prevent pathogen propagation (Thornber et al., 2020). Therefore, the development of pharmaceutical products to effectively prevent and treat infections is a prime need in shrimp aquaculture that could be undertaken by the field of nanotechnology (Govindaraju et al., 2019).

Nanotechnology is a growing interdisciplinary field involving the engineering of nano-sized materials (1−100 nm), whose physicochemical properties can greatly differ from bulk-sized forms (Thorley and Tetley, 2013). Because nanomaterials are similar in size to biomolecules within living cells and viruses, they have become valuable tools for diagnostics and therapy in human medicine and veterinary (Sanvicens and Marco, 2008). Particularly, metal nanoparticles have gain attention as powerful antimicrobial agents due its broad spectrum activity, durability, resistance, selectivity and specificity (Swain et al., 2014). Silver nanoparticles (AgNPs) have been investigated for disease control in aquaculture, due their properties against fungi (Johari et al., 2015a),

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Table 1
Common pathogens causative of diseases in shrimp*.

Pathogen	Disease (s)	Susceptible species
Viruses		
White Spot Syndrome Virus (WSSV)	White spot disease (WSD)	Penaeid shrimp and other decapod crustaceans
Yellow Head Virus (YHV) Genotype 1	Yellow head disease	*Metapenaeus affinis, Penaeus monodon, Litopenaeus vannamei, Litopenaeus stylirostris*
Infectious Hypodermal and Hematopoietic Necrosis Virus (IHHNV)	Infectious hypodermal and hematopoietic necrosis (IHHN)	*P. monodon, Penaeus californiensis, Penaeus setiferus, L. vannamei, L. stylirostris*
Hepatopancreatic Parvovirus (HPV)	Hepatopancreatic parvovirus disease	*Penaeus duorarum, Penaeus aztecus, P. setiferus, Penaeus marginatus, L. vannamei, Penaeus schmitii, Penaeus paulensis, Penaeus subtilis*
Taura Virus	Taura syndrome	*Metapenaeus ensis, P. aztecus, P. monodon, P. setiferus, L. stylirostris, L. vannamei*
Infectious myonecrosis virus (IMNV)	Infectious myonecrosis	*Penaeus esculentus, Penaeus merguiensis, L. vannamei.*
Penaeus monodon baculovirus (MBV)	Spherical baculovirosis	*P. monodon*
Baculovirus penaei (BP)	Tetrahedral baculovirosis	*P. duorarum, P. aztecus, P. setiferus, P.marginatus, L. vannamei, P.schmitii, P. paulensis, P. subtilis*
Lymphoid Organ Vacuolization Virus (LOVV)	Lymphoid organ vacuolization disease (LOVD)	*L. vannamei, P. monodon*
Bacteria		
Vibrio parahaemolyticus	Acute hepatopancreatic necrosis disease (AHPND)	*P. monodon, L. vannamei*
Vibrio harveyi	Luminescent vibriosis	Penaeid shrimp
Vibrio spp.	Brown spot disease, Black splinter, Seagull syndrome	Penaeid shrimp
Leucothrix mucor	Black gill disease	Penaeid shrimp
Hepatobacter penaei	Necrositing hepatopancreatitis	*L. vannamei*
Fungus		
Fusarium solani	Fungal infections	Juvenile and adult penaeid shrimp
Lagenidium spp.	Fungal Infections	Penaeid shrimp larvae
Parasites		
Microsporidian protozoa	Cotton shrimp disease	Penaeid shrimp and other decapod crustaceans
Gregarine	Gregarine infections	Penaeid shrimp

* Information taken from OIE website (https://www.oie.int/en/animal-health-in-the-world/) and Gomez-Gil et al. (2001).

bacteria (Bahabadi et al., 2016a; Dananjaya et al., 2016) and virus (Juarez-Mreno et al., 2017). For instance, AgNPs and silver nanocomposites have been tested for culture disinfection by the direct application into rearing water (Barakat and Yousry, 2016), or indirectly as materials for water filtration systems (Johari et al., 2015b; Nemati and Johari, 2019). In addition to this, AgNPs have been evaluated as treatments against infections, either as food additives (Barakat and Yousry, 2016), as well as, by the direct application into cultured animals (Das et al., 2020; Meneses-Márquez et al., 2019). Nonetheless, although those methods are still under development, they exemplify the potential and versatility of AgNPs for disease management in aquaculture industry.

Recently, the experimental use of AgNPs has shown favorable results against shrimp pathogens in microbiological assays (Bahabadi et al., 2016b; RathnaKumari et al., 2018; Sivaramasamy et al., 2017) but also in cultured shrimp exposed to microbes (Acedo-Valdez et al., 2017; Delavar et al., 2018; Romo-Quiñonez et al., 2020; Sivaramasamy et al., 2016). However, the administration of AgNPs over antibiotics and other commercial pharmaceuticals is still far to be extensive in aquaculture, mainly because the lack of information about AgNPs safety for organisms and environment (Gambardella et al., 2015). In this review, we summarize the advances, potential applications, and challenges of AgNPs against bacterial and viral diseases in shrimp farming.

2. AgNPs: synthesis and characteristics

AgNPs can be synthesized through physical, chemical, and biological methods (Beyene et al., 2017). Chemical reduction of colloidal silver is perhaps the most popular approach to produce AgNPs (Beyene et al., 2017; Song et al., 2009). This method involves the usage of organic and inorganic reducing agents in the presence of a stabilizer that prevent nanoparticle aggregation (Song et al., 2009). However, the main disadvantages of chemical synthesis are the high costs of production and the use of chemical reagents that could be hazardous for living organisms and environment (Prabhu and Poulose, 2012). These issues can be addressed through biological synthesis methods ("green synthesis") that are "eco-friendly" and low cost (Sharma et al., 2009). The reduction of silver compounds may be achieved with natural extracts containing amines, phenolic compounds, protein, pigments, alkaloids and other substances with reducing power that are present in living organisms (Asmathunisha and Kathiresan, 2013). For instance, AgNPs synthesized using plant extracts have shown antibacterial activity against *Vibrio* spp. in *Fenneropenaeus indicus* (Vaseeharan et al., 2010) *Penaeus monodon* (Kandasamy and Alikunhi, 2013; RathnaKumari et al., 2018) and *L. vannamei* (Alvarez-Cirerol et al., 2019).

Size and shape are characteristics influencing antimicrobial properties of AgNPs (Dakal et al., 2016). In general, it has been suggested that nanoparticles must be <50 nm to be effective, but small particle sizes (<10 nm) seems to have enhanced antibacterial capacity as they can interact better with surfaces and be easily internalized into cells (Agnihotri et al., 2014). The relevance of size for biological activity of AgNPs is exemplified for herpes simplex virus type 2 (HSV-2) infection treated with particles of 13, 33 and 46 nm; although all particle sizes had activity *in vitro* and *in vivo*, 33 nm AgNPs were the most effective against HSV-2, since they induced immune response and had the lowest toxicity for host cells (Orlowski et al., 2014). Regarding to shape, it appears to affect the surface area interacting with microorganisms; for example, in some studies, cubic and icosahedral shapes displayed stronger efficacy against *Escherichia coli* than triangular or spherical nanoparticles (El-zahry et al., 2015; Hong et al., 2016), while in other cases triangular and spherical shapes had a better biocidal action than other shapes (Kim et al., 2017; Pal et al., 2007).

Particle dispersion is also crucial for AgNPs activity since aggregates are prone to lack of antimicrobial effect. Particle aggregation can be avoided using polymers and other non-silver compounds as stabilizers, such as polyvinyl pyrrolidone (PVP), polyvinile alchol (PVA), polyethylene glycol (PEG), ethylenediaminetetraacetic acid (EDTA), among others (Ajitha et al., 2016). Stabilizers capping nanoparticles vary in their anti-aggregation capacity as they present distinct functional groups that can interact with the positive charges on the AgNPs surfaces (Bae et al., 2011). These interactions may also affect nanoparticle size as well as their activities. For example, PVA and PVP have demonstrated to render lower particle sizes than PEG and EDTA, but also to produce a higher inhibition of growth in plate cultures of *E. coli* and *Pseudomonas* spp. (Ajitha et al., 2016). All the properties mentioned above should be carefully considered for the design and synthesis of AgNPs, to generate nanoparticles with the desirable properties for specific medical or veterinary applications.

