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Historical Perspective

Macroalgae as biofactories of metal nanoparticles; biosynthesis and food applications

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ABSTRACT

Nanotechnology has opened a new frontier in recent years, capable of providing new ways of controlling and structuring products with greater market value and offering significant opportunities for the development of innovative applications in food processing, preservation, and packaging. Macroalgae (MAG) are the major photoautotrophic group of living beings known as a potential source of secondary metabolites, namely phenolic compounds, pigments, and polysaccharides. Biosynthesis based on the abilities of MAG as "nanobiofactories" targets the use of algal secondary metabolites as reducing agents to stabilize nanoparticles (NPs). Nowadays, most of the studies are focused on the use of metal (Ag, Au) and metal-oxide (CuO, ZnO) NPs derived from algae. The eco-friendly biosynthesis of metal NPs reduces the cost and production time and increases their biocompatibility, due to the presence of bioactive compounds in MAG, making them suitable for a wide variety of applications. These compounds have been attributed to the antimicrobial and antioxidant properties responsible for their application through innovative technologies such as nanoencapsulation, nanocomposites, or biosensors in the food industry. Nevertheless, toxicity is a key factor that should be considered, so the applicable regulation needs to guarantee the safe use of metal NPs. Consequently, the aim of this review will be to compile the available information on MAG-mediated metal NPs, their biosynthesis, and potential food applications.

1. Introduction

Nanotechnology is a multidisciplinary field that combines science and engineering at the nanoscale, between 1 and 100 nm, to develop nanomaterials (NMs) with different and unique properties [1]. Particularly, nanotechnology in the food sector has revolutionized the industry starting from processing to security, enhancing the flavor and shelf-life of food products [2]. Recent advancements in the field of NMs-based applications have shown prospects to re-frame processing lines, re-structure the production chain, promote natural resource conservation, and even re-define food habits. The target is to guarantee the presence of safe and advanced nanotechnology in the food industry focused on the consumer through safe and sustainable food with improved functional properties. It highlights the use of NMs to encapsulate bioactive components, as well as its application on food packaging and nanosensors. For instance, nanosensors incorporated into packaging could detect moisture, lipids or several gases released as a result of spoilage at all stages of the food chain, which in turn would reduce food waste, benefiting producers, retailers, and consumers [3,4]. Furthermore, they are being introduced in the control of environmental contamination in the food sector [5]. In food processing, NMs bring

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Abbreviations

Generic

NMs	Nanomaterials
NPs	Nanoparticles
nm	Nanometer
QDs	Quantum dots
SLNs	Solid lipid Nanoparticles
NLCs	Nanostructured lipid carriers
NDs	Nanodots
AuNPs	Gold Nanoparticle
AgNPs	Silver Nanoparticles
ROS	Reactive oxygen species
MIONPs	Magnetic Iron Oxide Nanoparticles
EC	Extracellular
IC	Intracellular
S	Spherical
I	Irregular
C	Cubic
P	Polygonal
PD	Poly-dispersed
T	Triangular
E	Ellipsoidal
PS	Pseudospherical
R	Rectangle
H	Hexagonal
A	Angular
(G)	Green algae
(B)	Brown algae
(R)	Red algae
CR	Crystalline
M	Metal
MO	Metal oxide
DA	Dopamine
HQ	Hydroquinone
NS	No significant
rpm	revolutions per minute
UV	Ultraviolet
IUPAC	International Union of Pure and Applied Chemistry
UE	European Union
EC	The European Commission
Reg	Regulation
EFSA	European Food Safety Authority
FDA	Food and Drug Administration

Compounds

Ag	Silver
Au	Gold
Pd	Palladium
Cu	Copper
Se	Selenium
Pt	Platinum
AgCl	Silver chloride
CuO	Copper oxide
ZnO	Zinc oxide
MgO	Magnesium oxide
Fe_3O_4	Iron (II, III) oxide
TiO_2	Titanium (IV)
Co_3O_4	Cobalt (II, III) oxide
CdS	Cadmium sulfide
CeO_2	Cerium (IV) oxide
ZrO_2	Zirconium dioxide
SiO_2	Silicon dioxide
H_2O_2	Hydrogen peroxide
Al_2O_3	Aluminum (III) oxide
$HAuCl_4$	Chloroauric acid
$AgNO_3$	Silver nitrate
CuS	Copper sulfide

Materials and methods

TEM	Transmission electron microscopy
FTIR	Fourier transform infrared spectroscopy
SEM	Scanning electron microscope
AFM	Atomic force microscopy
XRD	X-ray diffraction
DLS	Dynamic light scattering
XPS	X-ray photoelectron spectroscopy
HR-TEM	High-resolution transmission electron microscopy
EDS	Energy dispersive spectroscopy
WD-XRF	Wavelength Dispersive X-ray Fluorescence
PL	Photoluminescence
SPR	Surface plasmon resonance
UV-vis	Ultraviolet spectroscopy
SR	Raman spectroscopy
BET	Brunauer-Emmett-Teller technique
WD-XRF	Wavelength dispersive X-ray fluorescence
ζ	Zeta potential
CDZ	Clear zone diameter
MBC	Minimum bactericidal concentration
MIC	Minimum inhibitory concentration
Amp	Ampicillin
LB	Luria-Bertani
IC_{50}	Half maximal inhibitory concentration
MHA	Mueller Hinton agar
SDA	Sabouraud Dextrose agar
CDA	Czapek-Dox agar
CV	Crystal violet
TPC	Tissue culture plate assay
BHI	Brain Heart Infusion
PDA	Potato Dextrose agar
AAE	Ascorbic acid
GAE	Gallic acid
BET	Brunauer-Emmett-Teller
RSM	Response surface methodology
SERS	Surface enhancement Raman spectroscopy
SEMEDS	Scanning electron microscopy/ Energy dispersive spectroscopy
FESEM	Field emission scanning microscope X-ray photoelectron spectroscopy
TPC	Total phenolic content
FRAP	Ferric ion reducing antioxidant power
DPPH	2,2-diphenyl-1-picrylhydrazyl
ABTS	2,2'-azino-bis (3-ethylbenzothiazoline-6-sulfonic acid
LC-MS	Liquid chromatography-mass spectrometry
GC-MS	Gas chromatography-mass spectrometry
CILE	Composite modified carbon ionic liquid electrode

unique ideas such as the nanoencapsulation to enhance flavor release and retention, as well as to create new culinary products [6]. Food packaging with NMs is a trend that promotes the replacement of non-degradable materials with biodegradable ones, ensures safe food supply and delivery, and can be used as pathogen sensors, anti-counterfeiting devices and impermeable films [7,8]. Nevertheless, to apply any new NMs in the food industry, it must be taken into account that it needs to be environmentally friendly and provide zero or minimal toxic impact to the consumers of final product or service [9].

According to the number of dimensions at the nanoscale, nanoparticles (NPs) such as metal NPs have all three dimensions in nm range (<100 nm); so-called zero-dimensional (0D) NMs [10,11]. Based on their composition, NPs of metal oxides (Fe_3O_4, TiO_2, ZnO and QD) or pure metals (Ag, Au, Pd, Cu, …) are inorganic NMs [12,13]. These particles are crystalline or amorphous solids at room temperature, that can be spherical or non-spherical; they have different surface characteristics and sizes depending on the starting materials and fabrication conditions [14]. This study will focus on the review of metal-based NPs and natural polymeric NPs obtained from macroalgae (MAG) extracts. All NPs are NMs but not all NMs are NPs. NPs and NMs can be made of a single material (metals, carbon or polymers) or multiple materials (polymer-metal, silica-metal or graphene-metal). Following these concepts, other useful concepts can be defined such as "nanocomposite", which would be an NM with a multiphase structure that has one or more dimensions at the nanoscale or "nanobject" a NM that possesses one or more peripheral dimensions at the nanoscale [8,15]. The best-known shape of NMs is spherical, but there are examples of triangular, cubic, rectangular, polygonal, hexagonal, or ellipsoidal NMs [16]. There are different ways to classify NMs, depending on their origin, their dimensions or on their composition [17], as shown in Fig. 1. According to their origin; NMs are classified into two large groups: natural NMs, present in nature such as viruses, proteins, enzymes and minerals, and synthetic NMs that are not found in nature and require some processes for their production [18].

The two common approaches for the synthesis of NMs are top-down and bottom-up. The top-down approach involves breaking bulk materials by milling to reduce their size to the nanoscale, whereas the bottom-up approach involves building NMs from individual atoms that can self-assemble in a self-regulating manner. Metal NPs can be generated through three routes involving physical, chemical, and biological pathways. The physical and chemical route has disadvantages such as thermal instability or the use of aggressive chemical agents. Instead, the biological synthesis reduces toxicity problems, among others, by means of a simple process that uses metabolites present in plant or algae extracts as reducing agents [9,19]. This study was conducted with the purpose of compiling, analyzing, and organizing the available information on MAG-mediated NPs biosynthesis, including aspects related to their context, classification, the toxicity of metallic NMs mediated by MAG, their characterization, and subsequent biological potential and application focused on the food industry. Finally, a summary of the current legal framework applicable to the field of study was also included.

2. Biosynthesis of macroalgae-mediated metal nanoparticles; an overview

Algae are photosynthetic aquatic organisms that can be classified depending on certain aspects such as morphology, size, or habitat. Fundamentally, algae can be found in fresh or marine waters; microalgae are unicellular organisms while MAG are multicellular organisms that form complex structures [20,21]. MAG are classified into three lineages that have evolved independently, this is, brown algae (Phaeophyta), red algae (Rhodophyta) and green algae (Chlorophyta) [22]. The biosynthesis of NPs from algae is possible as either micro-mediated or macro-mediated biosynthesis. Algae have been postulated as model organisms for the fabrication of bio-NMs due to their ability to hyperaccumulate heavy metal ions. In addition, they possess an exceptional ability to remodel them into more malleable forms [23]. On the side, the reduced cultivation cost, shorter production time and sustainable biosynthesis minimize the use of hazardous chemicals, making algae an alternative platform for the synthesis of NPs [24]. This gives rise to what is currently recognized as green nanotechnology, or the use of pathways for the synthesis of NPs with the help of various biotechnological techniques [25].

The biosynthesis of NPs using algae can be performed in three important steps:

- The preparation of algae extracts in water or in organic solvents by heating or boiling it for a certain time;
- The preparation of molar solutions of ionic metal compounds;
- The incubation of algae solutions and molar solutions of ionic metal compounds, followed by continuous or non-agitation agitation under controlled conditions.

The algae-mediated synthesis of NPs is performed in shorter periods depending on the dose and type of algae used. This is due to the presence of several biomolecules in the composition of algae, including polysaccharides, peptides, phenolic compounds and pigments, that are responsible for the reduction and stabilization of metals [26]. The chemical composition of MAG is likely to vary from species to species and as a function of harvest time, growth habitat, or environmental conditions. Even within the same geographic area, growth rate and chemical composition may vary depending on, for example, harvest time, pH, sunlight intensity, salinity, nutrient availability, temperature, dissolved oxygen concentration, sea depth, local water currents, or proximity to aquaculture plants, among other culture parameters [27,28].

The production of monometallic, bimetallic, and metal oxide NPs from algae covers a wide range of possibilities and challenges that allow the study of a multitude of species.

