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# Mycosporine-Like Amino Acids from Coral Dinoflagellates[▽]

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**Coral reefs are one of the most important marine ecosystems, providing habitat for approximately a quarter of all marine organisms. Within the foundation of this ecosystem, reef-building corals form mutualistic symbioses with unicellular photosynthetic dinoflagellates of the genus *Symbiodinium*. Exposure to UV radiation (UVR) (280 to 400 nm) especially when combined with thermal stress has been recognized as an important abiotic factor leading to the loss of algal symbionts from coral tissue and/or a reduction in their pigment concentration and coral bleaching. UVR may damage biological macromolecules, increase the level of mutagenesis in cells, and destabilize the symbiosis between the coral host and their dinoflagellate symbionts. In nature, corals and other marine organisms are protected from harmful UVR through several important photoprotective mechanisms that include the synthesis of UV-absorbing compounds such as mycosporine-like amino acids (MAAs). MAAs are small (<400-Da), colorless, water-soluble compounds made of a cyclohexenone or cyclohexenimine chromophore that is bound to an amino acid residue or its imino alcohol. These secondary metabolites are natural biological sunscreens characterized by a maximum absorbance in the UVA and UVB ranges of 310 to 362 nm. In addition to their photoprotective role, MAAs act as antioxidants scavenging reactive oxygen species (ROS) and suppressing singlet oxygen-induced damage. It has been proposed that MAAs are synthesized during the first part of the shikimate pathway, and recently, it has been suggested that they are synthesized in the pentose phosphate pathway. The shikimate pathway is not found in animals, but in plants and microbes, it connects the metabolism of carbohydrates to the biosynthesis of aromatic compounds. However, both the complete enzymatic pathway of MAA synthesis and the extent of their regulation by environmental conditions are not known. This minireview discusses the current knowledge of MAA synthesis, illustrates the diversity of MAA functions, and opens new perspectives for future applications of MAAs in biotechnology.**

In coral reef ecosystems, scleractinian (hard) corals from the phylum Cnidaria build a three-dimensional (3D) calcium carbonate structure similar to a sea forest that provides a habitat for hundreds of thousands of marine species. Reef-building corals have been demonstrated to form mutualistic symbioses with unicellular photosynthetic dinoflagellates of the genus *Symbiodinium* (63, 103). This mutualistic symbiosis between the coral host and their algal endosymbionts is based on the exchange of nutrients, where the coral host provides shelter and carbon, nitrogen, and other inorganic nutrients to their algal symbionts, while symbiotic dinoflagellates supply coral hosts with their photosynthetic metabolites, meeting up to 95% of the coral's energy requirements (34–36, 40, 105, 116). Coral dinoflagellates also have symbiotic relationships with other invertebrates from the phyla Cnidaria, Platyhelminthes, Mollusca, Porifera, and Foramnifera, as well as with some protists (96, 103). These single-cell dinoflagellate protists are divided into 9 clades (clades A to I) and additional phylogenetically distinct subclades or types based on their nuclear and chloroplast ribosomal genes (70, 71, 82). The body of evidence regarding differences in the stress responses of various *Symbiodinium* clades and even subclades has been accumulating, and differences in the coral susceptibility to bleaching depend partially on their algal symbionts (11, 23, 76). Previous research has revealed that the susceptibility of coral to stress and bleaching varies, depending on the clade or type of algal symbionts they harbor; for instance, thermally tolerant clade D can increase the resistance of corals to elevated sea temperatures (11, 23, 76).

Rapid changes in the environment, such as global warming, UV radiation (UVR) and ocean acidification, are known to destabilize the symbiosis between corals and their dinoflagellate symbionts, leading to the loss of symbionts (and/or their pigments) and coral bleaching (2, 33, 43, 52, 67, 109). Exposure to UV radiation (280 to 400 nm) has been recognized as an important abiotic factor leading to coral bleaching (39), especially when combined with thermal stress (58, 102). High UVR reaches the Earth's surface, particularly in optically clear, shallow waters of tropical ecosystems such as coral reefs (Fig. 1). Furthermore, in aquatic organisms, solar UVR can also negatively affect reproduction and development and increase mutagenesis (42). Organisms exposed to UVR have developed different types of photoprotective mechanisms to reduce the damaging effects of UVR. The mitigation strategies in reducing UV-induced damage include the following: DNA repair mechanisms via processes such as photoreactivation; excision and mismatch repair; and a reactive oxygen species (ROS) response via the accumulation of antioxidants and a UVR interception response via the accumulation of photoprotective compounds with UVR absorption capabilities (51, 75, 90, 92). In many marine organisms, an important photoprotective mechanism that has been evolutionarily conserved involves UV-absorbing mycosporine-like amino acids (MAAs).