3. Toxicity tests (acute and chronic)

Silver nanoparticles have been extensively investigated for toxicity

during the last two decades (McShan et al., 2014). The toxicity of AgNPs in water media has been mainly attributed to their dissolution into free silver ions (Ag^{+}) and to their aggregation behavior, which are greatly influenced by electrolyte composition of media (Li et al., 2011). Certain ligands in water media like oxygen, chloride and phosphate can react with nanomaterial surfaces and substantially transform their physicochemical properties (Xiu et al., 2011). Moreover, in complex solute mixtures like seawater, other aspects like salinity or organic matter amount also influence AgNPs activity (Wang et al., 2014a). For example, AgNPs have proven to be more stable in the presence of dissolved organic matter (in the form of humic acid) at low salinities (5 ppt) in contrast to high salinities (30 ppt) (Wang et al., 2014a). However, the increase in salinity conditions has shown to decrease AgNPs toxicity in some marine animals, like in the rainbow trout *Oncorhynchus mykiss*, in which the exposure to brackish water reduced the mortality caused by nanoparticle treatment when compared to freshwater (Salari-Joo et al., 2012). Reduction in nanoparticles toxicity at high salinities could be related to a lower silver bioavailability, as has been found in the marine medaka (*Oryzias melastigma)* exposed to citrate-AgNPs at high salinities (15 and 30 ppt) (Wang and Wang, 2014). In contrast, in the clam *Scrobicularia plana*, the bioaccumulation of AgNPs was higher at 15 ppt than at 30 ppt (Bertrand et al., 2016). Thus, it seems that the behavior of nanosilver in seawater is very complex, but also the response of organisms to AgNPs-salinity interactions. Nonetheless, salinity is a key factor to consider during toxicological evaluations of silver nanomaterials in marine species.

Acute toxicity tests have demonstrated that very few designs of AgNPs could be approved for their application as drugs. For the same reason, reports on chronic toxicity tests are still limited not only in vertebrates, but also in crustaceans and other marine invertebrates (Magesky and Pelletier, 2018). With respect to nanoparticle designs, the composition, particle size, particle shape, concentration, aggregation behavior, and finally, the coating agent for the purpose for the incorporation into specific cells, are characteristics that have been investigated for toxicity (Kruszewski et al., 2011). Different types of nanoparticles have been studied, mainly those that are made of silver nitrate ($AgNO_3$), which have been combined with different stabilizing agents such as sodium dodecyl sulfate (SDS), PEG, oleilamine and oleic acid, chitosan, carboxymethyl cellulose and PVP. Other nanocomposites that have been also studied for toxicity are: silver acetate, silver borate, silver allantoinate, zinc, silver carbonate, silver chloride, silver chromate, silver glycerolate, colloidal silver iodide, silver lactate, silver manganese, nylon polymers with silver (Cardoso, 2016). Depending on their nature, these materials can have a significant impact in nanoparticle dissolution rate in seawater, which is a factor influencing their toxicity (Toncelli et al., 2017). For example, citrate-AgNPs are more stable in waters with high humic acid, but have faster dissolution rates in seawater than PVP coated nanosilver (Angel et al., 2013). In fact, the use of coating agents is one of the most explored strategies to improve biocompatibility of nanoparticles. For example, along with its stabilizing properties, PVP can considerably decrease toxicity of nanoparticles (Hou et al., 2017). PVP was successfully used in AgNPs formulations like Argovit® (Juarez-Moreno et al., 2017) and Argovit-4® (Romo-Quiñonez et al., 2020), which have presented remarkable antiviral activity in whiteleg shrimp without cause any mortality associated to toxicity during acute testing. Biocompatibility of AgNPs also can be improved through "Green synthesis methods". As example, AgNPs coated with seaweed bioactive compounds (proteins, polysaccharides and polyphenols) have demonstrated to do not cause any mortality in shrimp related to side effects when are used as short-term antibacterial (Maldonado-Muñiz et al., 2019).

With respect to size, AgNPs toxicity in marine animals appears to increase when size is reduced (Hou et al., 2017; Liu et al., 2019). Bouallegui et al. (2018) reported in the mussel *Mytilus galloprovincialis* that acute exposure to AgNPs with a size of <100 nm alter digestive gland tissue. Concentration is also limiting factor for AgNPs applications. In brine shrimp *Artemia salina* experiments, acute toxicity (indicated by the rise in immobilization rate, failed hatching and increase in mortality) increased together with nanoparticles concentration (An et al., 2019; Arulvasu et al., 2014). According to lethal median concentration (LC_{50}) found in different studies, tolerance to AgNPs appears to be variable among marine species; a LC50 of 8.9 mg/L at 96 h was found in *O. mykiss* (Shabrangharehdasht et al., 2020), whereas in the estuarine copepod *Amphiascus tenuiremis* and *L. vannamei* was 0.1 mg/L at 96 h (Sikder et al., 2018), and 35.5 mg/L at 48 h (Lam et al., 2020), respectively. These differences in tolerance between species suggest that shrimp might be less sensitive to metal nanoparticles than some fishes and other marine invertebrates.

Chronic toxicity in invertebrates have been demonstrated to be greater for naked AgNPs, but lesser for coated AgNPs (Lekamge et al., 2020). Chan and Chiu (2015), investigated sub-lethal and chronic toxicity of AgNPs in some larvae of marine invertebrate species; after 8 days of exposure, they observed that bioaccumulation of Ag from nanoparticles was minor in larvae exposed to $AgNO_3$ coated with PVP or oleinic acid. Still, the larvae treated with nanoparticles experienced a significant retardation in growth and development, and also a reduction in larval settlement rate. The authors suggested that the toxicity of coated AgNPs might not be solely evoked by the release of silver ions (Ag^{+}) to the test medium (Chan and Chiu, 2015). In vertebrates such as the rats, subchronic toxicity tests have been carried out up to 90 days, and orally administered AgNPs were found accumulated in the liver and kidneys of rodents (Kim et al., 2010). This could suggest that analog tissues in marine invertebrates such as shrimp (for example, shrimp hepatopancreas) could be the target organs where AgNPs will bioaccumulate (Kim et al., 2010). In the marine shrimp *Penaeus duorarum* exposed to silver in medium, metal became accumulated in hepatopancreas in a dose-dependent way, suggesting a key role of this organ in silver detoxification (Bianchini et al., 2007). Silver bioaccumulated through diet or environmental exposure can be transferred to upper trophic levels. Mansouri et al. (2016) and Lacave et al. (2017), proven the trophic transfer in fish fed during 14-21 days with *Artemia salina* previously treated with AgNPs. Therefore, silver bioaccumulation either during short or long administrations would be a prime aspect to consider before any actual application in aquaculture to avoid any harm to human or environmental health.

Biochemical and microscopic analyses have revealed that AgNPs and their products can trigger diverse changes in cells and tissues of marine organisms (Magesky and Pelletier, 2018). It has been reported in *M. galloprovicialis* that silver accumulation following AgNPs chronic exposure is accompanied by toxicopathic signs in tissues (gills and digestive gland), such as membrane destabilization, atrophy, necrosis and vacuolization, among others (Jimeno-Romero et al., 2017). Likewise, in the oyster *Crassostrea virginica* embryos and hepatopancreatic cells of adults suffered alterations due lysosomal destabilization by nanosilver toxicity in a dose-dependent way (Ringwood et al., 2010). As for molecular effects, in *O. mykiss* hepatic and blood cells, AgNPs toxicity was evidenced by the rise in reactive oxygen species (ROS), damage to DNA and lipids, diminished antioxidant (glutathione) levels, and up-regulation of activity of antioxidant enzymes like glutathione reductase and glutathione S-transferase (Massarsky et al., 2014). Similarly, in the oyster *Saccostrea glomerata* acute exposure to AgNPs promoted oxidative damage to DNA and lipids and activation of antioxidant defenses (Carrazco-Quevedo et al., 2019). Interestingly, a study in *A. salina*, showed that although AgNPs caused a dose-dependent rise in ROS, superoxide dismutase (SOD) activity was higher at the lowest concentration (6.25 mg/L) than at greater concentrations tested (25 and 100 mg/L) (An et al., 2019). Nonetheless, it appears that ROS bursts and oxidative damage are some of the most important consequences of exposure to nanosilver at cellular level, leading to activation of antioxidant defense mechanisms to counteract damage to biomolecules (Yu et al., 2020).

4. Therapeutic and prophylactic uses of AgNPs in the control of shrimp diseases

While AgNPs have proven to inhibit different types of pathogens infecting humans (Lara et al., 2011), the information about the action of AgNPs on shrimp diseases is still limited. However, all the evidence from *in vivo* studies highlights that AgNPs with diverse characteristics have antimicrobial effects in shrimp (Table 2), mostly against WSSV and bacteria from *Vibrio* genus. White spot disease caused by WSSV, can rapidly spread and cause the total loss of a shrimp culture, making it a latent danger for farms (Sánchez-Martínez et al., 2007). On the other hand, *Vibrio* bacteria that are ubiquitous in all coastal ecosystems of the world, may also cause serious illness in shrimp like vibriosis, acute hepatopancreatic necrosis syndrome (AHPNS), brown spot disease, among others, generating considerable economic losses in hatcheries and farms (Acedo-Valdez et al., 2017; Chandrakala and Priya, 2017). We can distinguish two principal approaches in the application of nanoparticles to cope viral and bacterial infections in shrimp cultures: the prophylactic and therapeutic uses. Prophylactic uses imply the protective administration of drugs to healthy individual before the onset of disease, whereas therapeutic uses concern to the applications to change the course of an active disease (Bhardwaj et al., 2020).