Table 1 details a choice of different metal and metal oxide NPs biosynthesized from various marine MAG, along with the size of NPs and the activity associated with them. For example, a study employed the aqueous extract of the algae *Sargassum wightii* to synthesize stable AuNPs by chloroauric acid ($HAuCl_4$) reduction. The obtained results confirmed the production of uniform AuNPs. It was detailed that the probable reason was the presence of sugars and/or terpenes that help the reduction of metal ions resulting in pure metallic NPs and bi-metallic NPs with a size ranging from 8 to 12 nm. Detailed observations by transmission electron microscopy (TEM) specified an average size of 11 nm. In addition, the presence of extracellular polysaccharides in the algae (35%) may facilitate the stabilization of NPs [29]. In another study, the antimicrobial activity against common fish pathogens like *Vibrio parahaemolyticus, Vibrio vulnificus, Vibrio harveyii* or *Vibrio anguillarum* was revealed by using a red alga named *Portieria hornemannii* to synthetize AgNPs (35-50 nm) [30].

Bioactive compounds from algal matrices can help in the synthesis of NPs acting as reducing, stabilizing, and coating agents, being able to provide a robust coating on NPs in a single step [31]. From carbohydrates, minerals, vitamins, or polyunsaturated fatty acids to bioactive compounds that act as antioxidants (polyphenols and tocopherols), pigments, such as carotenoids or chlorophylls, these are some molecules present in MAG extracts with great value for the synthesis of NPs with optimal properties [32–34]. Among MAG resources, one of the outstanding compounds currently acquiring great value for research, are polysaccharides, e.g. agar, alginate, carrageenan, ulvan, fucoidan and laminarin. These hydrocolloids are mainly composed of small sugar units joined with glycosidic bonds formed by hydrophilic groups [35]. In addition, polysaccharides, together with proteins and enzymes, are target groups of biomolecules also present in the cell wall. Many studies focused on the use of these molecules and their action as biocatalysts in the production of precursor metal salts to nucleate into metal and metal

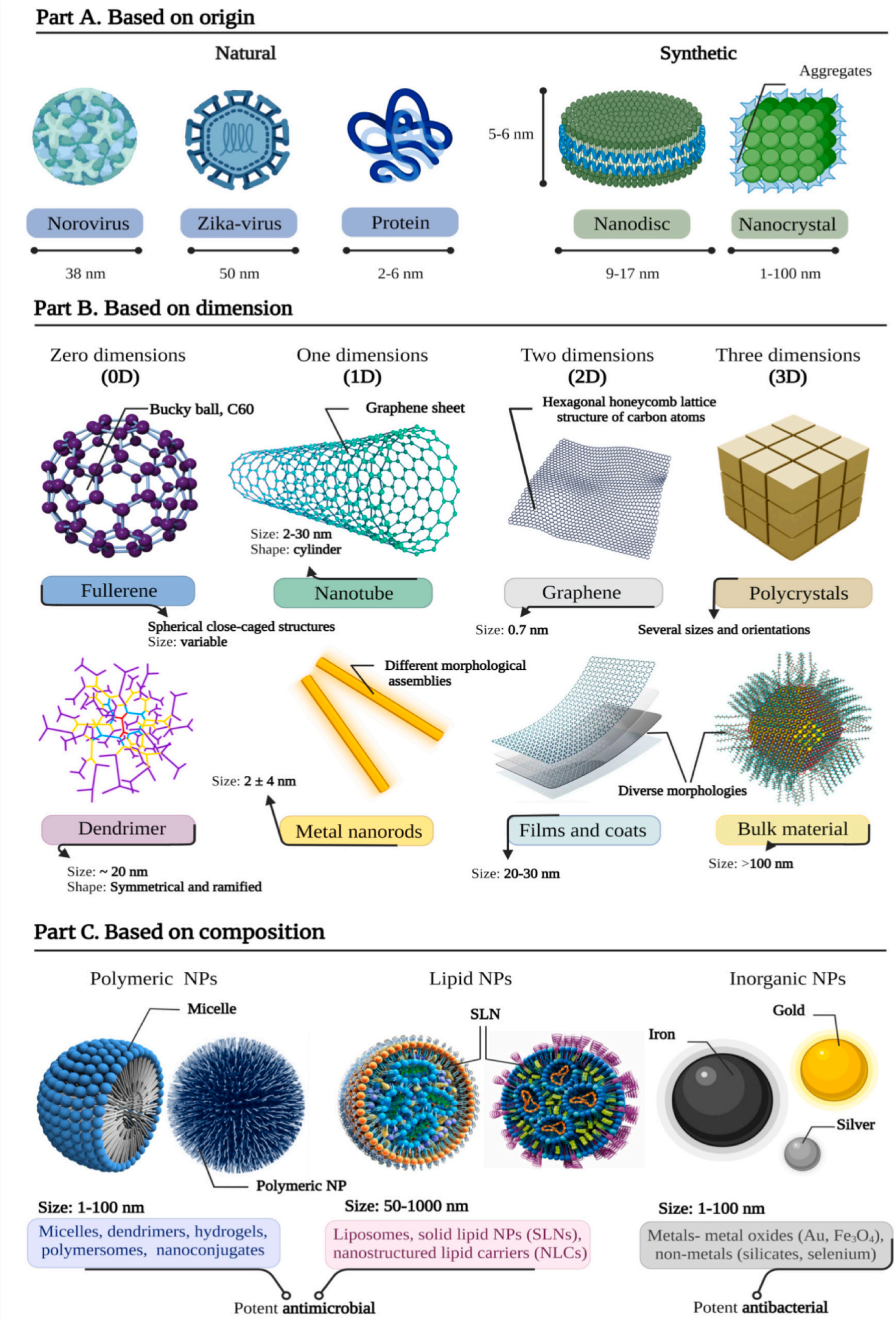

Fig. 1. Examples of nanomaterials (NMs) based on their origin, dimensions, and composition. Created with BioRender.com.

oxide NPs [24]. On the contrary, the remaining larger amphipathic molecules act as surfactants, driving and controlling the growth of NPs [24]. De Aragao et al. [36] studied a polysaccharide isolated from *Gracinalaria birdiae* as a reducing and stabilizing agent to synthesize spherical AgNPs. The employed polysaccharide acted by forming complexes with the Ag ions, controlling the reduction process, and protecting the particles from aggregation thus, affecting the shape and size of AgNPs. In addition, the influence of AgNPs morphology and size was

Table 1
Main characteristics and biological properties of macro/microalgae mediated biosynthesis of metal and metal-oxide NPs.

Species	NP	Size (nm)	Activity								Ref.
			Antibacterial	Antifungal	Antibiofilm	Antioxidant	Anticancer	Cytotoxicity	Anti-inflammatory	Anti-plasmodial	
MACROALGAE											
Metal											
Ulva fasciata **(G)**		7–20	✓								[40]
Ulva rigida **(G)**		12	✓	✓			✓				[41]
Enteromorpha prolifera **(G)**		18				✓					[42]
Enteromorpha fexuosa **(G)**		30–90				✓	✓		✓		[43]
Enteromorpha compressa **(G)**		4–24	✓	✓				✓			[44]
Caulerpa racemosa **(G)**		5–25	✓								[45]
Caulerpa serrulata **(G)**		8–12	✓								[46]
Gracilaria corticata **(R)**		52		✓							[47]
Gracilaria foliifera **(R)**		24	✓	✓			✓	✓			[41]
Gracilaria birdiae **(R)**		20–95	✓								[36]
Gelidiella acerosa **(B)**		–	✓								[48]
Gelidium corneum **(R)**	Ag	20–50	✓	✓	✓						[49]
Palmaria decipiens **(R)**		7				✓					[50]
Chondrococcus hornemannii **(R)**		–	✓			✓					[36]
Sargassum ilicifolium **(B)**		25	✓								[51]
Sargassum polycystum **(B)**		28				✓	✓				[52]
Padina sp. **(B)**		25–60	✓			✓					[53]
Padina pavonica **(B)**		46	✓								[54]
Turbinaria conoides **(B)**		2–17			✓						[55]
Turbinaria ornata **(B)**		49–75			✓						[56]
Desmarestia menziesii **(B)**		18				✓					[50]
Laurencia papillosa **(B)**		–	✓	✓							[57]
Cytoseira myrica **(B)**		17	✓	✓			✓	✓			[41]
Ulva rigida **(G)**		9	✓	✓			✓	✓			[58]
Gracilaria Pygmea **(R)**		27–36				✓					[59]
Gracilaria foliifera **(R)**		13	✓	✓			✓	✓			[58]
Lemanea fluvitilis (L.) **(R)**		5–15				✓					[40]
Corallina officinalis **(R)**		14–16						✓			[60]
Palmaria decipiens **(R)**		31–42	✓								[50]
Chondrus crispus **(R)**		14.4–19.4				✓			✓		[61]
Turbinaria decurrens **(B)**		10–20				✓					[62]
Cystoseira myrica **(B)**		11				✓		✓			[58]
Desmarestia menziesii **(B)**		8–15				✓					[50]
Dictyota bartayresiana **(B)**	Au	–		✓							[63]
Stoechospermum marginatum **(B)**		19–94	✓								[64]
Cystoseira baccata **(B)**		8.4				✓					[65]
Galaxaura elongata **(B)**		4–77	✓								[66]
Padina pavonica **(B)**		3–70	✓								[67]
Sargassum cymosum **(B)**		5–22									[68]
Sargassum ilicifolium **(B)**		13.61	✓								[51]
Sargassum glaucescens **(B)**		2– 5					✓				[69]
Sargassum polycystum **(B)**		30–60	✓								[70]
Sargassum muticum **(B)**		9–12	✓			✓					[71]
Sargassum glaucescens **(B)**		2–5				✓					[69]
Halymenia dilatata **(R)**	Pt	13–17				✓	✓				[72]
Padina gymnospora **(B)**		5-50	✓			✓	✓	✓			[73]
Corallina mediterránea **(R)**	Cu	13–14						✓			[74]
Metal oxides											
Cystoseira trinoids **(B)**	CuO	7–10	✓			✓					[75]
Sargassum muticum **(B)**	CuO/ZnO	15–20			✓						[76]

(*continued on next page*)

Table 1 (*continued*)

Species	NP	Size (nm)	Activity								Ref.
			Antibacterial	Antifungal	Antibiofilm	Antioxidant	Anticancer	Cytotoxicity	Anti-inflammatory	Anti-plasmodial	
Bifurcaria bifurcate **(B)**	CuO	5–45 (~21)	✓								[77]
Ulva flexuosa (wulfen) **(G)**		12	✓	✓							[78]
Ulva fasciata **(G)**		23–34			✓						[79]
Jania rubens **(R)**		22.22–33.33			✓						[79]
Pterocladia capillacea **(R)**	Fe_3O_4	17–22.5	✓	✓							[80]
Gracilaria edulis **(R)**		20–26	✓	✓							[81]
Colpomenia sinuosa **(B)**		11.2–34	✓	✓							[80]
Sargassum vulgare **(B)**		17–34			✓						[79]
Halimeda opuntia **(G)**		33	✓								[82]
*Cladophora glomerata***(G)**		14.4–37.5		✓							[83]
Gracilaria edulis **(R)**	ZnO	65–95					✓	✓			[84]
Cystoseira crinite **(B)**		23–140	✓	✓		✓					[85]
Sargassum myriocystum **(B)**		36	✓	✓							[33]
Valoniopsis pachynema **(G)**	CdS	<100								✓	[86]
Sargassum wightii **(B)**	MgO	68	✓	✓							[87]
Sargassum wightii Greville **(B)**	CeO_2	35.68				✓					[88]
Sargassum wightiic **(B)**	ZrO_2	6	✓								[89]
Sargassum plagiophyllum **(B)**	AgCl	18–42	✓								[90]
MICROALGAE											
Chlamydomonas reinhardtii **(G)**	Ag	5–15	✓								[91]
Anabaena flos-aquae **(G)**		5–25					✓	✓			[92]
Spirogyra variants **(G)**		18	✓								[93]
Phenerochaete chrysosporium **(G)**		34–90	✓								[94]
Chlorococcum humicola **(G)**		16	✓								[95]
Origanum onites **(G)**		54.2				✓					[96]
Desmodesmus sp. **(G)**		15–30									[97]
Dunaliella salina **(G)**		15.26					✓				[98]
Coelastrella **(G)**	Au	30				✓					[99]
Nitzschia diatom **(G)**		43	✓								[100]
Trichodesmium erythraeum **(BG)**	Ag	~26.5	✓			✓	✓				[101]
Stephanopyxis turri **(B)**	Au	10–30	✓								[102]

Abbreviations: (G): green algae; (R): reed algae; (B): brown algae; (BG): blue-green algae.

associated with the development of antibacterial activity.