AgNPs synthesized by chemical or biological methods, have proven to inhibit the growth *in vitro* of *Vibrio* species that are pathogenic for marine shrimp (Alvarez-Cirerol et al., 2019; Bahabadi et al., 2016b; Kandasamy and Alikunhi, 2013; RathnaKumari et al., 2018; Sivaramasamy et al., 2017, 2016). Concordantly, nanoparticles also have proven to prevent, in some extent, shrimp diseases caused by *Vibrio* like vibriosis in *F. indicus* (Vaseeharan et al., 2010), *P. monodon* and juvenile *L. vannamei* (Kandasamy and Alikunhi, 2013; Sivaramasamy et al., 2016) and AHPNS in *L. vannamei* postlarvae (Alvarez-Cirerol et al., 2019). In those cases, prophylactic effects of nanoparticles were translated to a higher survival of individuals exposed to bacteria after AgNPs administration over a period of time, in contrast to untreated animals that presented the expected elevated mortalities (Alvarez-Cirerol et al., 2019; Kandasamy and Alikunhi, 2013; Sivaramasamy et al., 2016; Vaseeharan et al., 2010). These findings make obvious a lower contagion frequency of shrimp treated with nanoparticles, whose bactericidal effects are associated to a damage in cellular components of pathogens (Alvarez-Cirerol et al., 2019), but also to a boosted immune response in treated animals (Kandasamy and Alikunhi, 2013; Sivaramasamy et al., 2016). On the other hand, therapeutic effects of AgNPs were have been tested to counteract active infections of *Ricketsia*, an emerging bacteria producing necrotizing hepatopancreatitis in *L. vannamei* (Acedo-Valdez et al., 2017). Oral administration of AgNPs during a 24 days scheme diminished the presence of bacterial nodes in hepatopancreas of infected shrimp and raised their survival up to 100 % (Acedo-Valdez et al., 2017).

Antiviral effects of AgNPs *versus* WSSV have been confirmed using the patented formulations Argovit® (Juarez-Moreno et al., 2017; Ochoa-Meza et al., 2019) and Argovit-4® (Romo-Quiñonez et al., 2020), which are a suspension of PVP-coated spheroid silver nanoparticles. The Anti-WSSV effects reported for these drugs are dependent on the dose, delivery scheme, and the type viral challenge used (Juarez-Moreno et al., 2017; Ochoa-Meza et al., 2019; Romo-Quiñonez et al., 2020). Argovit-4® was tested for prophylaxis when was simultaneous applied with a WSSV inoculum, showing to reduce mortality of shrimp in a maximum of 50 % with a 1000 ng dose. Also, oral administration of this drug seems to effectively protect shrimp exposed to infected tissue, a common way of viral propagation in farms. A minimal dose of 10 μg/g was enough to protect shrimp against WSSV, as treated animals showed only a mortality of 16 % after 192 h, in contrast to the null survival in positive control group. It is important to highlight that no toxic effects were observed at this concentration of AgNPs (Romo-Quiñonez et al., 2020). Moreover, Argovit® was effective to treat WSSV in *L. vannamei* by increasing survival rates of infected shrimp between 70–80 % depending on the dose, together with a decrease in viral load quantified by molecular analyses. Interestingly, WSSV-positive shrimp treated with this drug did not develop signs and symptoms of white spot disease, indicating that virions within shrimp lost their infectivity in some way (Juarez-Moreno et al., 2017). It has been suggested that Argovit® exerts its antiviral effects by inducing innate immunity in WSSV-infected shrimp, through the mechanism of cell membrane protein recognition of AgNP metal silver or by its interaction with the WSSV envelope

Table 2
In vivo studies using AgNPs against pathogens in shrimp.

Reference	Synthesis of AgNPs	AgNPs Characteristics	Type of administration	Pathogen (s)	Shrimp species	Use *	Effect in Survival
Vaseeharan et al. (2009)	Synthesis with extract of green tea (*Camellia sinensis*) as reducing agent	No data	Oral	*Vibrio harveyi*	*Feneropenaeus indicus*	T	↑
Kandasamy et al. (2013)	Synthesis with extract of plant *Prosopis chilensis* as reducing agent	Shape: spherical Size: 5−25 nm	Oral	*Vibrio cholerae* *V. harveyi* *V. parahaemolyticus.*	*P. monodon*	P	↑
Sivaramasamy et al. (2016)	Extracellular synthesis by bacteria (*Bacillus subtillis*)	Shape: spherical Size: 10−25 nm	Oral	*V. harveyi* *V. parahaemolyticus.*	*L. vannamei*	P	↑
Acedo-Valdez et al. (2017)	Synthesis with infusion of green tea (*C. sinensis*) and neem (*Azadirachta indica*) as reducing agent	Shape: polyhedral, semi-hemispherical and flattened Size: 5−45 nm	Oral	*Rickettsia* like bacteria	*L. vannamei*	T	↑
Juarez-Moreno et al. (2017)	Suspension of AgNPs coated with PVP (Argovit®)	Shape: spheroid Size: 1−90 nm	Injection	WSSV	*L. vannamei*	T	↑
Alvarez-Cirerol et al. (2019)	Synthesis with extract of plant *Rumex hymenosepalus* as reducing agent	Shape: quasi-spherical Size: 2−10 nm	Oral	*V. parahaemolyticus* (bacteria)	*L. vannamei*	P	↑
Ochoa-Meza et al. (2019)	Suspension of AgNPs coated with PVP (Argovit®)	Shape: spheroid Size: 1−90 nm	Injection	WSSV	*L. vannamei*	T	↑
Romo-Quiñonez et al. (2020)	Suspension of AgNPs coated with PVP (Argovit-4®)	Shape: spheroid Size: 1−90 nm	Oral	WSSV	*L. vannamei*	P	↑

* Type of use: P, prophylactic; T, therapeutic.

(Ochoa-Meza et al., 2019). As far we know, no other AgNPs formulation has been proven yet either for prevention and/or therapy of viral diseases in shrimp.

5. Challenges: the best way to administer AgNPs in shrimp culture

The latest studies on AgNPs against viral and bacterial pathogens in human and veterinary medicine has accelerated their applications in other industries such as shrimp aquaculture that currently contributes with more than 50 % of cultured aquatic species worldwide (Thornber et al., 2020). Tests have been carried out to apply AgNPs directly to culture systems (Lam et al., 2020), sometimes supported with adjuvants like chitosan (Dananjaya et al., 2016) and plant derived compounds (RathnaKumari et al., 2018; Vaseeharan et al., 2010), or by the incorporation into living organisms such as brine shrimp *Artemia* (Acedo-Valdez et al., 2017). Some advances have shown that administration of AgNPs directly into shrimp ponds can be done (Lam et al., 2020), however, this method can make nanoparticles overused and cause serious environmental problems, like the generation of silver waste that can be dispersed into aquatic ecosystems and accumulated in other species (Wang et al., 2014b).

Alternatively, the administration of AgNPs in shrimp has been done by injecting nanoparticles in suspension (Juarez-Moreno et al., 2017; Ochoa-Meza et al., 2019). Intramuscular injection has been tried as method for the delivery of Argovit® as anti-WSSV therapy in broodstock shrimp with positive results on survival, virus scavenging, and stimulation of immune response (Juarez-Moreno et al., 2017; Ochoa-Meza et al., 2019). However, in open-sky shrimp farms, where huge amounts of animals must be treated, injection protocols would be impractical and expensive. To address this issue, the incorporation of AgNPs in formulated food is currently under research as an alternative for a large-scale administration. Recently, our group has reported the application of nanosilver through food against viral pathogens such as WSSV, that has affected shrimp cultures for more than two decades. In the work done by Romo-Quiñonez et al. (2020), high concentrations of AgNPs were incorporated into commercial pelleted food and were tested in cultured shrimp obtaining quite encouraging results in survival to viral challenges, since no toxicity was found in a short-term (196 h), indicated by changes in shrimp behavior, abnormal body color, alteration of feeding rate and a null mortality (Romo-Quiñonez et al., 2020). Oral administration in food of AgNPs was also applied to treat *Vibrio* infections in juvenile *L. vannamei* (Maldonado-Muñiz et al., 2019; Sivaramasamy et al., 2016) and juvenile *F. indicus* (Vaseeharan et al., 2010) and *P. monodon* (RathnaKumari et al., 2018). Maldonado-Muñiz et al. (2019) and Sivaramasamy et al. (2016) reported that shrimp fed with nanoparticles presented a high resistance to *Vibrio parahaemolyticus* without exhibit alterations in growth and feed conversion ratios. However, diets with high amounts (1000−10000 ppm) of Ag/AgCl nanoparticles administrated to *L. vannamei* during 7 days, caused a decrease in hepatosomatic index and dose-dependent silver bioaccumulation in tissues (hepatopancreas and cuticle), suggesting that more efforts are necessary to find safe parameters for oral administration of these formulations (Maldonado-Muñiz et al., 2019).

Another alternative studied for AgNPs inclusion in diet, is the utilization of other organisms as nanoparticles carriers that can be eaten by shrimp. Sivaramasamy et al. (2016), showed that feeding whiteleg shrimp with the AgNPs producing bacteria (*Bacillus subtilis*) offered a protective effect against vibriosis by increasing survival from 10 % to 71 %, although it was lower than the obtained by giving food enriched with purified AgNPs (91 %) (Sivaramasamy et al., 2016). In a similar way, nauplii of *Artemia franciscana* loaded with AgNPs were used for post-larvae feeding as preventive treatment of bacterial diseases (Acedo-Valdez et al., 2017). Nonetheless, even if these biocarriers showed low sensitivity to AgNPs in these experiments (Acedo-Valdez et al., 2017), there are other reports about the capacity of microcrustaceans to bioaccumulate silver and transfer it to other trophic levels (Lacave et al., 2017; Mansouri et al., 2016). Thus, a major challenge for dietary inclusion of AgNPs is to minimize the toxic effects due bioaccumulation of silver, not only for shrimp, but for non-target organisms. Moreover, it would be also important to have a proper waste management in farms that prevent the escape of nanoparticles and silver residues to marine environment.

The AgNPs have been also tested for the improvement of water quality, with the purpose of reducing the use of traditional disinfectants and antibiotics that can be expensive, generate microbial resistances, and have noxious effects in non-target organisms (Khosravi-Katuli et al., 2017). Immobilization of AgNPs on support matrixes have shown to increase their stability and to reduce the leaching of colloidal silver, making this type of materials suitable for filtration technologies (Agnihotri et al., 2013). Distinct types of silver nanocomposites like AgNPs-coated polyurethane foams (Jain and Pradeep, 2005), AgNPs-gelatin sponges (Wei et al., 2018), AgNPs-chitosan films (Vimala et al., 2010), Ag-NPs-coated porous ceramic (Delavar et al., 2018), AgNPs-coated zeolite (Johari et al., 2015b), AgNPs-silica beads (Sarkheil et al., 2016), graphene oxide-AgNPs membranes (Sun et al., 2015), among others, have been developed for membranes in water filtration systems, since they combine the porosity of support matrixes with the antimicrobial capacities of nanoparticle coats. Concerning to shrimp farming, AgNPs immobilized in silica beads (Ag/TEPA-Den-SiO_2) have demonstrated to effectively kill luminous *Vibrio* bacteria isolated from *L. vannamei* culture (Sarkheil et al., 2017, 2016). This type of filters seems to have a relatively high stability of material due the aminated surface on silica beads that keep leakage below of 0.033 mg/mL at a flow rate 500 mL/min (Sarkheil et al., 2016). Also, it has been demonstrated that the survival and growth performance of shrimp postlarvae is improved by filtering infected seawater with Ag/TEPA-Den-SiO_2 (Sarkheil et al., 2017). In a similar way, AgNPs-coated porous ceramic modified by an aminosilane coupling agent, known as 3-Amino-Propyl-Triethoxysilane (APTES), also has proven to be effective for the elimination of pathogenic bacteria from whiteleg shrimp culture (Delavar et al., 2018). Other materials like AgNPs-coated zeolite might be also useful for seawater filtration in shrimp hatcheries. In this sense, Johari et al. (2015b) investigated the effectiveness of zeolite filters coated with nanosilver (0.5, 1, and 1.5 %) against fungal infections during incubation of fertilized rainbow trout eggs. They found that filters coated with 0.5 % AgNPs increased the survival from fertilization to larval stage without development of infections. Thus, the indirect use of filtering materials with immobilized AgNPs for seawater disinfection, seems to be safer than the direct application of nanosilver into shrimp culture media.

6. Advances in action mechanisms

AgNPs exert their antimicrobial activities through multiple and complex mechanisms, most of them were investigated for vertebrate pathogens. Concerning to viruses, evidence found for human immunodeficiency virus 1 (HIV-11) (Lara et al., 2010) and Peste des petits ruminants virus (PPRV) (Khandelwal et al., 2014), suggest that AgNPs can bind virion surface elements (e.g. envelope proteins) and also penetrate to the core, which in turn, may impair interactions with host cells and inhibit viral replication. Moreover, AgNPs can destroy morphological structures in the viral surface as occurred for H3N2 influenza virus (Xiang et al., 2013). According to studies with hepatitis B virus (a double-stranded DNA virus), the inhibition of viral proliferation could be mediated by the blocking of nucleic acids synthesis (DNA and RNA) through the binding of nanoparticles to genetic material of virus (Lu et al., 2008).

AgNPs are known for having antibacterial properties even at very low concentrations, which are attributed to the Ag^+ ion releasement that is extremely toxic for most of bacteria (Lara et al., 2011). Nanoparticles or Ag^+ ions could interact with functional groups of proteins, nucleic acids and lipids present in the surface and interior of cells, leading to

structural and functional alterations of biomolecules (Tang and Zheng, 2018). Internalized AgNPs have shown to increase the generation of ROS in *V. parahaemolyticus*, causing oxidative damage to cell membranes and to the biomolecules dispersed in cytoplasm (Alvarez-Cirerol et al., 2019). In the Gram-negative bacteria *E. coli*, AgNPs disrupt the permeability of outer membrane, leading to the leakage of inner biomolecules to the extracellular medium. This is followed by the inactivation of respiratory dehydrogenases and the inhibition of growth of bacterial cells. At the same time, the damage in membrane lipids and proteins may cause its collapse, and finally produce cell death (Li et al., 2010).

Host responses can also contribute to enhance the effects of nanoparticles against infections. Specifically in shrimp, Ochoa-Meza et al. (2019) reported that the AgNPs injection into WSSV infected shrimp up-regulates the expression of lipopolysaccharide and β-1,3-glucan binding protein (LGBP) gene at 30 h post-treatment, which encodes a pathogen-associated molecular patterns (PAMPs) recognition protein that would be involved in the recognition of WSSV to trigger innate immunity (Ochoa-Meza et al., 2019). In agreement, Kandasamy et al. (2013) found that shrimp fed during 30 days with commercial food supplemented with AgNPs increased total hemocyte count and phenoloxidase activity, a defense protein in hemolymph (Kandasamy and Alikunhi, 2013). On the contrary, in a short molecular study, Romo--Quiñones et al. (2020), did not find any change in expression of genes that are involved in phagocytosis (Phagocytosis-activating protein, Rab6), antimicrobial peptides (peneidin 4 and crustin) and pro-phenoloxidase, in shrimp infected with WSSV and fed with AgNPs during 96 h, suggesting that nanoparticles do not stimulate an early immune response to virus when are orally administrated (Romo-Quiñonez et al., 2020).

Although effects of nanoparticles could vary according to their particular physicochemical characteristics, the method of administration, and type of pathogen, the existence of a multiplicity of molecular targets in viruses and bacteria contribute to the broad-spectrum activity of nanosilver (Lara et al., 2011; Tang and Zheng, 2018). A better understanding of mechanistic bases of AgNPs activities using a multi-level approach, from genome to whole organisms, surely will make nanoparticles more precise and specific against microbes but also less harmful to host organisms.

7. Other potential applications

The management of high stock densities in shrimp cultures, the increased global trade of cultured species, climate change and the anthropogenic impact in aquatic ecosystems have led to the emergence of diverse virus and bacteria that can cause disastrous outbreaks in shrimp hatcheries and farms (Walker and Winton, 2010). In particular, there is a rising concern for the presence of multi-resistant bacteria in marine ecosystems that cannot be treated with traditional antibiotics, being a continuous risk for aquaculture activities in coastal areas worldwide (Labella et al., 2013). Due their broad-spectrum of activities, AgNPs offer a potential alternative to antibiotics and other traditional drugs, as some experimental efforts have exhibited their effectiveness against bacteria and viruses commonly affecting shrimp (Kandasamy and Alikunhi, 2013; Romo-Quiñonez et al., 2020). From a positive point of view, current advances suggest that silver nanoparticles have a low toxicity for breeded shrimp (Juarez-Moreno et al., 2017), which opens the door to more research about their direct pharmaceutical applications, but also as adjuvants to potentiate the effects of antibiotics and other drugs that are already available for veterinary use, since in some cases, AgNPs have shown to stimulate innate immunity in shrimp (Kandasamy and Alikunhi, 2013; Ochoa-Meza et al., 2019). In this sense, biological synthesis methods seems to favor immunostimulant activities of metallic nanoparticles, as diverse bioactive compounds are present in the natural extracts (Ibrahim et al., 2019; Rather et al., 2017).

Diagnosis of diseases is another opportunity area for AgNPs utility in shrimp medicine. Because spectrum of absorption varies with size and shape of nanoparticles, AgNPs with different characteristics can be conjugated with biomolecules (like antibodies) for detection of pathogens (Yen et al., 2015). This probe design was tested for other metallic nanoparticles (gold) that were conjugated to a polyclonal antibody for detection of WSSV protein Vp28 (Kulabhusan et al., 2017). Other examples are the applications of DNA-functionalized nanoparticles in loop-mediated isothermal amplification (LAMP) for colorimetric detection of genetic material from WSSV, *Penaeus stylirostris* densovirus (PstDNV), and microsporidian (*Enterocytozoon hepatopenaei*) (Arunrut et al., 2019; Seetang-Nun et al., 2013; Suebsing et al., 2013). The main advantages of these methods over more traditional molecular tests, are their quickness, simplicity, as well as their potential for portability and multiplexing, that would make them suitable for rapid "in field" detection of pathogens in shrimp farms (Kulabhusan et al., 2017; Seetang-Nun et al., 2013).