Several studies have inquired about the growth mode of NPs, deducing that it begins with the conversion or reduction of metal ions from their mono or divalent oxidation states to zero valent states after mixture of a metal salt solution with the solution holding the algae extract. This is followed by nucleation mediated mainly by enzymes present in the algae composition and detected by the color change in the reaction [37]. Following nucleation, thermodynamic stability (Ostwald ripening) takes place, a kinetic process in which the immediate small particles adhere to the lower energy faces of the forming crystal [38]. This aims to give rise to larger NPs of different sizes and shapes. During growth, this is where the compositional biomolecules act as natural surfactants as described in the previous section. Dhas et al. [39] evaluated the antimicrobial and antioxidant activity of AuNPs biosynthesized from the extract of MAG *Sargassum plagiophyllum.* The formation of NPs was observed by color change during the reduction of Au^3 to Au^0 after the addition of auric chloride ($HAuCl_4$). The result were NPs with efficient antimicrobial and antioxidant activity that reached an average size of 65.87 nm. Finally, the termination phase directly affected by physical factors (pH, incubation time, temperature, substrate concentration, stirring frequency, etc.) [37] and adsorption of natural surfactants or coating agents that interact on the crystal facets influencing the orientation and final assembly [24].

Two routes exist for the completion of metal NPs biosynthesis process depending on the location of NPs once formed (Fig. 2): the dose-dependent intracellular (IC) mode in which the biosynthesis of NPs occurs inside the algal cell and consists of adding metallic salts to the culture medium for uptake and reduction by the organism; or the extracellular (EC) mode in which the metal ions adhere to the surface of the algal cells. In this route, the reduction is carried out by metabolites such as proteins, lipids or enzymes secreted by the cells, or with derived components [3,103]. The EC method is more widespread when MAG are used because it does not require specific cultivation conditions. The MAG are harvested directly from seas or lakes and are subjected to simple pretreatments to later adapt the synthesis process by adjusting the influential physical parameters (pH, temperature, biomass, etc.). Unlike IC synthesis, the EC route does not allow the permanent production of NMs in photobioreactors. IC synthesis, more common when using microalgae, is based on the metabolism of living algal cells to carry out the synthesis of various NMs through control and automation in photobioreactors [104]. Table 1 shows a brief overview of relevant studies focused on microalgae.

In the case of microalgae-mediated synthesis, recent research has developed a novel approach to isolate organic nanodots (NDs) derived from *Spirulina platensis*. The goal was to obtain an innovative alternative preservative that can increase the shelf life and sensory quality of food and drinks. TEM analysis revealed that the NDs obtained reached an average size of 40-45 nm. Although the results were favorable, it was concluded that further investigation is needed about the efficacy of NDs as preservatives, because they could guarantee a new promising approach for food storage, with higher commercial profitability [105].

3. Factors in the macroalgae-mediated biosynthesis of metal nanoparticles

Temperature, light, extract or biomass concentration, precursor concentration, frequency of agitation, incubation period, exposure time or pH of the medium are some physical factors that regulate the stabilization, nucleation and formation of NPs [37]. All kinds of effects on morphology, yield, stability, and abundance have been reported during the synthesis of NPs due to various critical factors involved in the process. Currently, to ensure process control, response surface methodology (RSM) is resorted to find the optimal operating conditions [129]. The factors that show the greatest relevance will be discussed below:

3.1. Temperature

In some cases, the biosynthesis of metallic NPs is carried out at room temperature and continuous stirring [130]. This avoids destabilization of bioactive compounds in algal extracts and allows obtaining complex mixtures of sizes and shapes in NPs [34,131]. Nonetheless, some authors have reported that an increase in temperature favorably affects the reaction rate and production of NPs. It also influences the regulation of the shape and size of NPs [103]. In studies of AuNPs biosynthesis with MAG such as *Actinotrichia fragilis, Ecklonia cava* or *Galaxaura elongata* carried out at room temperature, different shapes, e.g. spherical, cubic, triangular or hexagonal, were obtained [114,133,134]. Rajeshjumar. et al. [135] showed the highest conversion rate of Au ions into NPs after increasing the process temperature. While larger AuNPs were obtained at 20 and 40°C, the fastest reaction rate and maximum synthesis of small size NPs were obtained at 80°C. In another study, at low temperatures (<65°C), the rate of ion reduction was very slow with peaks as low as

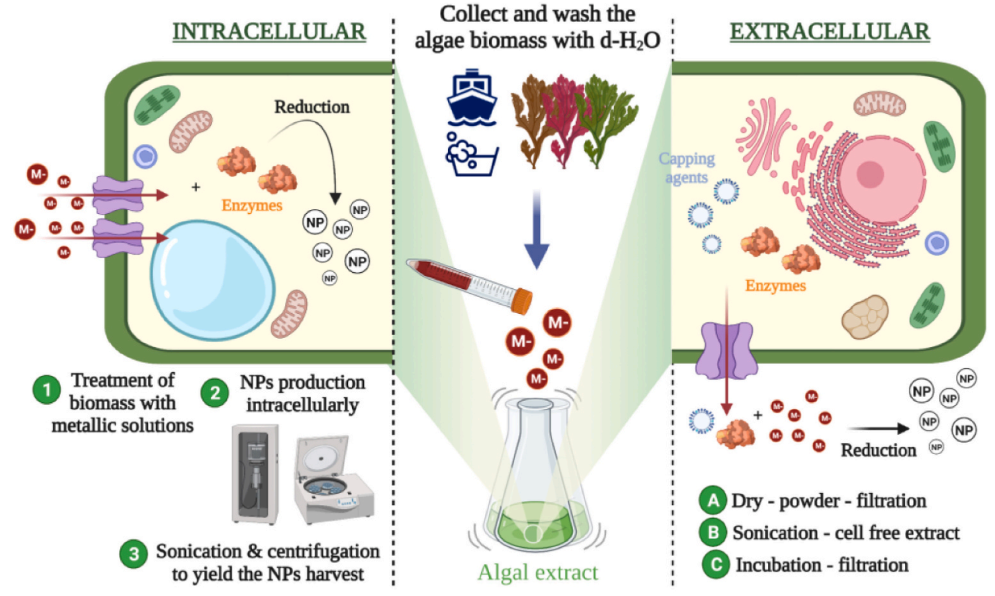

Fig. 2. Protocols employed for extracellular and intracellular synthesis of nanoparticles [22,38]. Created with BioRender.com.

480 nm. With an increase in temperature from 65 to 75°C, the surface plasmon resonance (SPR) absorption peaks were smooth and broad, showing an increase in size (>2 μm) of the spherical NPs and polydisperse NPs. Agglomeration of NPs was reported at temperatures from 85 to 95°C [117]. The chosen temperature depends mainly on the algal stain and the method used for synthesis. Its optimization can facilitate obtaining NPs of different sizes and shapes [132].

3.2. The extract concentration

The extract concentration is directly related to the content of bioactive compounds used as reducing agents, directly influencing the stabilization of metal ions and therefore, the final size and shape of NPs. Several studies have obtained a higher applicability when an increase in biomass concentration is reported. Also, on the agglomeration of NPs after increasing the extract concentration [34,37,136]. Babu et al. [137] conducted a diffusion assay to find out the dose-dependent impact of As-AuNPs at various As concentrations (25, 50, 75 and 100 μg/mL). The best result was obtained at 100 μg/mL while the lowest activity was recorded at 25 μg/mL. Aboelfetoh et al. [46] observed that further increase in extract concentration (25%) reduces the intensity of the SPR band due to the agglomeration of NPs. In another study, it was found that algal extract can play a role in the stabilization of NPs through adsorption on the surface of AuNPs. It was also shown that the extract did not influence the size and shape of NPs [45]. Hamouda et al. [138] through a comparison study in the synthesis of AgNPs showed that the NPs differed in shape depending on the type of algae.

3.3. The precursor concentration

The precursor concentration directly affects the size, shape, and yield during synthesis. The higher the concentration, the greater the yield. Generally, the effect on the color of the reaction is visualized by varying the concentration used [43]. The effect on the synthesis of AgNPs was studied by varying the silver nitrate ($AgNO_3$) concentration from 0.5 to 4 mM. At higher $AgNO_3$ concentrations, AgNPs started to aggregate and increase in size. Using the maximum concentration, the collision frequency was increased and resulted in aggregation of the NPs. It was concluded that the optimum Ag concentration was 1 mM [139]. In another study, it was shown that a low precursor concentration implies that particle growth in the system is limited due to the presence of a sufficient amount of coating agent [140]. Finally, some authors observed the color change in the green algae extract upon addition of colorless $AgNO_3$. The color changed to dark brown, this transition usually signals the oxidation of the metal (Ag^+ to Ag^0) and hence indicating the formation of the NPs [141,142].

3.4. Contact time

The rate and properties of NPs synthesized from algal extracts are affected by the incubation time of the reaction. An increase in contact time results in accelerated biosynthesis [143]. In a study about the synthesis of AgNPs using the alga *Caulerpa serrulata,* the reaction between Ag ions and reducing materials in the extract was monitored for 8 days. As the contact time increased, there was an increase in the intensity of the SPR band, with no shift and thus, a rapid increase in the number of AgNPs [46]. Reactions have been carried out from fast reactions of 10 min to slower reactions of 72 h, both at room temperature [144,145].

3.5. The pH

pH is recognized as a critical parameter that drastically affects the size, shape, and synthesis rate of metallic NMs [146]. The production of NPs has been described in the bibliography at alkaline, acidic, and neutral pH. It is true that, for the three cases, studies have detailed changes in the size and morphology of the synthesized NPs largely due to alterations in the electrical charge of the biomass and the coating agents or functional groups that cause repulsion or attraction of the metals in solution, and modify the conformation of the cell structures, determining the binding sites available for the metals. Higher pHs are associated with a higher production of spherical NPs with a reduced diameter whereas more acidic pHs are associated with different shapes (cylindrical and triangular) and larger particle size and agglomeration. On the other hand, biosynthesis is usually carried out at neutral pH [34,37,132]. In a study to prove the efficacy of the antifungal activity, the effect on the production of AuNPs was investigated by altering the pH value of synthesis between 4 and 9. According to the intensity of the SPR bands and the color of the reaction, it was concluded that pH= 8 was the optimal [147]. On the other hand, Rajeshkumar et al. [135] obtained large AuNPs at pH= 8 and 9 and smaller and more stable AuNPs at pH= 6 and 7.

3.6. Capping agent

Overall, secondary metabolites present in the algae act as reducing and coating agents in the synthesis of NPs [148]. Most of the reviewed studies support the theory that functional groups such as proteins, phenolic compounds, terpenoids, flavones, and polysaccharides can encapsulate the surface of the ions acting as essential capping agents in the stabilization of NPs. Nevertheless, the precise mechanism involved in the formation of NPs is still a matter of debate [116]. In a study using MAG *Chaetomorpha linum* to synthesize AgNPs, biomolecules such as secondary amines, peptides, flavonoids, and terpenoids were found to be effective in coating and stabilizing AgNPs [149]. In the synthesis of AuNPs by *Cystoseira baccata*, it was suggested that the polysaccharides and polyphenols present in the cell wall contain hydroxyls as functional groups that aid in the bioreduction of the bulk material to its elemental form and the presence of proteins acts as a coating agent and prevents agglomeration, resulting in stable AuNPs [150]. The results of another study on the synthesis of AgNPs showed that coating agents such as proteins, flavonoids, and tannins may be responsible for the biosynthesis of NPs and reduction of metal ions to NPs [138].

3.7. Additional effects

The influence of agitation frequency is not always remarkable. A few studies have reported that by varying the revolutions per minute (rpm), they obtained variations only in the diameter of the synthesized NPs. Consequently, they are usually more associated with experimental errors than with the stirring rate. For instance, in the synthesis of AuNPs at 300, 800 and 1000 rpm, it was concluded that the stirring speed did not promote significant changes in the NPs produced [68]. Concerning light, it is necessary to initiate the reduction process during the biosynthesis of NPs. In the synthesis of AgNPs using the microalga *Neochloris oleoabundans*, the dependence on light for synthesis was demonstrated by studying a varied range of wavelengths and concluding that for some cases, synthesis without light was unfeasible [151]. Finally, the effect of pressure was tested in some studies; the reduction rate of metal ions through phytochemical agents and the synthesis rate of NPs was higher at ambient pressure [19,152].

4. Main macroalgae-mediated metal nanoparticles

4.1. Silver nanoparticles

One of the most remarkable types of metallic NPs are AgNPs. The tunable chemical and physical properties of AgNPs make the study of their applicability stand out from other inorganic metals [153]. Target properties such as functionality under varying extremes of temperature, pressure and pH, unique plasmonic properties, high surface to volume ratio or catalytic effect in determinative oxidation reactions make

AgNPs capable of limiting the growth of resistant microbial strains at exceptionally low concentrations [154,155]. AgNPs have enhanced toxicity against multidrug-resistant microorganisms and, although the specific mechanism of action is still unknown, the effect is attributed to the generation of Ag^+ ions influenced by the surface field of NPs. In particular, NPs with larger surface area generate higher Ag^+ concentrations, leading to higher antimicrobial activity [8].

In terms of applicability, the antimicrobial efficacy of AgNPs may enhance the activity of drugs such as fluconazole as well as their use as food packaging material. In addition, SPR allows AgNPs to be developed as biosensors for the detection of contaminants or biomarkers [156]. However, the excessive use of AgNPs can be cytotoxic and their unregulated release into the environment can have detrimental effects on aquatic and terrestrial biota [156]. The embedding of AgNPs as antimicrobial agents in food and in packaging materials can promote dispersion and persistent yield, leading to sustained release of AgNPs in the packaging and risking migration to the food product [154]. Therefore, their use and development should be actively investigated to ensure the reliability of the potential benefits described. The properties of algae-synthesized AgNPs are determined according to the results obtained by different spectroscopic, diffractographic and microscopic techniques mentioned above [143]. The following points (Fig. 3) summarize the important indications for AgNPs biosynthesis using a MAG extract [121].

1. Synthesis of AgNPs with algal extracts as source of reducing agents is ensured by the color change from brownish yellow to brown. The appearance of the brown color is due to the excitation of SPR effect and the reduction of $AgNo_3$.
2. The reduction of these AgNPs is monitored by UV-vis, which indicates their formation in the absorbance range of 350-600 nm.
3. FTIR evaluation is used to confirm the presence of bioactive groups interacting between synthesized Ag-NPs and algal extracts. Hydroxyl and carbonyl groups are confirmed among the active groups.
4. The zeta potential indicates the inter-particle efficiency of the coating compounds in stabilizing AgNPs. Negative values clarify the repulsion between the particles, which means the achievement of higher stability in their formation, avoiding agglomeration in aqueous solutions [138].

4.2. *Gold nanoparticles*

Another outstanding type of metallic NPs is AuNPs, which stand out for their ability to interact with light through SPR; they improve the sensitivity and actively target biomarkers due to high surface-to-volume ratio [157]. Their solutions show a range of colors from red and purple to violet, depending on the magnification of violet and the increase in particle size. This color is related to the strong absorption and scattering of radiation at 520 nm, which results from the collective oscillation of conduction electrons on the surface of AuNPs when excited by incident light. For instance, metallic gold is golden yellow, gold nanorods are blue or black in solution, while spherical AuNPs have a visible wine-red color. In terms of shape, Au nanospheres, nanorods or nanobelts to nanoprims and nanostars have been fabricated. Both the size and shape of AuNPs have a decisive effect on their chemical, optical and electromagnetic properties [69]. In addition, they can enhance the scattering of Raman radiation, manipulate the fluorescence of a fluorophore depending on the resistance they show to fluoroscopy among some optical properties. Recent scientific advances have proven their ability to be reinforced as building blocks for plasmonic devices [111,158]. Studies for AuNPs are promising in areas such as catalysis involving organic reactions or plasmodium-mediated photocatalysis [159]. Other notable properties include redox behavior, ease of preparation, non-toxicity, performance and bioconjugation or biocompatibility [160,161].

A potential association has been set up between MAG and AuNPs due to their composition rich in bioactive compounds that are used as reducing and stabilizing agents during the biosynthesis. In addition, their resistance to oxidation due to the development of defense cells positions them as potent antioxidants against free radicals and other oxidative agents [111,161]. AuNPs are usually obtained by chemical reduction of tetrachloroauric acid ($HAuCl_4$) with sodium citrate or

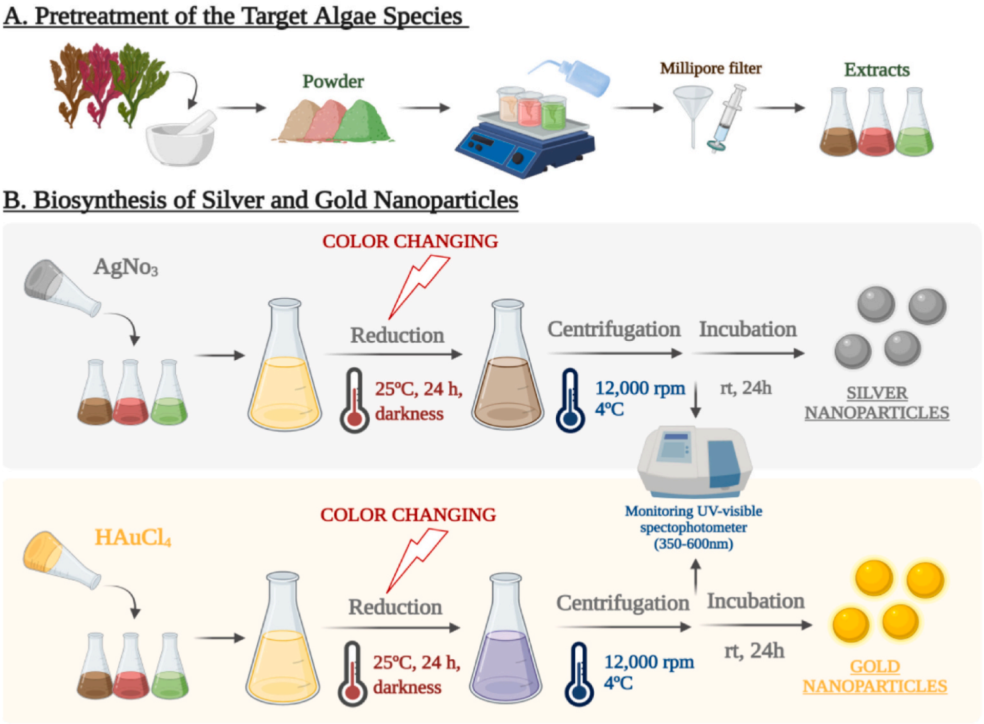

Fig. 3. Silver and Gold NPs biosynthesis process mediated by algae. Created with BioRender.

$NaBH_4$. For instance, Costa et al. [68] synthesized AuNPs using the extract of MAG *Sargassum cymosum* by several concentrations of the metal precursor $HAuCl_4$, temperature, pH, and stirring speed. The metal NPs exhibited strong staining due to their SPR, which facilitated identification and detection by UV-Vis spectrophotometry. In all experiments, the formation of AuNPs was evidenced by the color change from light yellow to purple in an average time of 10 min and with a progressive increase in the color intensity. The ideal range for the extract was a precursor ratio of 5:20. Likewise, the optimal synthesis temperature ranged from 60 to 80°C and pH <5. Finally, the stirring speed had no influence on the process. Spherical AuNPs with a size of 5 to 22 nm were obtained.

5. Characterization techniques for metal nanoparticles

Characterization techniques help us to understand the specific properties of NPs in a fast and reliable way in order to control and apply them later on [81]. In most cases, the final NPs are characterized by spectroscopic and diffractographic techniques. Ultraviolet-visible spectroscopy (UV-vis), dynamic light scattering (DLS), energy dispersive spectroscopy (EDS), X-ray diffraction (XRD) and Raman spectroscopy (SR) are used to characterize the composition, structure, and crystalline phase. In contrast, the size and morphological characteristics of NPs are evaluated using scanning electron microscopy (SEM), TEM, high resolution TEM (HR-TEM) and atomic force microscopy (AFM) [23,162]. The functional groups involved in bio-reduction are studied by Fourier transform infrared (FTIR) spectroscopy [31]. Finally, the hydrodynamic diameter, surface charge and distribution of NPs in the liquid, as well as their stability, are determined by the zeta potential (ζ) and the Brunauer-Emmett-Teller technique (BET), which facilitate determination of the specific area of NPs [22]. Fig. 4 summarizes the most used characterization methods for NPs.