8. Concluding remarks

Nanotechnology, is an emerging field with multiple applications in shrimp culture, including the treatment of diseases caused by pathogens. Although information on AgNPs effectiveness against viruses and bacteria affecting shrimp is still scanty, the studies carried over with *Vibrio* spp. and WSSV have shown that infectious diseases in shrimp might be managed by the administration of these type of nanoparticles either by intramuscular injection, inclusion in formulated food, as well as immobilized in filters for culture water disinfection. However, even if experimental AgNPs formulations have been apparently innocuous for marine shrimp, most of studies on toxicity have been done only under acute exposures. There is a considerable gap in the knowledge of specific mechanisms for antimicrobial activity in shrimp, but also about in-host bioaccumulation and toxicity, from the cellular to systemic level. Potential adverse effects in shrimp must be assessed in both acute and chronic toxicity assays considering specie-specific characteristics, like developmental stages and sex differences. Such information would serve to generate less toxic, more effective and pathogen-directed formulations.

Declaration of Competing Interest

The authors report no declarations of interest.

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References

Acedo-Valdez, M.R., Grijalva-Chon, J.M., Larios-Rodríguez, E., Maldonado-Arce, A.D., Mendoza-Cano, F., 2017. Antibacterial effect of biosynthesized silver nanoparticles in Pacific white shrimp Litopenaeus vannamei (Boone) infected with necrotizing hepatopancreatitis bacterium (NHP-B). Lat. Am. J. Aquat. Res. 45, 421–430. https://doi.org/10.3856/vol45-issue2-fulltext-17.

Agnihotri, S., Mukherji, Soumyo, Mukherji, Suparna, 2013. Immobilized silver nanoparticles enhance contact killing and show highest efficacy: elucidation of the mechanism of bactericidal action of silver. Nanoscale 5, 7328–7340. https://doi.org/10.1039/c3nr00024a.

Agnihotri, S., Mukherji, Soumyo, Mukherji, Suparna, 2014. Size-controlled silver nanoparticles synthesized over the range 5–100 nm using the same protocol and their antibacterial efficacy. RSC Adv. 4, 3974–3983. https://doi.org/10.1039/c3ra44507k.

Ajitha, B., Reddy, Y.A.K., Reddy, P.S., Jeon, H., Ahn, C.W., 2016. Role of capping agents in controlling silver nanoparticles size, antibacterial activity and potential application as optical hydrogen peroxide sensor. RSC Adv. 6, 36171–36179. https://doi.org/10.1039/C6RA03766F.

Alvarez-Cirerol, F.J., López-Torres, M.A., Rodríguez-León, E., Rodríguez-Beas, C., Martínez-Higuera, A., Lara, H.H., Vergara, S., Arellano-Jimenez, M.J., Larios-Rodríguez, E., Martínez-Porchas, M., Vega, E., Iñiguez-Palomares, R.A., 2019. Silver nanoparticles synthesized with Rumex hymenosepalus: a strategy to combat early mortality syndrome (EMS) in a cultivated white shrimp. J. Nanomater. https://doi.org/10.1155/2019/8214675.

An, H.J., Sarkheil, M., Park, H.S., Yu, I.J., Johari, S.A., 2019. Comparative toxicity of silver nanoparticles (AgNPs) and silver nanowires (AgNWs) on saltwater microcrustacean, Artemia salina. Comp. Biochem. Physiol. Part C 218, 62–69. https://doi.org/10.1016/j.cbpc.2019.01.002.

Angel, B.M., Batley, G.E., Jarolimek, C.V., Rogers, N.J., 2013. The impact of size on the fate and toxicity of nanoparticulate silver in aquatic systems. Chemosphere 93, 359–365. https://doi.org/10.1016/j.chemosphere.2013.04.096.

Arulvasu, C., Jennifer, S.M., Prabhu, D., Chandhirasekar, D., 2014. Toxicity effect of silver nanoparticles in Brine Shrimp Artemia. Transfus. Apher. Sci. 2014, 256919 https://doi.org/10.1155/2014/256919.

Arunrut, N., Jitrakorn, S., Saksmerprome, V., Kiatpathomchai, W., 2019. Double-loop-mediated isothermal amplification (D-LAMP) using colourimetric gold nanoparticle probe for rapid detection of infectious Penaeus stylirostris densovirus (PstDNV) with reduced false-positive results from endogenous viral elements. Aquaculture 510, 131–137. https://doi.org/10.1016/j.aquaculture.2019.05.049.

Asmathunisha, N., Kathiresan, K., 2013. A review on biosynthesis of nanoparticles by marine organisms. Colloids Surf. B Biointerfaces 103, 283–287. https://doi.org/10.1016/j.colsurfb.2012.10.030.

Bae, E., Park, H., Park, J., Yoon, J., Kim, Y., Choi, K., Yi, J., 2011. Effect of chemical stabilizers in silver nanoparticle suspensions on nanotoxicity. Bull. Korean Chem. Soc. 32, 613–619. https://doi.org/10.5012/bkcs.2011.32.2.613.

Bahabadi, N.M., Delavar, F.H., Mirbakhsh, M., Niknam, K., Johari, S.A., 2016a. Assessing antibacterial effect of filter media coated with silver nanoparticles against Bacillus spp. Iran. South Med. J. 19, 1–14. https://doi.org/10.7508/ismj.1395.01.001.

Bahabadi, N.M., Delavar, F.H., Mirbakhsh, M., Niknam, K., Johari, S.A., 2016b. Assessment of antibacterial activity of two different sizes of colloidal silver nanoparticle (cAgNPs) against Vibrio harveyi isolated from shrimp Litopenaeus vannamei. Aquac. Int. 25, 463–472. https://doi.org/10.1007/s10499-016-0043-8.

Barakat, K.M., Yousry, H.S.E., 2016. Protective effect of squilla chitosan – silver nanoparticles for Dicentrarchus labrax larvae infected with Vibrio anguillarum. Int. Aquat. Res. 8, 179–189. https://doi.org/10.1007/s40071-016-0133-2.

Benzie, J.A.H., 2009. Use and exchange of genetic resources of penaeid shrimps for food and aquaculture. Rev. Aquac. 1, 232–250. https://doi.org/10.1111/j.1753-5131.2009.01018.x.

Bertrand, C., Zalouk-Vergnoux, A., Giambérini, L., Poirier, L., Devin, S., Labille, J., Perrein-Ettajani, H., Pagnout, C., Châtel, A., Levard, C., Auffan, M., Mouneyrac, C., 2016. The influence of salinity on the fate and behavior of silver standardized nanomaterial and toxicity effects in the estuarine bivalve Scrobicularia plana. Environ. Toxicol. Chem. 35, 2550–2561. https://doi.org/10.1002/etc.3428.

Beyene, H.D., Werkneh, A.A., Bezabh, H.K., Ambaye, T.G., 2017. Synthesis paradigm and applications of silver nanoparticles (AgNPs), a review. Sustain. Mater. Technol. 13, 18–23. https://doi.org/10.1016/j.susmat.2017.08.001.

Bhardwaj, P., Bhatia, E., Sharma, S., Ahamad, N., Banerjee, R., 2020. Advancements in prophylactic and therapeutic nanovaccines. Acta Biomater. 108, 1–21. https://doi.org/10.1016/j.actbio.2020.03.020.

Bianchini, A., Playle, R.C., Wood, C.M., Walsh, P.J., 2007. Short-term silver accumulation in tissues of three marine invertebrates: shrimp Penaeus duorarum, sea hare Aplysia californica. and sea urchin Diadema antillarum 84, 182–189. https://doi.org/10.1016/j.aquatox.2007.02.021.

Bouallegui, Y., Younes, R.Ben, Bellamine, H., Oueslati, R., 2018. Histopathological indices and inflammatory response in the digestive gland of the mussel Mytilus galloprovincialis as biomarker of immunotoxicity to silver nanoparticles. Biomarkers 23, 277–287. https://doi.org/10.1080/1354750X.2017.1409803.

Cardoso, P.C., 2016. Nanopartículas de plata: obtención, utilización como antimicrobiano e impacto en el área de la salud. Rev. Hosp. Niños (B. Aires) 58, 19–28.

Carrazco-Quevedo, A., Römer, I., Salamanca, M.J., Poynter, A., Lynch, I., Valsami-Jones, E., 2019. Ecotoxicology and environmental safety bioaccumulation and toxic effects of nanoparticulate and ionic silver in Saccostrea glomerata (rock oyster). Ecotoxicol. Environ. Saf. 179, 127–134. https://doi.org/10.1016/j.ecoenv.2019.04.032.

Chan, C.Y.S., Chiu, J.M.Y., 2015. Chronic effects of coated silver nanoparticles on marine invertebrate larvae: a proof of concept study. PLoS One 10. https://doi.org/10.1371/journal.pone.0132457 e0132457.

Chandrakala, N., Priya, S., 2017. Vibriosis in shrimp aquaculture a review. Int. J. Sci. Res. Sci. Eng. Technol. 3, 27–33.

Dakal, T.C., Kumar, A., Majumdar, R.S., Yadav, V., 2016. Mechanistic basis of antimicrobial actions of silver nanoparticles. Front. Microbiol. 7, 1831. https://doi.org/10.3389/fmicb.2016.01831.