Likewise, MAG-mediated synthesis of inorganic NPs such as Ag and Au, which are the most used metals as biomass, is mainly investigated. Table 2 shows some examples of EC and IC MAG synthesis of Au and Ag NPs. The EC method is more widespread when MAG are used because it does not require specific cultivation conditions while IC synthesis is rarely used. Also, spherical shape is the most common NPs shape although others have been reported. The most used techniques for the characterization of NPs are the following: (i) due to its cost-effectiveness, availability, simplicity and speed, UV-Vis spectroscopy is the crucial tool to confirm the formation of metallic NPs at the initial stage of synthesis [153,163]. The optical properties due to SPR are overseen by UV-Vis [22]. These radiations interact with the metals and promote the electronic energy transition and a specific SPR band can be obtained, helping to obtain the size and shape of NPs up to a certain limit [23,34]. (ii) advanced TEM and SEM techniques are used to study the size and morphology of NPs. TEM through a 2D image of the 3D NPs provides information on the morphology of NPs. In addition, it informs about the role of coating agents and metabolite encapsulation [153]. This technique has a higher resolution than SEM to determine the size, shape, distribution and aggregation of NPs in aqueous environments, with high surface spatial resolution, and the dispersion of NPs in the matrix [23,34]. (iii) the combination of the latter two techniques with EDS provides further information on the elemental composition. In addition, FTIR is used to identify the functional groups attached onto

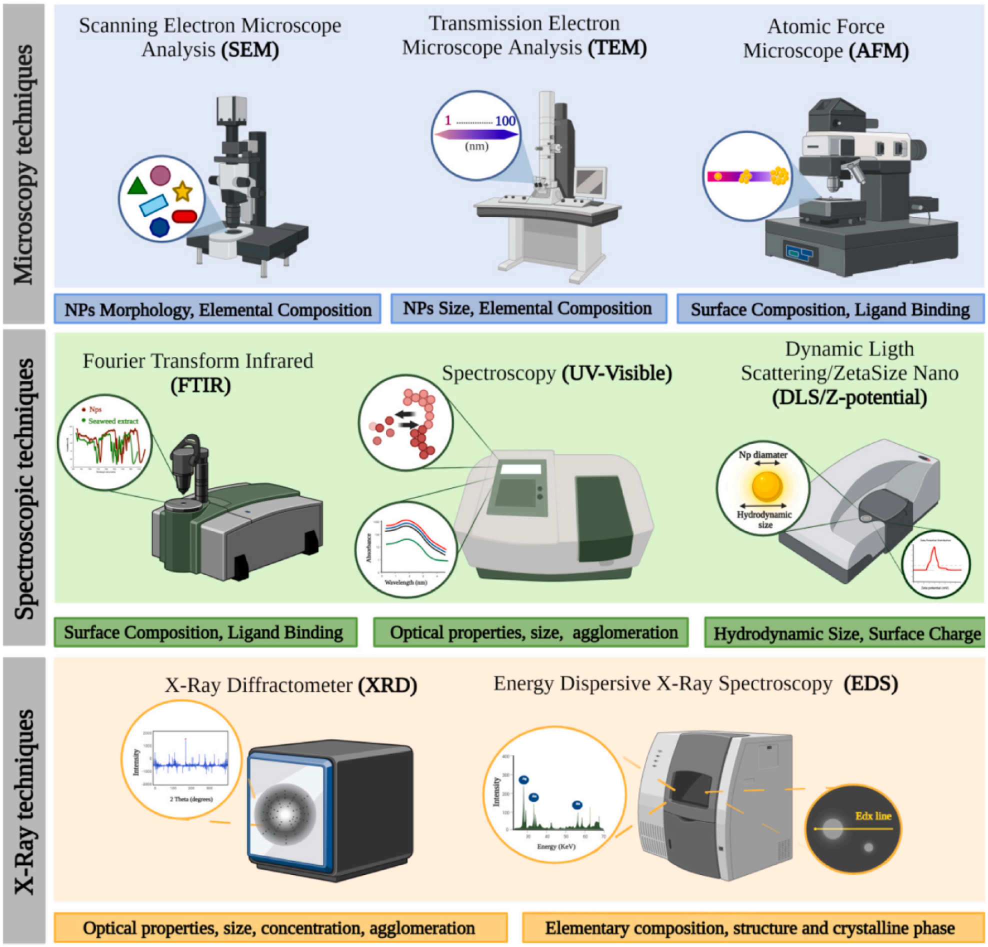

Fig. 4. Overview of the most used methods to characterize NPs [22]. Created with BioRender.

Table 2
Characterization techniques, shape, and type of synthesis in macroalgae mediated Au-Ag NPs.

Species	NP	Shape	Synthesis	Characterization techniques																Ref.
				UV-Vis	SEM	TEM	XRD	FTIR	AFM	EDS	DLS	FESEM	HR-TEM	CP-MS	PL	ζ	SR	WD-XRF	SEMEDS	
Padina pavonica ***(B)***	Au	S	EC	✓		✓	✓	✓		✓										[67]
Padina gymnospora ***(B)***		S		✓	✓		✓	✓	✓											[106]
Lemanea fluviatilis (L.) ***(R)***		S		✓		✓	✓	✓			✓		✓							[107]
Stoechospermum marginatum ***(B)***		S		✓	✓	✓	✓	✓							✓			✓		[64]
Sargassum polycystum ***(B)***		S		✓	✓		✓	✓		✓										[70]
Ulva intestinalis ***(G)***		S, I		✓		✓	✓													[108]
Chondrus crispus ***(R)***		S, P		✓	✓	✓		✓		✓										[109]
Stoechospermum marginatum ***(B)***		S, H, T		✓	✓	✓	✓	✓							✓			✓		[110]
Osmudaria obtusiloba ***(R)***		S, T		✓			✓	✓					✓				✓		✓	[111]
Fucus vesiculosus ***(B)***		S			✓	✓	✓	✓		✓										[112]
Turbinaria conoides ***(B)***		CR		✓	✓		✓			✓		✓								[113]
Ecklonia cava ***(B)***		S, T		✓		✓	✓	✓		✓		✓								[114]
Galaxaura elongata ***(R)***		S	IC	✓		✓		✓									✓			[66]
Colpomenia sinuosa ***(B)***	Ag	S	EC	✓		✓		✓												[40]
Corallina mediterranea ***(R)***		S, H		✓	✓	✓	✓	✓		✓										[59]
Sargassum plagiophyllum ***(B)***		S	IC	✓	✓		✓	✓												[115]
Sargassum siliquosum ***(B)***		S	EC	✓	✓			✓		✓	✓	✓				✓				[116]
Caulerpa racemosa ***(G)***		S, T		✓		✓	✓	✓												[45]
Cystophora moniliformis ***(B)***		C		✓	✓		✓	✓		✓	✓									[117]
Hypnea musciformis ***(R)***		S		✓	✓		✓	✓		✓										[118]
Chaetomorpha antennina ***(G)***		S		✓			✓	✓		✓	✓	✓				✓				[119]
Ulva fasciata ***(G)***		S	IC	✓	✓		✓	✓		✓										[120]
Padina boeregeseni ***(B)***		S	EC	✓	✓		✓	✓												[121]
Sargassum muticum ***(B)***		S		✓		✓	✓	✓		✓						✓				[122]
Sargassum tenerrimum ***(B)***		S		✓		✓		✓			✓									[123]
Spyridia fusiformis ***(R)***		S, T, P, R		✓		✓	✓	✓												[124]
Sargassum dentifolium ***(B)***		S, E, I		✓		✓		✓								✓				[125]
Jania rubens ***(R)***		S, E, I		✓		✓		✓								✓				[125]
Sargassum cinereum ***(B)***		T		✓	✓															[126]
Gelidium corneum ***(R)***		S, A		✓		✓	✓	✓						✓						[127]
Pterocladia capillacae ***(R)***		S		✓		✓		✓												[40]
Sargassum incisifolium ***(B)***	Ag/Au	S		✓		✓	✓			✓	✓					✓				[128]

Abbreviations: (G): green algae; (R): reed algae; (B): brown algae; EC: extracellular; IC: intracellular; S: spherical; I: irregular; C: cubic; P: polygonal; T: triangular; E: ellipsoidal; R: rectangle; H: hexagonal; A: angular; CR: crystalline; UV-Vis: ultraviolet spectroscopy; SEM: scanning electron microscopy; TEM: transmission electron microscopy; XRD: X-ray diffraction; FTIR: Fourier transform infrared spectroscopy; AFM: atomic force microscopy EDS: energy dispersive spectroscopy; DLS: dynamic light scattering; FESEM: field emission scanning electron microscope X-ray photoelectron spectroscopy; HR-TEM: high resolution transmission electron microscopy; PL: photoluminescence; ζ: zeta potential; SR: Raman spectroscopy; WD-XRF: wavelength dispersive X-ray fluorescence; SEMEDS: scanning electron microscopy/ energy disperse spectroscopy.

Table 3

Antibacterial and antifungal activity of macroalgae-mediated metal NPs compared to commercial antibiotic and antifungal drugs.

Species	NP	Medium (**)	Dose (*)	Gram (+)				Gram (-)					Fungi					Ref.
				B. cereus	*B. subtilis*	*S. aureus*	*S. pneumoniae*	*E. coli*	*S. typhii*	*P. aeruginosa*	*K. pneumoniae*	*V. cholerae*	*C. albicans*	*C. neoformans*	*A. niger*	*T. cutaneum*	*T. mantigrophytes*	
U. rigida ***(G)***	Au	MHA	0–80	$0^{(18b)}$ (19d)	-	$11^{(18d)}$	-	$17^{(20b)}$ (17c) (10d)	-	-	-	-	$0^{(30a)}$	$11^{(28a)}$	-	30	$25^{(35a)}$	[58]
G. foliifera ***(R)***				$13^{(18b)}$ (19d)	-	$12^{(18d)}$	-	$11^{(20b)}$ (17c) (10d)	-	-	-	-	$0^{(30a)}$	$11^{(28a)}$	-	22	$15^{(35a)}$	[58]
C myrica ***(B)***				$0^{(18b)}$ (19d)	-	$11^{(18d)}$	-	$11^{(20b)}$ (17c) (10d)	-	-	-	-	$12^{(30a)}$	$11^{(28a)}$	-	15	$0^{(35a)}$	[58]
U. rigida ***(G)***	Ag	PDA	-	$16^{(18b)}$	-	$14^{(20b)\ (17c)}$ (10d)	-	$12^{(20b)}$ (17c) (10d)	-	-	-	-	$12^{(30a)}$	$11^{(28a)}$	-	$29^{(28a)}$	$18^{(35a)}$	[171]
G. foliifera ***(R)***				$4^{(18b)}$	-	$18^{(20b)\ (17c)}$ (10d)	-	$11^{(20b)}$ (17c) (10d)	-	-	-	-	$13^{(30a)}$	$14^{(28a)}$	-	$18^{(28a)}$	$0^{(35a)}$	[171]
C myrica ***(B)***				$19^{(18b)}$	-	$17^{(20b)\ (17c)}$ (10d)	-	$13^{(20b)}$ (17c) (10d)	-	-	-	-	$0^{(30a)}$	$13^{(28a)}$	-	$19^{(28a)}$	$0^{(35a)}$	[171]
S. marginatum ***(B)***	Au	-	250	-	-	-	6	0	$6^{(13e)}$	$8^{(13e)}$	$6^{(12e)}$	$8^{(15e)}$	-	-	-	-	-	[64]
E.flexuosa ***(G)***	Ag	-	-	-	$18^{(14g)}$	$14^{(13g)}$	-	$13^{(12g)}$	-	$0^{(10g)}$	10		$14^{(18h)}$	-	$0^{(16h)}$	-	-	[172]
H. musciformis ***(R)***		SDA	5	-	$30^{(29g)}$	$25^{(27g)}$	-	$22^{(20g)}$	-	$0^{(15g)}$	$17^{(17g)}$		$32^{(42h)}$	-	$20^{(22h)}$	-	-	[144]
Padina sp. ***(B)***		MHA	1000	-	12.67 (25.33g)	$15.17^{(12.67g)}$	-	12.67 (20.50g)	11.50 (23.50g)	$13.33^{(21.33g)}$	-	-	-	-	-	-	-	[148]
S. tenerrimum ***(B)***		LB		-	-	16	-	15	17	16	16	18	-	-	-	-	-	[123]
Padina sp. ***(B)***		MHA	1	-	$14^{(25g)}$	$15^{(12g)}$	-	$12^{(20g)}$	$11^{(23g)}$	$15^{(21g)}$	-	-	-	-	-	-	-	[53]
L. papillosa ***(B)***		MHA	50	-	$17^{(24g)}$	$16^{(21g)}$	$15^{(20g)}$	$14^{(21g)}$		$13^{(16g)}$	$15^{(20g)}$	-	-	-	$10^{(16i)}$	-	-	[57]
P. gymnospora ***(B)***	Pt	LB	10^{4}-2x10^{5}	3	-	2.2	2.5	-	2.1	-	2	-	-	-	-	-	-	[73]
C. crinita ***(B)***	ZnO	MHA	10	26	-	27.3	-	24.3	26.3	-	-	-	22.3	-	$31^{(29.7f)}$	-	-	[85]
C. sinuosa ***(B)***				-	$9^{(5g)}$	$7^{(1g)}$	-	$7^{(2g)}$	$11^{(5g)}$	$9^{(5g)}$	-	$15^{(7g)}$	-	-	-	-	-	
P. capillacea ***(R)***	Fe_3O_4	CDA	30	-	$5^{(5g)}$	$3^{(1g)}$	-	$6^{(2g)}$	$5^{(5g)}$	$5^{(5g)}$	-	$9^{(7g)}$	-	-	-	-	-	[80]