Dananjaya, S.H.S., Godahewa, G.I., Jayasooriya, R.G.P.T., Lee, J., Zoysa, M.De, 2016. Antimicrobial effects of chitosan silver nano composites (CAgNCs) on fish pathogenic Aliivibrio (Vibrio) salmonicida. Aquaculture 450, 422–430. https://doi.org/10.1016/j.aquaculture.2015.08.023.

Das, S., Aswani, R., Midhun, S.J., Ek, R., Mathew, J., 2020. Advantage of zinc oxide nanoparticles over silver nanoparticles for the management of Aeromonas veronii infection in Xiphophorus hellerii. Microb. Pathog. 147, 104348 https://doi.org/10.1016/j.micpath.2020.104348.

Delavar, F.H., Bahabadi, N.M., Mirbakhsh, M., Niknam, K., Johari, S.A., Baghmollaii, M. E., 2018. Application of porous ceramic substrates containing silver nanoparticles in water filtration system for infection control of Vibrio harveyi in white leg shrimp (Litopenaeus vannamei). J. Fish. Sci. Technol. 7, 311–319.

El-zahry, M.R., Mahmoud, A., Refaat, I.H., Mohamed, H.A., Bohlmann, H., Lendl, B., 2015. Antibacterial effect of various shapes of silver nanoparticles monitored by SERS. Talanta 138, 183–189. https://doi.org/10.1016/j.talanta.2015.02.022.

FAO, 2020a. Fishery and aquaculture statistics. Global aquaculture production 1950-2018 (FishstatJ) [WWW Document]. FAO Fish. Div. [online]. https://doi.org/www.fao.org/fishery/statistics/software/fishstatj/en.

FAO, 2020b. Fishery and Aquaculture Statistics. Global Production by Production Source 1950-2018 (FishstatJ) [WWW Document]. FAO Fish. Div. [online]. URL. www.fao.org/fishery/statistics/software/fishstatj/en.

Flegel, T.W., 2019. A future vision for disease control in shrimp aquaculture. J. World Aquac. Soc. 1–18. https://doi.org/10.1111/jwas.12589.

Gambardella, C., Costa, E., Piazza, V., Fabbrocini, A., Magi, E., Faimali, M., Garaventa, F., 2015. Effect of silver nanoparticles on marine organisms belonging to different trophic levels. Mar. Environ. Res. 111, 41–49. https://doi.org/10.1016/j.marenvres.2015.06.001.

Gomez-Gil, B., Roque, A., Guerra-Flores, A.L., 2001. Enfermedades infecciosas más comunes en la camaronicultura en méxico y el impacto del uso de antimicrobianos. In: Paez-Osuna, F. (Ed.), Camaronicultura Y Medio Ambiente. UNAM, México, pp. 315–346.

Govindaraju, K., Itroutwar, P.D., Veeramani, V., Kumar, T.A., Tamilselvan, S., 2019. Application of nanotechnology in diagnosis and disease management of white spot syndrome virus (WSSV) in aquaculture. J. Clust. Sci. https://doi.org/10.1007/s10876-019-01724-3.

Hong, X., Wen, J., Xiong, X., Hu, Y., 2016. Shape effect on the antibacterial activity of silver nanoparticles synthesized via a microwave-assisted method. Environ. Sci. Pollut. Res. 23, 4489–4497. https://doi.org/10.1007/s11356-015-5668-z.

Hou, J., Li, S., Wang, X., 2017. Toxic effects and molecular mechanism of different types of silver nanoparticles to the aquatic crustacean Daphnia magna. Environ. Sci. Technol. 51, 12868–12878. https://doi.org/10.1021/acs.est.7b03918.

Ibrahim, E.H., Kilany, M., Ghramh, H.A., Khan, K.A., Islam, S., 2019. Cellular proliferation/cytotoxicity and antimicrobial potentials of green synthesized silver nanoparticles (AgNPs) using Juniperus procera. Saudi J. Biol. Sci. 26, 1689–1694. https://doi.org/10.1016/j.sjbs.2018.08.014.

Jain, P., Pradeep, T., 2005. Potential of silver nanoparticle-coated polyurethane foam as an antibacterial water filter. Biotechnol. Bioeng. 90, 59–63. https://doi.org/10.1002/bit.20368.

Jimeno-Romero, A., Bilbao, E., Izagirre, U., Cajaraville, M.P., Marigómez, I., Soto, M., 2017. Digestive cell lysosomes as main targets for Ag accumulation and toxicity in marine mussels, Mytilus galloprovincialis, exposed to maltose- stabilised Ag nanoparticles of different sizes. Nanotoxicology 11, 168–183. https://doi.org/10.1080/17435390.2017.1279358.

Johari, S.A., Kalbassi, M.R., Soltani, M., Yu, I.J., 2015a. Study of fungicidal properties of colloidal silver nanoparticles (AgNPs) on trout egg pathogen, Saprolegenia sp. Int. J. Innov. Stud. Aquat. Biol. Fish. 3, 191–198.

Johari, S.A., Kalbassi, M.R., Soltani, M., Yu, I.J., 2015b. Application of nanosilver-coated zeolite as water filter media for fungal disinfection of rainbow trout (Oncorhynchus mykiss) eggs. Aquac. Int. 24, 23–38. https://doi.org/10.1007/s10499-015-9906-7.

Juarez-Moreno, K., Mejía-Ruiz, C.H., Díaz, F., Reyna-Verdugo, H., Denisse, A., Vazquez-Felix, E.F., Bogdanchikova, N., 2017. Effect of silver nanoparticles on the metabolic rate, hematological response, and survival of juvenile white shrimp Litopenaeus vannamei. Chemosphere 169, 716–724. https://doi.org/10.1016/j.chemosphere.2016.11.054.

Kandasamy, K., Alikunhi, N.M., 2013. Synthesis of silver nanoparticles by coastal plant Prosopis chilensis (L.) and their efficacy in controlling vibriosis in shrimp Penaeus monodon. Appl. Nanosci. 65–73. https://doi.org/10.1007/s13204-012-0064-1.

Khandelwal, N., Kaur, G., Kumar, K., Singh, P., Sharma, S., Tiwari, A., Vir, S., Kumar, N., 2014. Silver nanoparticles impair Peste des petits ruminants virus replication. Virus Res. 190, 1–7. https://doi.org/10.1016/j.virusres.2014.06.011.

Khosravi-Katuli, K., Prato, E., Lofrano, G., Guida, M., Vale, G., Libralato, G., 2017. Effects of nanoparticles in species of aquaculture interest. Environ. Sci. Pollut. Res. 24, 17326–17346. https://doi.org/10.1007/s11356-017-9360-3.

Kim, Y.S., Song, M.Y., Park, J.D., Song, K.S., Ryu, H.R., Chung, Y.H., Chang, H.K., Lee, J. H., Oh, K.H., Kelman, B.J., Hwang, I.K., Yu, I.J., 2010. Subchronic oral toxicity of silver nanoparticles. Part. Fibre Toxicol. 7, 20. https://doi.org/10.1186/1743-8977-7-20.

Kim, D.H., Park, J.C., Jeon, G.E., Kim, C.S., Seo, J.H., 2017. Effect of the size and shape of silver nanoparticles on bacterial growth and metabolism by monitoring optical density and fluorescence intensity. Biotechnol. Bioprocess Eng. 22, 210–217. https://doi.org/10.1007/s12257-016-0641-3.

Kobayashi, M., Msangi, S., Batka, M., Vannuccini, S., Dey, M.M., Anderson, J.L., 2015. Fish to 2030: the role and opportunity for aquaculture. Aquac. Econ. Manag. 193, 282–300. https://doi.org/10.1080/13657305.2015.994240.

Kruszewski, M., Brzoska, K., Brunborg, G., Asare, N., Dobrzynska, M., Dusinská, M., Fjellsbø, L.M., Georgantzopoulou, A., Gromadzka-ostrowska, J., Gutleb, A.C., Lankoff, A., Pran, E.R., Rinna, A., Instanes, C., Sandberg, W.J., Schwarze, P., Tomasz, S., Wojewódzka, M., Refnes, M., 2011. Toxicity of silver nanomaterials in higher eukaryotes. Adv. Mol. Toxicol. https://doi.org/10.1016/B978-0-444-53864-2.00005-0, pp. 179–2018.

Kulabhusan, P.K., Rajwade, J.M., Sugumar, V., Taju, G., Sahul, A.S., Paknikar, K.M., 2017. Field-usable lateral flow immunoassay for the rapid detection of white spot syndrome virus (WSSV). PLoS One 12. https://doi.org/10.1371/journal.pone.0169012 e0169012.

Labella, A., Gennari, M., Ghidini, V., Trento, I., Manfrin, A., Borrego, J.J., Lleo, M.M., 2013. High incidence of antibiotic multi-resistant bacteria in coastal areas dedicated to fish farming. Mar. Pollut. Bull. 70, 197–203. https://doi.org/10.1016/j.marpolbul.2013.02.037.