Abbreviations: (G): green algae; (R): reed algae; (B): brown alga; Fluconazole (a); Choramphenicol (b); Augmentin (c); Gentamycin (d); Tetracycline (e); Bacitracin (f);Ampicillin (g); Nystalin (h); Muller Hinton Agar (MHA); Sabouraud Dextrose Agar (SDA); Luria-Bertani (LB);Potato dextrose Agar (PDA); Czapek-Dox Agar (CDA); *Bacillus cereus (B. cereus; Bacillus subtilis (B. subtilis); Staphylococcus aureus (S. aureus); Streptococcus* pneumoniae (S. pneumoniae); *Escherichia coli (E. coli); Salmonella typhi (S. typhi); Pseudomonas aeruginosa (P. aeruginosa); Klebsiella pneumoniae (K. pneumoniae); Vibrio cholerae (V. cholerae); Candida albicans (C. albicans); Cryptococcus neoformans (C. neoformans); Aspergillus niger (A. niger); Trichosporon cutaneum (T. cutaneum); Trichophyton mantigrophytes (T. mantigrophytes).* * Dose expressed in μg/mL. ** Medium: In all cases agar well diffusion assay (AWD) was employed.

Note: Numbers in superscript refer to clear zone diameters (CDZ) of the control antibiotics.

NPs. It provides a clear picture of the reducing agents responsible for coating, reduction and stabilization [23]. It is fast, inexpensive, requires zero sample preparation, and highly reproducible. However, it is less sensitive to nanoscale analysis and provides only qualitative information [164]. (iv) XRD is used to identify and characterize crystalline NMs. This non-destructive technique is useful to determine purity, crystal size, geometry, orientation, phases and other structural parameters such as average grain size, crystallinity, deformation and crystal faults [165]. On the other hand, DLS explores several physicochemical characteristics, such as hydrodynamic size, shape, structure, aggregation state, and biomolecular conformation. It is non-invasive, short, and reproducible [153,164]. DLS also measures the zeta potential (ζ) of NPs, where the high magnitude value indicates electrostatically stabilized NPs, showing no aggregation [166].

6. Biological properties of macroalgae-mediated metal nanoparticles in the food industry

Metal NPs mediated by various MAG extracts open a multidisciplinary approach in biological systems [23]. It has been proven that the production of bioactive metabolites by algae may be the answer to specific applications in industries such as biomedical, pharmaceutical, or food among others. Bacteria are common harmful agents, as evidenced by the widespread clinical use of antibiotics. This fact implies a threat to global health because the overuse of antibiotics has caused the emergence of multidrug-resistant microbial strains that reduce their efficacy [167]. New classes of antibiotics with novel structures are needed to combat this trend. At the same time, antimicrobial activity is key to combating food spoilage and extending shelf life. On the other hand, it has been demonstrated that MAG have developed mechanisms through metabolic routes to suppress or eliminate the oxygen radicals that are inevitably produced during photosynthesis and electron transport, a phenomenon known as oxidation. The antioxidant activity of MAG could reduce the lipid oxidation and so, one of the main causes of food waste due to the deterioration [168–170]. In conclusion, antimicrobial and antioxidant properties have received most attention and are key in food processing and packaging. For this reason, they will be discussed below.

6.1. Antimicrobial activity

Different works have supported the antimicrobial activity of algae, attributed to their specific compounds. At the same time, the use of natural alternatives instead of synthetic additives have been researched to improve the quality and safety of the food products during storage, to keep their nutritional and organoleptic properties while controlling food-borne pathogens. Table 3 compiles different studies about the use of MAG-mediated metal NPs and their results compared to commercial antibiotics.

For instance, the antimicrobial and antifungal activity was assessed for AgNPs synthesized by the algae (*U. rigida **(G)**, C. myrica **(B)** and G. foliifera **(R)***). The presence of secondary metabolites produced by MAG were reported to be responsible for the antimicrobial effect. The direct relationship of AgNPs with antimicrobial activity was demonstrated by not detecting antibacterial or antifungal effects in ethanolic or aqueous extracts of the same algae [41]. In another study, the minimum inhibitory concentration (MIC) and minimum bactericidal concentration (MBC) in the case of AgNPs synthesized from *K. alvarezii* (KaNPs) showed that the treatment decreased the bacterial growth of the different strains from 62-82% compared to the control at 24 h. This antimicrobial effect is reinforced by the synergistic impact of the Ag ions released inside the cell and the presence of phytochemicals such as lipids, phenolics or terpenoid derivatives of the algal extract in the same way as in the previous assay. In this study, KaNPs inhibited biofilm formation by 31-72% dose-dependently and presented better results than the antibiotic used as positive control. Therefore, KaNPs showed their potential as an effective alternative to antibiofilm and antibacterial agents against multidrug-resistant bacteria [148]. In the case of AgNPs synthesized by *E. cava* extract, effective antimicrobial activity was achieved using only 40 μg of biosynthesized AgNPs, showing the compatibility of the extract and the metal [145]. Another study using photosynthesized ZnONPs with MAG *C. crinita* showed considerable antimicrobial activity against all strains tested and it was found that such activity was dose-dependent on ZnONps [85]. Also, with ZnONPs obtained through by *H. opuntia* MAG extract, it was found that the bacterial activity not only increased with ZnONPs concentration, but also with exposure time [82].

Although the mechanism of NPs as antimicrobial agents is not transparent and is unknown, theories have been proposed such as that their small size facilitates the ability to prevent bacterial growth through inhibition of cellular proteins by fusion with thiol (-SH) groups, the accumulation of NPs in the cell membrane and consequent increase in membrane permeability leading to alteration of physiological function, cell death by the interaction of ions with the bases and phosphorus groups of DNA, generation of ROS that damage cellular components, denaturation of proteins or inactivation of enzymes [56,85,145]. In the case of fungi, an increase in hydroxyl radicals by NPs leads to apoptotic cell death [47]. Within NPs, those of smaller size with relatively large contact areas show higher bacterial efficacy compared to larger ones [36]. The presence of organic biomolecules in the MAG extracts that act as chelators during the synthesis of metal NPs seems to be responsible for their antimicrobial potential as reported in the reviewed literature.

6.2. Antioxidant activity

Oxidative damage is caused by the interactions of ROS with any compound susceptible to be oxidized and suffer structural changes in the process. ROS also exert several undesirable and significant changes in foods such as limiting their shelf-life, lowering nutritional value, loss of color, flavor, and odor [173]. So, MAG-mediated metal NPs could be used as agents to counteract the imbalance of the oxidant/antioxidant ratio by donating an electron or breaking the oxidation chain [35]. The presence of organic biomolecules in MAG extracts that act as chelators during the synthesis of metal NPs seems to be responsible for their antioxidant potential as reported in the reviewed literature. Additionally, it has been found that the reason for the free radical scavenging activity of biosynthesized NPs is the high surface-to-volume ratio [119].

Table 4 is an overview of different assays that determine the free radical scavenging of 2,2-diphenyl-1-picrylhydrazyl (DPPH), 2,2`-azino-bis (3-ethylbenzothiazoline-6-sulfonic acid (ABTS) and ferric ion reducing antioxidant power (FRAP). The results are shown through the IC_{50} and, in some cases, the comparison with a standardized antioxidant agent is shown. In addition, total phenolic content (TPC) has been reported due to its direct correlation with the antioxidant activity [174]. The implication is that the higher the TPC of the extract, the higher the antioxidant activity [145]. For instance, AuNPs mediated by the brown algae *T. decurrens* showed half antioxidant activity (49.38 and 33.02 μg/mL, for ABTS and DPPH respectively) as compared with commercial agent Trolox. However, applying the same dose of AgNPs synthetized using the red algae *C. hornemannii*, the IC_{50} for DPPH assay was similar to the commercial agent ascorbic acid (92.3 and 96.1 μg/mL, respectively). The diversity of antioxidant assays and the absence of controls make difficult the interpretation of results.

6.3. Toxicity of metal nanoparticles

As mentioned earlier, nanotechnology has multiple applications, but it is essential to pay attention to the downside of NMs: nanotoxicity. The toxicological effects of NPs depend on several factors such as the variety, concentration, shape, and size of NPs, the species of the test organism, the employed synthesis method, and the loading, agglomeration, and surface modification [179,180]. For example, higher toxicity is usually

Table 4

Antioxidant activity of macroalgae-mediated metal NPs measured in terms of total phenolic content (TPC) and FRAP, ABTS and DPPH assays; and compared to commercial controls.

Information		Quantity	Methods				Reference	
Species	NP	*Dose*	*TPC*	*FRAP*	*ABTS*	*DPPH*	*Control*	*Ref.*
		(μg/mL)	(mg GAE/g)	(mg AAE/g)	(*IC_{50}*, μg/mL)	(*IC_{50}*, μg/mL)	(*IC_{50}*, μg/mL)	
E. flexuosa ***(G)***		200	-	-	50.9	140.38	-	[43]
G. elongata ***(B)***		200	-	-	48.12	98.37	-	[43]
T. ornata ***(B)***		200	-	-	50.63	98.68	-	[43]
C. hornemannii ***(R)***	Ag	100	-	-	-	96,1	AAE = 92.3	[175]
C. antennina ***(G)***		100-500	-	-	-	384.13	-	[119]
E. prolifera ***(G)***		100-500	-	-	-	142.0	-	[42]
E. cava ***(B)***		50-500	-	-	-	198	-	[145]
T. decurrens ***(B)***		100	28.86	-	70.64	51.16	TE = 33.02 (DPPH), 49.38 (ABTS)	[62]
G. pygmaea ***(R)***	Au	5-25	1.82	0.53	-	0.89	-	[176]
S. incisifolium ***(B)***		-	235	95	-	-	-	[128]
H. dilatate ***(R)***	Pt	100	-	49.43	-	78,91	-	[72]
D. menziessi ***(B)***		2-0.1	0.84	126.35	-	68.70	-	[50]
P. decipiens ***(R)***		2-0.1	0.34	43.66	-	127.21	-	[50]
I. cordata ***(R)***		2-0.1	NS	NS	-	NS	-	[177]
D. antarctica ***(B)***	Au-Ag	2-0.1	0.37	-	-	63.3	-	[177]
U. lactuca L. ***(G)***		-	0,13	24.3	-	153.8	-	[174]
U. intestinalis L. ***(G)***		-	0.200	25.3	-	140.1	-	[178]
S. muticum ***(B)***		25-500	0.55	81.5	-	69.50	-	[71]
C. crinita ***(B)***	ZnO	3-1000	-	-	-	201.45	AAE = 21.46	[85]
C. trinodis ***(B)***	CuO	-	-	-	-	543	-	[75]

Abbreviations: (G): green algae; (R): reed algae; (B): brown algae; TPC: total phenol content; FRAP: ferric ion reducing antioxidant power; ABTS: 3-ethylbenzothiazoline-6-sulfonic acid: DPPH 2,2-diphenyl-1-picrylhydrazyl; NS: no significant; AAE: ascorbic acid equivalent; GAE: gallic acid equivalent; TE: Trolox equivalent; IC_{50}: half maximal inhibitory concentration; *Durvillaea antarctica (D.antarctica); Iridaea cordata (I. cordata); Desmarestia menziesii (D. menziesii).*

observed for finer-sized metallic NPs compared to bulk materials [48]. The key factors implicated in the toxicity of NPs can promote two main adverse effects [181]:

- Oxidative stress due to the generation of reactive oxygen species (ROS) that affects proteins responsible in cell membrane repair, leakage of cellular components and inflammatory reactions.
- Genotoxicity leading to DNA damage and mutations.

In a study on the toxic effects of 12 NPs at different trophic levels (algae, bacteria, and protozoa), it was found that the growth inhibition assay on the microalga *Pseudokirchneriella subcapitat* was the most sensitive with half maximal inhibitory concentration (IC_{50}) of 10 out of the 12 NPs ranging from 0.1 to 58 mg/L. Toxicity was related to ROS production and agglomeration of NPs trapping algal cells. This concluded in the evidence of toxicity responses by the metal NPs due to a combination of the above factors and other mechanisms [182]. In particular, great attention has been paid to the over-production of ROS by food nanostructures which, although not having direct effects on human health, their nanoscale nature may lead to some inevitable side effects such as oxidative stress or alteration of physiological processes in cells [1]. In the case of food NMs, one of the main concerns is the interaction with the food product using nanosensors or food packaging that may induce the migration of NMs into the human body by ingestion. Studies indicate the biocompatibility of metallic NPs without significant toxic effects. However, responses have also been reported where oxidative stress and other effects are evidenced by their presence [183].

For instance, a study investigated the migration of several metal oxide NPs, such as TiO_2, ZnO, SiO_2 and Al_2O_3, used in food packaging. The study concluded that there was no significant migration although it is recommended to add a functional barrier to the packaging to separate the food from the nanocomposite [184]. Nevertheless, the uncertainty about the possible toxicological effects of NMs is still considerable and requires satisfactory answers that will prevent safety problems and allow the widespread commercialization of nanotechnology that has proven its efficacy.

7. Potential applications of macroalgae-mediated metal nanoparticles in food industry

The major hurdle in the food industry is the limited shelf life of food products as a result of microbial spoilage and reactions such as degradation, enzymatic browning or oxidative rancidity [185]. The use of MAG-mediated NPs offers new insight into the ecological problem since NPs are usually biocompatible and free of toxic chemicals entangled on their surfaces because they do not use any external coating or reducing agents during the synthesis. Therefore, they show less toxicity than chemically synthesized NPs [20,186]. The diversity of algae species does not implicate the use of any toxic substances during the reduction and stabilization of the NPs since they are rich in bioactive compounds that act as reducing and coating agents and are primarily responsible for the potential of these "nanobiofactories" to behave as competent antimicrobial or antioxidant agents [23].

7.1. Nanoencapsulation

Encapsulation is a technique in which a substance in solid, liquid, or gaseous state is trapped and/or coated in another material, called wall material. In this case, the encapsulation takes place at the nanometric scale, being able to change the desired size range of the particles. This technology is a novel alternative since it allows to preserve and protect labile bioactive agents present in the food matrix from adverse conditions. As explained previously, algae are rich in bioactive compounds such as carotenoids, essential oils, fatty acids, and phenolic compounds. This group of molecules are mostly hydrophobic and poorly soluble. They are also responsible for the antimicrobial and antioxidant activity present in many varieties of MAG-mediated NPs. The use of nanoencapsulation allows to cover these bioactive compounds with a wall material that protects them from external agents. This is particularly useful in applications such as active packaging, as it enhances the bioavailability and stability of the naturally occurring antimicrobial compounds, thus favoring their subsequent application [187,188]. By reducing the size of NPs, the area per unit volume increases, resulting in advantages such as the ones depicted in Fig. 5 [188–191].

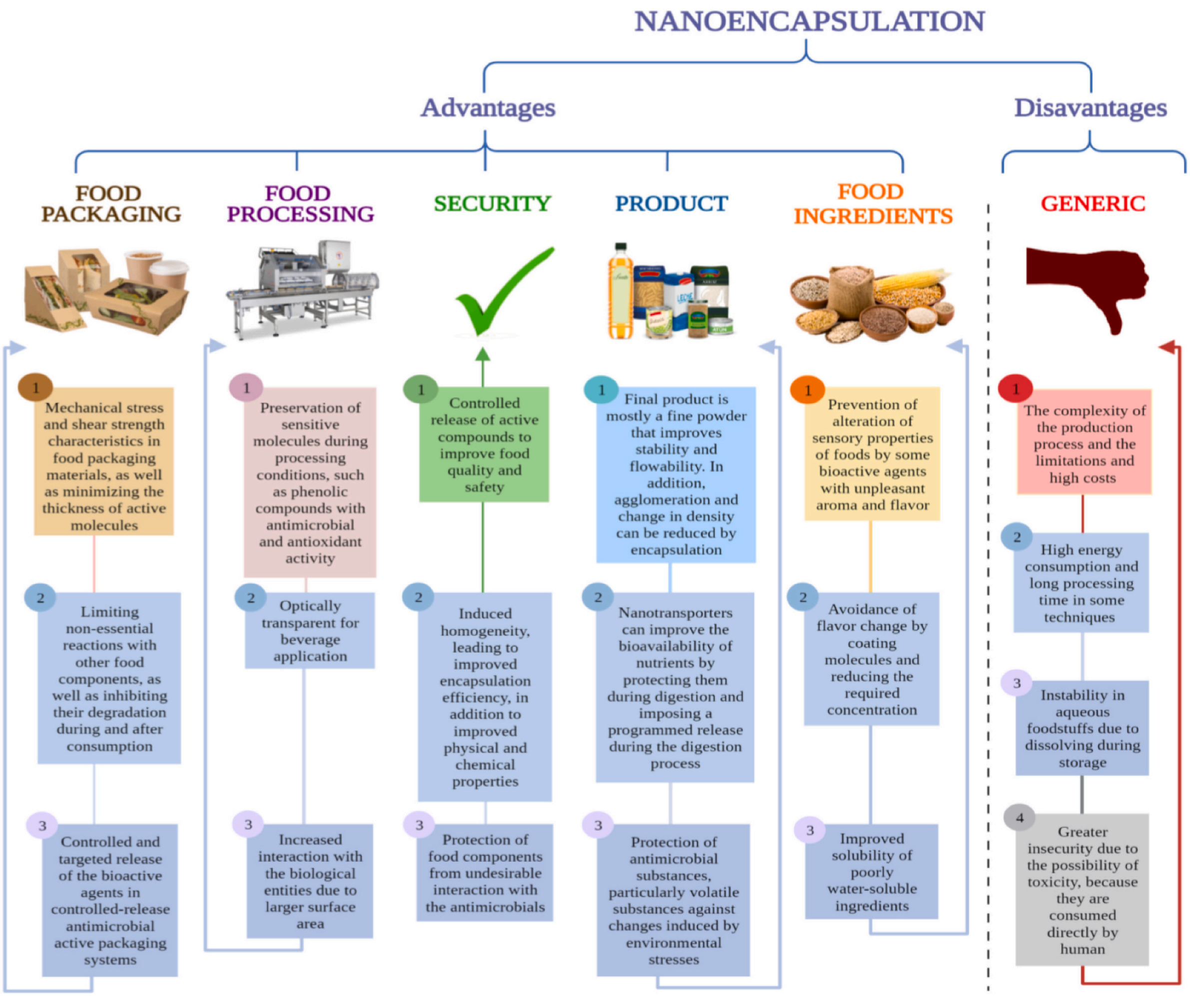

Fig. 5. Main advantages of using macroalgae-mediated metal nanoparticles for nanoencapsulation in the food processing, preservation, and packaging industry. Created with BioRender.com.

7.2. Food packaging

Packaging plays a key role in the modern food industry as the main process for preserving the quality of food products from manufacture to consumption. The recent trend is based on replacing synthetic/chemical antimicrobial agents and antioxidants while new concepts such as "biodegradable packaging", "active packaging" and "smart packaging" are currently guiding food packaging research and development [187]. Biopolymer-derived films have been shown to have excellent potential to contain various additives, such as antimicrobial agents and antioxidants, in their matrix and release them during storage [190,192]. On the one hand, inorganic NPs have been widely investigated along with efficient demonstrations of antimicrobial activities attributed to their high surface area/volume ratio. The trend is based on the development of barriers against the diffusion of oxygen, carbon dioxide, aromatic compounds, and water vapor [193]. Ag, Au and Cu NPs are the most exploited elements to develop packaging systems that extend the shelf life of food products. Using nanotechnology, it is possible to detect the presence or growth of bacteria in packaging, moderate food flavors, improve the functions of edible films or regulate gas exchange through the packaging, among other functions. The ability of these NMs is influenced by their shape, size, concentration, surface charge, metal ion release and type of surrounding medium. Therefore, the different existing scenarios for the formulation and application of nano-packaging must be taken into account [194].

Seaweeds are also considered one of the best alternative to the traditional material when combined with any biodegradable polymer, as they are a rich source of polysaccharides with the ability to improve the sustainability, functionality and sensory property of the product [195]. Polysaccharides have been extensively investigated as a part of active and smart packaging. Their potential includes some properties such as inherent protective, film and gel-forming or barrier capabilities against oxygen and carbon dioxide under low and moderate relative humidity conditions [196]. Nevertheless, they present a poor barrier against water vapor due to their hydrophilic nature and poor mechanical stability which slows down their industrial application [197]. This disadvantage can be solved by combining a new reactive group that allows advanced modifications to be made for specific applications [198]. This way, nanocomposites emerge as biopolymers stabilized by NPs and able to improve their technical properties, such as barrier, thermal, chemical or mechanical stability due to their interfacial interactions with polymer branches, higher surface area and high surface energy [199,200]. The most commonly used seaweed polysaccharides as food contact materials are alginate (Phaeophyceae), agar (Rhodophyceae), and carrageenan (Rhodophyceae) [201,202].