Lacave, J.M., Fanjul, Á., Bilbao, E., Gutierrez, N., Barrio, I., Arostegui, I., Cajaraville, M. P., Orbea, A., 2017. Acute toxicity, bioaccumulation and effects of dietary transfer of silver from brine shrimp exposed to PVP/ PEI-coated silver nanoparticles to zebra

fish. Comp. Biochem. Physiol. - C Pharmacol. Toxicol. Endocrinol. 199, 69–80. https://doi.org/10.1016/j.cbpc.2017.03.008.
Lam, P.H., Le, M.T., My, D., Dang, T., Chanh, T., Doan, D., Phuc, N., Tu, C., 2020. Safe concentration of silver nanoparticles in solution for white leg shrimp (Litopeaneus vannamei) farming. Biol. Chem. Res. 7, 35–45.
Lara, H.H., Ayala-nuñez, N.V., Ixtepan-turrent, L., Rodriguez-padilla, C., 2010. Mode of antiviral action of silver nanoparticles against HIV-1. J. Nanobiotechnology 8. https://doi.org/10.1186/1477-3155-8-1.
Lara, H.H., Garza-Treviño, E.N., Ixtepan-Turrent, L., Singh, D.K., 2011. Silver nanoparticles are broad-spectrum bactericidal and virucidal compounds. J. Nanobiotechnology 9, 2–9. https://doi.org/10.1186/1477-3155-9-30.
Lekamge, S., Miranda, A.F., Pham, B., Ball, A.S., Shukla, R., Lekamge, S., 2020. The toxicity of non-aged and aged coated silver nanoparticles to the freshwater shrimp Paratya australiensis. J. Toxicol. Environ. Heal. Part A 00, 1–16. https://doi.org/10.1080/15287394.2019.1710887.
Li, W., Xie, X., Shi, Q., 2010. Antibacterial activity and mechanism of silver nanoparticles on Escherichia coli. Appl. Microbiol. Biotechnol. 85, 1115–1122. https://doi.org/10.1007/s00253-009-2159-5.
Li, X., Lenhart, J.J., Walker, H.W., 2011. Aggregation kinetics and dissolution of coated silver nanoparticles. Langmuir 25, 1095–1104. https://doi.org/10.1021/la202328n.
Liu, H., Wang, X., Wu, Y., Hou, J., Zhang, S., Zhou, N., 2019. Toxicity responses of different organs of zebrafish (Danio rerio) to silver nanoparticles with different particle sizes and surface coatings. Environ. Pollut. 246, 414–422. https://doi.org/10.1016/j.envpol.2018.12.034.
Lu, L., Sun, R.W., Chen, R., Hui, C., Ho, C., Luk, J.M., Lau, G.K.K., 2008. Silver nanoparticles inhibit hepatitis B virus replication. Antivir. Ther. (Lond.) 13, 253–262.
Magesky, A., Pelletier, É., 2018. Cytotoxicity and physiological effects of silver nanoparticles on marine invertebrates. In: Saquib, Q., Faisal, M., Al-Khedhairy, A., Alatar, A. (Eds.), Cellular and Molecular Toxicology of Nanoparticles. Springer, Cham, pp. 285–309. https://doi.org/10.1007/978-3-319-72041-8.
Maldonado-Muñiz, M., Luna, C., Mendoza-Reséndez, R., Barriga-Castro, E.D., Soto-Rodriguez, S., Ricque-Marie, D., Cruz-Suarez, L.E., 2019. Silver nanoparticles against acute hepatopancreatic necrosis disease (AHPND) in shrimp and their depuration kinetics. J. Appl. Phycol. https://doi.org/10.1007/s10811-019-01948-w.
Mansouri, B., Johari, S.A., Azadi, N., Davari, B., Asghari, S., Dekani, L., 2016. Trophic transfer potential of silver nanoparticles from Artemia salina to Danio rerio. Bioflux 9, 101–104.
Massarsky, A., Abraham, R., Nguyen, K.C., Rippstein, P., Tayabali, A.F., Trudeau, V.L., Moon, T.W., 2014. Nanosilver cytotoxicity in rainbow trout (Oncorhynchus mykiss) erythrocytes and hepatocytes. Comp. Biochem. Physiol. Part C 159, 10–21. https://doi.org/10.1016/j.cbpc.2013.09.008.
McShan, D., Ray, P.C., Yu, H., 2014. Molecular toxicity mechanism of nanosilver. J. Food Drug Anal. 22, 116–127. https://doi.org/10.1016/j.jfda.2014.01.010.
Meneses-Márquez, J.C., Hamdan-Partida, A., Monroy-Dosta, M.C., Castro-Mejía, J., Faustino-Vega, A., Soria-Castro, E., Bustos-Martínez, J., 2019. Use of silver nanoparticles to control Vibrio fluvialis in cultured angelfish Pterophyllum scalare. Dis. Aquat. Organ. 137, 65–72. https://doi.org/10.3354/dao03423.
Nemati, T., Johari, S.A., 2019. Will the antimicrobial properties of ZnONPs turn it into a more suitable option than AgNPs for water filtration? Comparative study in the removal of fish pathogen, Aeromonas hydrophila from the culture of juvenile common carp (Cyprinus carpio). Environ. Sci. Pollut. Res. 26, 30907–30920. https://doi.org/10.1007/s11356-019-06178-8.
Ochoa-Meza, A.R., Álvarez-Sánchez, A.R., Romo-Quiñonez, C.R., Barraza, A., Toledano-Magaña, Y., Bogdanchikova, N., Pestryakov, A., 2019. Silver nanoparticles enhance survival of white spot syndrome virus infected Penaeus vannamei shrimps by activation of its immunological system. Fish Shellfish Immunol. 84, 1083–1089. https://doi.org/10.1016/j.fsi.2018.10.007.
Orlowski, P., Tomaszewska, E., Gniadek, M., Baska, P., Nowakowska, J., Sokolowska, J., Nowak, Z., Donten, M., Celichowski, G., Grobelny, J., 2014. Tannic acid modified silver nanoparticles show antiviral activity in herpes simplex virus type 2 infection. PLoS One 9. https://doi.org/10.1371/journal.pone.0104113 e104113.
Pal, S., Tak, Y.K., Song, J.M., 2007. Does the antibacterial activity of silver nanoparticles depend on the shape of the nanoparticle? A study of the gram-negative bacterium Escherichia coli. Appl. Environ. Microbiol. 73, 1712–1720. https://doi.org/10.1128/AEM.02218-06.
Prabhu, S., Poulose, E.K., 2012. Silver nanoparticles: mechanism of antimicrobial action, synthesis, medical applications, and toxicity effects. Int. Nano Lett. 2, 1–10. https://doi.org/10.1186/2228-5326-2-32.
Rather, M.A., Bhat, I.A., Sharma, N., Gora, A., Ganie, P.A., Sharma, R., 2017. Synthesis and characterization of Azadirachta indica constructed silver nanoparticles and their immunomodulatory activity in fish. Aquac. Res. 48, 3742–3754. https://doi.org/10.1111/are.13199.
RathnaKumari, P., Kolanchinathan, P., Siva, D., Abirami, B., Masilamani, V., George, J., Shanmugam, A., Balasundaram, A., 2018. Antibacterial efficacy of seagrass Cymodocea serrulata- engineered silver nanoparticles against prawn pathogen Vibrio parahaemolyticus and its combative effect on the marine shrimp Penaeus monodon Padmanabhan. Aquaculture 493, 158–164. https://doi.org/10.1016/j.aquaculture.2018.04.061.
Ringwood, A.H., Mccarthy, M., Bates, T.C., Carroll, D.L., 2010. The effects of silver nanoparticles on oyster embryos. Mar. Environ. Res. 69, S49–S51. https://doi.org/10.1016/j.marenvres.2009.10.011.
Romo-Quiñonez, C.R., Álvarez-Sánchez, A.R., Álvarez-Ruiz, P., Chávez-Sánchez, M.C., Bogdanchikova, N., Pestryakov, A., 2020. Evaluation of a new Argovit as an antiviral agent included in feed to protect the shrimp Litopenaeus vannamei against White Spot Syndrome Virus infection. PeerJ 8, 1–22. https://doi.org/10.7717/peerj.8446.
Salari-Joo, H., Kalbassi, M.R., Johari, S.A., 2012. Effect of water salinity on acute toxicity of colloidal silver nanoparticles in rainbow trout (Oncorhynchus mykiss) larvae. Iran. J. Heal. Environ. 5, 121–132.
Sánchez-Martínez, J.G., Aguirre-Guzmán, G., Mejía-Ruíz, C.H., 2007. White spot syndrome virus in cultured shrimp: a review. Aquac. Res. 38, 1339–1354. https://doi.org/10.1111/j.1365-2109.2007.01827.x.
Sanvicens, N., Marco, M.P., 2008. Multifunctional nanoparticles – properties and prospects for their use in human medicine. Trends Biotechnol. 26, 425–433. https://doi.org/10.1016/j.tibtech.2008.04.005.
Sarkheil, M., Sourinejad, I., Mirbakhsh, M., Kordestani, D., 2016. Aquacultural engineering application of silver nanoparticles immobilized on TEPA-Den-SiO 2 as water filter media for bacterial disinfection in culture of Penaeid shrimp larvae. J. Aquac. Eng. Fish. Res. 74, 17–29. https://doi.org/10.1016/j.aquaeng.2016.05.003.
Sarkheil, M., Sourinejad, I., Mirbakhsh, M., Kordestani, D., Johari, S.A., 2017. Antibacterial activity of immobilized silver nanoparticles on TEPA-Den-SiO 2 against shrimp pathogen, Vibrio sp. Persian1. Aquac. Res. 48, 2120–2132. https://doi.org/10.1111/are.13048.
Seetang-Nun, Y., Jaroenram, W., Sriurairatana, S., Suebsing, R., Kiatpathomchai, W., 2013. Visual detection of white spot syndrome virus using DNA-functionalized gold nanoparticles as probes combined with loop-mediated isothermal amplification. Mol. Cell. Probes 27, 71–79. https://doi.org/10.1016/j.mcp.2012.11.005.
Shabrangharehdasht, M., Mirvaghefi, A., Farahmand, H., 2020. Effects of nanosilver on hematologic, histologic and molecular parameters of rainbow trout (Oncorhynchus mykiss). Aquat. Toxicol. 225, 105549 https://doi.org/10.1016/j.aquatox.2020.105549.
Sharma, V.K., Yngard, R.A., Lin, Y., 2009. Silver nanoparticles: green synthesis and their antimicrobial activities. Adv. Colloid Interface Sci. 145, 83–96. https://doi.org/10.1016/j.cis.2008.09.002.
Sikder, M., Eudy, E., Chandler, G.T., Baalousha, M., 2018. Comparative study of dissolved and nanoparticulate Ag effects on the life cycle of an estuarine meiobenthic copepod, Amphiascus tenuiremis. Nanotoxicology 12, 375–389. https://doi.org/10.1080/17435390.2018.1451568.
Sivaramasamy, E., Zhiwei, W., Li, F., Xiang, J., 2016. Enhancement of vibriosis resistance in Litopenaeus vannamei by supplementation of biomastered silver nanoparticles by Bacillus subtilis. J. Nanomed. Nanotechnol. 7, 1–10. https://doi.org/10.4172/2157-7439.1000352.
Sivaramasamy, E., Zagorsek, K., Li, F., Xiang, J., 2017. In situ synthesis of silver nanoparticles into TEMPO-mediated oxidized bacterial cellulose and their antivibriocidal activity against shrimp pathogens. Carbohydr. Polym. 166, 329–337. https://doi.org/10.1016/j.carbpol.2017.02.093.
Song, K.C., Lee, S.M., Park, T.S., Lee, B.S., 2009. Preparation of colloidal silver nanoparticles by chemical reduction method. Korean J. Chem. Eng. 26, 153–155. https://doi.org/10.1007/s11814-009-0024-y.
Stentiford, G.D., Neil, D.M., Peeler, E.J., Shields, J.D., Small, H.J., Flegel, T.W., Vlak, J. M., Jones, B., Morado, F., Moss, S., Lotz, J., Bartholomay, L., Behringer, D.C., Hauton, C., Lightner, D.V., 2012. Disease will limit future food supply from the global crustacean fishery and aquaculture sectors. J. Invertebr. Pathol. 110, 141–157. https://doi.org/10.1016/j.jip.2012.03.013.
Suebsing, R., Prombun, P., Srisala, J., Kiatpathomchai, W., 2013. Loop-mediated isothermal amplification combined with colorimetric nanogold for detection of the microsporidian Enterocytozoon hepatopenaei in penaeid shrimp. J. Appl. Microbiol. 114, 1254–1263. https://doi.org/10.1111/jam.12160.
Sun, X., Qin, J., Xia, P., Guo, B., Yang, C., Sun, X., Qin, J., Xia, P., Guo, B., Yang, C., Song, C., Wang, S., 2015. Graphene oxide-silver nanoparticle membrane for biofouling control and water purification. Chem. Eng. J. 281, 253–259. https://doi.org/10.1016/j.cej.2015.06.059.
Swain, P., Nayak, S.K., Sasmal, A., Behera, T., Barik, S.K., Swain, S.K., Mishra, S.S., Sen, A.K., Das, J.K., Jayasankar, P., 2014. Antimicrobial activity of metal based nanoparticles against microbes associated with diseases in aquaculture. World J. Microbiol. Biotechnol. 30, 2491–24502. https://doi.org/10.1007/s11274-014-1674-4.
Tang, S., Zheng, J., 2018. Antibacterial activity of silver nanoparticles: structural effects. Adv. Healthc. Mater. 1701503, 1–10. https://doi.org/10.1002/adhm.201701503.
Thorley, A.J., Tetley, T.D., 2013. New perspectives in nanomedicine. Pharmacol. Ther. 140, 176–185. https://doi.org/10.1016/j.pharmthera.2013.06.008.
Thornber, K., Verner-jeffreys, D., Hinchliffe, S., Rahman, M.M., Bass, D., Tyler, C.R., 2020. Evaluating antimicrobial resistance in the global shrimp industry. Rev. Aquac. 12, 966–986. https://doi.org/10.1111/raq.12367.
Toncelli, C., Mylona, K., Kalantzi, I., Tsiola, A., Pitta, P., Tsapakis, M., Pergantis, S.A., 2017. Silver nanoparticles in seawater: a dynamic mass balance at part per trillion silver concentrations. Sci. Total Environ. 601–602, 15–21. https://doi.org/10.1016/j.scitotenv.2017.05.148.
Vaseeharan, B., Ramasamy, P., Chen, J.C., 2010. Antibacterial activity of silver nanoparticles (AgNps) synthesized by tea leaf extracts against pathogenic Vibrio harveyi and its protective efficacy on juvenile Feneropenaeus indicus. Lett. Appl. Microbiol. 50, 352–356. https://doi.org/10.1111/j.1472-765X.2010.02799.x.
Vimala, K., Mohan, Y.M., Sivudu, K.S., Varaprasad, K., Ravindra, S., Reddy, N.N., Padma, Y., Sreedhar, B., Mohanaraju, K., 2010. Fabrication of porous chitosan films impregnated with silver nanoparticles: a facile approach for superior antibacterial application. Colloids Surf. B Biointerfaces 76, 248–258. https://doi.org/10.1016/j.colsurfb.2009.10.044.
Walker, P.J.W., Winton, J.R.W., 2010. Emerging viral diseases of fish and shrimp. Vet. Res. 4151. https://doi.org/10.1051/vetres/2010022.