Kanglong et al. [203] developed a new method based on the coordinated electrodeposition of alginate for the green synthesis of CuSNPs and the direct fabrication of a modified electrode with CuSNPs/alginate nanocomposite film. Alginate was the stabilizing biopolymer in the synthesis. The obtained nanocomposite film showed the electrochemical sensing ability of hydrogen peroxide (H_2O_2) and hydroquinone (HQ) and also, the colorimetric sensing ability of H_2O_2 and dopamine (DA) which shows great potential in sensing fields to create new detectors and sensors. In another study, agar-based bioactive nanocomposite films reinforced by Ag-Cu NPs and produced by casting method. They showed improved thermo-mechanical, structural, oxygen barrier, optical and antimicrobial properties. The agar achieved a significant increase in the tensile strength of the films. These results postulate agar/Ag-Cu nanocomposite films as UV barrier materials and active packaging materials to ensure food safety and prolong the shelf life of packaged foods [204]. AgNPs were also synthesized using melanin as a reducing and coating agent. AgNPs were incorporated into carrageenan to prepare antimicrobial films. The addition of AgNPs improved the barrier properties of the film against UV light, reduced the water contact angle and water vapor barrier properties, improved the thermal stability with color change, and increased the resilience of the nanocomposite films. In addition, the carrageenan/AgNPs nanocomposite films showed strong antimicrobial activity which together with the improved film properties create an optimal choice for application as a packaging material [205]. Other examples include a study in which ulvan, a less recognized polysaccharide extracted from MAG *U. lactuca*, was used to produce novel and safe bionanocomposite AgNPs films with antioxidant and antimicrobial activities for active packaging [206]. Furthermore, Guilin et al. [207] used sodium alginate and chitosan functionalized by CuONPs and ZnONPs as substrates to fabricate the layer-by-layer nanocomposite film (SA-CS@CuO/ZnO) and investigate its antibacterial mechanisms. Bacteria treated with the composite film showed signs such as loss of structural integrity in the cell wall and membrane or destabilization of normal physiological activities.

7.3. Biosensors

The International Union of Pure and Applied Chemistry (IUPAC) describes a biosensor as an integrated receiver-transducer device capable of providing specific quantitative or semi-quantitative analytical data using a biological recognition element [208]. Biosensors provide a key technology for food industries to improve food safety, control and maintain food quality. Biosensor technology is versatile, cost-effective, sustainable, and capable of detecting with high selectivity and sensitivity numerous contaminants, food additives, or number of permitted residues or possible hazardous analytes present in food matrices. This technology reduces false failures, is fast, and does not require extensive sample pretreatment unless it is necessary to filter or concentrate samples to improve sensitivity [209]. Nanobiosensor gives the advantages of being transportable and user-friendly. Furthermore, it is not a high-cost technology, so its use is spreading among researchers who need to perform analytical methods in an affordable and simple way [208].

Algae-mediated NPs show unique quantum effects and follow a green synthesis. The main advantage of using algae lies in their adaptability to diverse environments, as they are less vulnerable to physicochemical changes than other bioreceptors. In addition, dual optical and electrochemical signal transduction can be used to construct biosensors, allowing analysis in complex matrices with different turbidity and analyte concentrations [37,209]. Most scientific papers focus on microalgae for the development of biosensors. However, some applications have been found with MAG. For example, Rojas-Pérez et al. [70] and Li et al. [91] employed MAG *Osmundaria obtusiloba* for the synthesis of AuNPs and reported a high sensitivity for the detection of the compound 4-nitrothiophenol evaluated by Surface Enhanced Raman scattering (SERS). Mehrjo et al. [210] synthesized NPs by ZnO nanosheets with a film thickness of $\approx$ 23 nm, doped with PdNPs and, in the presence of MAG *Cystoceira baccata* extract. To investigate the possible application of the obtained NPs, the electrooxidation of ethanol on the surface of the ZnO-PdNPs modified carbon paste electrode was studied in an alkaline medium by cyclic voltammetry. The result was an electrode that showed high catalytic activity for the oxidation of ethanol and, at the same time, high sensitivity for the determination of the compound in a wide range of concentrations. At last, Momeni et al. [211] by synthesizing PdNPs using *Sargassum bovinum* MAG extract, developed a carbon ionic liquid electrode (PdNPs/CILE) for the determination of H_2O_2 in aqueous solutions. The obtained results showed a reliable, stable, non-enzymatic sensor with high selectivity and exhibiting a wide linear range of 5.0 μM-15.0 mM with a sensitivity of 284.35 mA/mM cm^2 and a detection limit of 1.0 μM.

8. Legislation

Nowadays, legislation has not yet been adopted to cover algae and nanotechnology as a unit applied to the agri-food industry. For this reason, the main current legislative frameworks for the development of activities related to MAG in different areas of food and the currently applicable regulations for nanotechnology in the food industry have been compiled in

Table 5 and resumed as follows.

Regulation (EC) N° 178/2002, the basis of food and feed legislation in the European Union (EU), stablishes the general legal framework for the development of food at EU level, implements the general principles and requirements of food legislation and covers all production processes for traceability and food safety [227]. Seaweeds are considered as novel food by *Regulation (EC) N° 2015/2283* [212]. The entry of MAG species and extracts that have not been used as food in the EU before May 15, 1997, must undergo an authorization procedure to ensure their safety. Another basic regulation for the management of MAG due to their tendency to easily accumulate heavy metals from the surrounding water is *Regulation (EC) N° 1881/2006* establishing maximum contaminant levels for water used for cultivation or harvesting of MAG. This regulation is not very extensive because the contribution of algae-based food products in European diets is relatively small [214]. Moreover, *Regulation (EC) N° 396/2005* and *Regulation (EC) N° 1881/2006* stablish other maximum levels of contaminants in food [214,215].

Regulation (EU) N° 2015/2283 on Novel Foods states that food composed of "engineered NMs" should be considered as novel foods [212] and *Regulation (EU) N° 1169/2011*, on the provision of food information to consumers, states that "all ingredients present in the form of engineered NMs shall be clearly indicated in the list of ingredients" [221]. *Regulation (EU) N° 10/2011* on plastic materials and articles intended for food contact emphasizes that NPs ("substances in nanoform") may exhibit toxicological properties different from those of the same substance in conventional particle size. Therefore, they must necessarily undergo a specific risk assessment and should be used only after explicit authorization [222]. It can be assumed that pairing nanoresearch with different biological entities to produce clean and safe NPs can lead us to new research horizons by producing application-based products. Despite this, large-scale utilization of algal sources as “nanobiofactories” is still immature [22]. An international regulatory system, complete government guidelines, as well as rigorous toxicological screening methodologies are essential in order to verify and validate the legal applications of nanotechnology [228]. In addition, significant studies exploring the potential and limitations of MAG -mediated NPs biosynthesis in the food industry are required.

9. Conclusions and future perspectives

Nanotechnology has been postulated as a versatile opportunity to be explored and applied in food science and industry. Through MAG-mediated biosynthesis of metal NPs such as Ag and Au, eco-friendly, non-toxic, and cost-effective NMs can be obtained. MAG represent a source of bioactive compounds that play a crucial role in coating and stabilizing NPs at both, intracellular and extracellular approaches. The production of NMs with desired morphologies and sizes requires the optimization of key factors influencing the synthesis process such as

Table 5
Main regulations applicable to macroalgae and NPs use in the food industry.

Regulation	Application	Specification	Ref.
Macroalgae			
Reg (EC) N° 2015/ 2283	Novel foods	Classifies according to whether the algae variety chosen has been used before or is novel, and for those macroalgae with a history of safe use of at least 25 years.	[212]
Reg (EU) N° 2017/ 2470	Novel foods	Establishes the list of novel foods compiles all novel foods authorized to date. Includes conditions of use, labeling requirements and specifications.	[213]
Reg (EC) N° 1881/ 2006	Foodstuffs	It establishes maximum contaminant contents in water used for algae cultivation or harvesting.	[214]
Reg (EC) N° 396/2005	Maximum limits for pesticide residues in food and feedstuffs	Maximum mercury content in seaweed is defined as 0.01 mg/kg.	[215]
Reg (EC) N° 1881/ 2006	Maximum level of certain contaminants in food.	Establishes a maximum limit of 3.0 mg/kg of cadmium in food supplements consisting mainly of dried seaweed or derived products and 0.01 mg/kg of mercury and lead for generic food supplements.	[214]
Reg (EC) N° 1333/ 2008	Food additives	Eight food additives based on macroalgae phytochemicals and used as a thickening and gelling agent have been reported.	[216]
Reg (EU) N° 2022/650	Food additives	Information on the source, composition, and use.	[217]
Reg (EU) N° 2018/848	Organic production and labeling of organic products	Usage of macroalgae as raw material to produce biofertilizers.	[218]
Reg (EU) N° 2019/ 1009	Commercialization of fertilizer products	Defines the maximum concentration limits for contaminants present in the culture substrate.	[219]
Reg (EC) N° 1935/ 2004	Food packaging	Safety of food contact materials should be based on a scientific risk assessment.	[220]
Nanoparticles			
Reg (EC) N° 2015/ 2283	Novel Foods	Food composed of "engineered nanomaterials" should be considered a novel food.	[212]
Reg (EU) N° 1169/ 2011	Food information provided to consumers	It states that "all ingredients present in the form of engineered nanomaterials shall be clearly indicated in the list of ingredients" (with the word "nano" in parentheses after the ingredient name)	[221]
Reg (EC) N° 10/2011	Plastic materials intended for food contact	NPs may exhibit toxicological properties different from those of the same substance in conventional particle size. They must undergo a specific risk assessment and should be used only after explicit authorization.	[222]
Reg (EC) N° 450/2009	Active and intelligent food packaging	Use of NPs as a functional barrier is since they exhibit chemical and physical properties that are very different from larger particles.	[223]
EFSA	Generic	"Guidance on risk assessment of nanomaterials applied in the food and feed chain: human health and animal health"	[224]
EFSA	Generic	"Guidance on technical requirements for regulated food and feed product applications to establish the presence of small particles including nanoparticles"	[225]
FDA	Generic	"Considering whether an FDA-regulated product involves the application of nanotechnology,"	[226]

Abbreviations: Reg: regulation; EC: The European Commission; EU: European Union; EFSA: European Food Safety Authority; FDA: Food and Drug Administration.

temperature, pH or concentration of the precursor metal and extract. In addition, following the formation of NPs, the use of characterization tools such as UV-VIS, TEM, SEM, FTIR or XRD help to understand their unique properties and characteristics. Although extensive research is needed to gather determinant aspects such as the specific mechanism of NPs biosynthesis, the involvement of the active biomolecules of MAG in it, as well as the risk and potential attributed nanotoxicity impact, the development of applications based on the demonstrated antimicrobial and antioxidant potential of metal NPs is promising in the food industry. In this field, nanotechnology has revolutionized conventional concepts and stimulates innovative ideas, such as encapsulation to enrich food products, the application of diverse techniques in packaging material with the aim of overcoming current challenges in the food sectors or nanosensors to express product characteristics and control the microbial load in the final product.

Future perspectives should include active lines of research that address the improvement of economic viability or applicability in the food industry. The yield of the MAG-mediated biosynthetic pathway for the formation of metal NPs has gaps and unknowns. The roles played by the active groups contained in MAG extracts during the biosynthesis process are not yet precisely known, which is essential to discern the biocompatibility with metal NPs. In turn, deepening the different stages of the biosynthesis process of these metal salts as well as their characterization by means of a coherent control process could enhance their final stability. MAG and metal NPs exhibit susceptibility to a wide range of factors, either separately or considered as a whole. These factors elicit heterogeneous responses and are hardly assessed from an optimized point of view. In another line, the evaluation of the impact of the proposed full-scale, cost, or manufacturing process of MAG-mediated NPs is scarcely reported. The comprehension of the associated risks, the lack of accessibility, confidence, or cost-effectiveness, and their management during the entire production chain (handling, storage or, final elimination) are responsible for the fact that the implementation of proposals with strong potential in the market is still in their initial stages.

Ultimately, these approaches should focus on improving the quality, shelf life, safety, and wholesomeness of food, which is closely linked to the need for powerful upgrades and investments in research and regulation to ensure that the proven benefits outweigh the prejudices attributed to an ambiguous field still growing and with progressive perspective on standard technology.

Declaration of Competing Interest

All authors declare that there is no conflict of interest.

Data availability

No data was used for the research described in the article.

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