Wang, J., Wang, W.-X., 2014. Salinity influences on the uptake of silver nanoparticles and silver nitrate by marine medaka (Oryzias melastigma). Environ. Toxicol. Chem. 33, 632–640. https://doi.org/10.1002/etc.2471.

Wang, H., Burgess, R.M., Cantwell, M.G., Portis, L.M., Perron, M.M., Wu, F., Ho, K.T., 2014a. Stability and aggregation of silver and titanium dioxide nanoparticles in seawater: role of salinity and dissolved organic carbon. Environ. Toxicol. Chem. 33, 1023–1029. https://doi.org/10.1002/etc.2529.

Wang, H., Ho, K.T., Scheckel, K.G., Wu, F., Cantwell, M.G., Katz, D.R., Horowitz, D.B., Boothman, W.S., Burgess, R.M., 2014b. Toxicity, bioaccumulation, and biotransformation of silver nanoparticles in marine organisms. Environ. Sci. Technol. 48, 13711–13717. https://doi.org/10.1021/es502976y.

Wei, F., Zhao, X., Li, C., Han, X., 2018. A novel strategy for water disinfection with a AgNPs/gelatin sponge filter. Environ. Sci. Pollut. Res. 25, 19480–19487. https://doi.org/10.1007/s11356-018-2157-1.

Xiang, D., Zheng, Y., Duan, W., Li, X., Yin, J., Shigdar, S., O'Connor, M.L., Marappan, M., Zhao, X., Miao, Y., Xiang, B., Zheng, C., 2013. Inhibition of A/Human/Hubei/3/2005 (H3N2) influenza virus infection by silver nanoparticles in vitro and in vivo. Int. J. Nanomedicine 8, 4103–4114. https://doi.org/10.2147/IJN.S53622.

Xiu, Z., Ma, J., Alvarez, P.J.J., 2011. Differential effect of common ligands and molecular oxygen on antimicrobial activity of silver nanoparticles versus silver ions. Environ. Sci. Technol. 45, 9003–9008. https://doi.org/10.1021/es201918f.

Yen, C., Puig, H.De, Tam, J.O., Gómez-márquez, J., Bosch, I., Hamad-schifferli, K., Gehrke, L., 2015. Multicolored silver nanoparticles for multiplexed disease diagnostics: distinguishing dengue, yellow fever, and Ebola viruses. Lab Chip 15, 1638–1641. https://doi.org/10.1039/C5LC00055F.

Yu, Z., Li, Q., Wang, J., Yu, Y., Wang, Y., Zhou, Q., Li, P., 2020. Reactive oxygen species-related nanoparticle toxicity in the biomedical field. Nanoscale Res. Lett. 15, 115. https://doi.org/10.1186/s11671-020-03344-7.