In 1969, "S-320" UV-absorbing compounds were discovered

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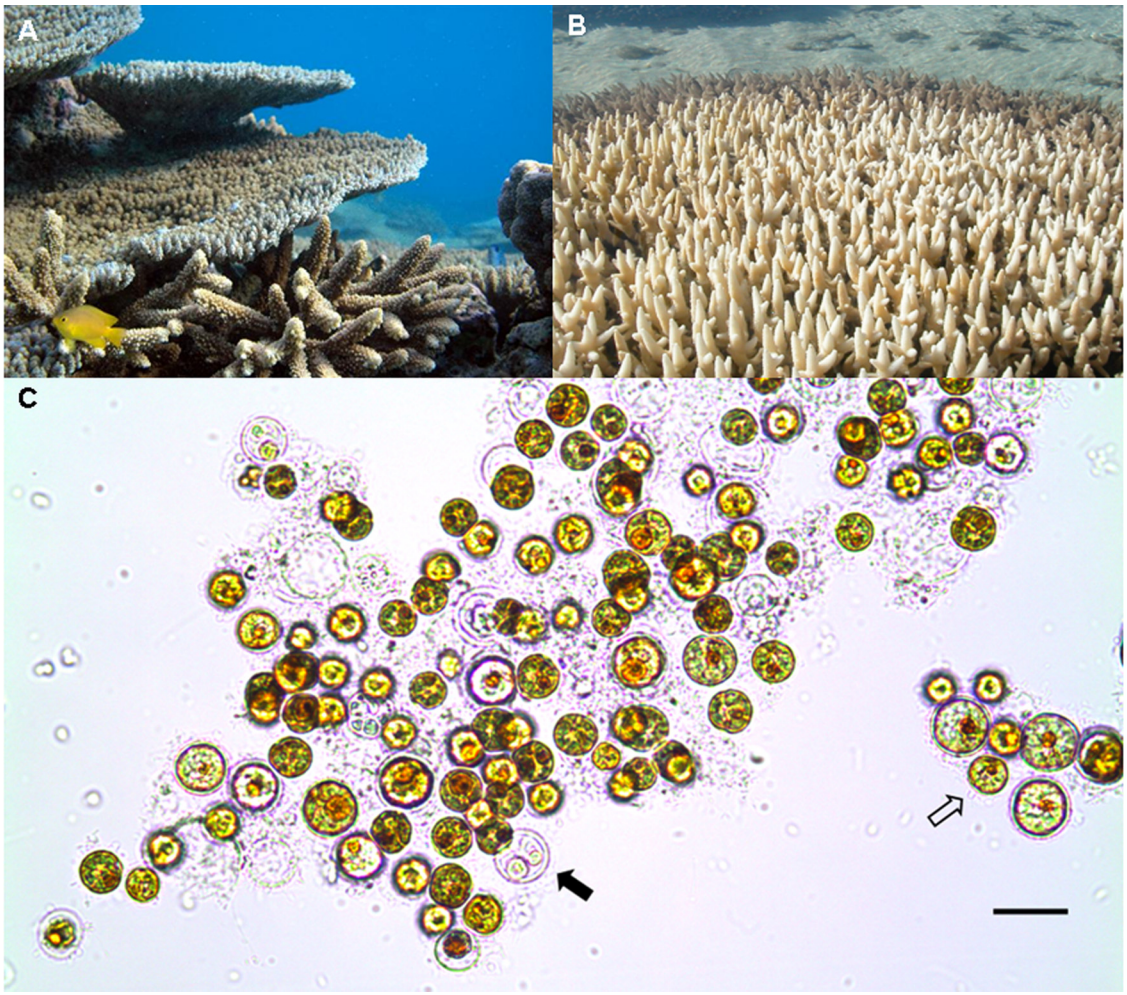


FIG. 1. (A) The shallow-water environment of tropical coral reefs (Heron Island, Queensland, Australia) is characterized by high levels of damaging UV radiation. (B) Bleached corals of *Acropora* species on the Great Barrier Reef. (C) Light micrograph of coral endosymbionts maintained in culture containing dead cells (indicated by black arrow) and viable (indicated by white arrow) *Symbiodinium* cells. Bar, 20 μm. (Photos in panels A and B were provided by O. Hoegh-Guldberg, University of Queensland.)

in different coral species by Shibata (83). Subsequently, these metabolites were identified as MAAs and characterized by maximum absorbance in the UV range of 310 to 362 nm, with a molar absorptivity of $\varepsilon = 28{,}100$ to $50{,}000\ M^{-1}\ cm^{-1}$ (reviewed by Shick and Dunlap [85] and Sinha et al. [94]). MAAs are found in many marine species (more than 380 marine species) and freshwater organisms (60, 85). MAAs are found not only in corals but also in other animals, cyanobacteria, and algae. It was originally thought that animals were not able to synthesize their own MAAs but had to acquire them from food or endosymbiotic algae. These ubiquitous secondary metabolites are transparent, water-soluble compounds with a low molecular mass (<400 Da) and contain a cyclohexenone or cyclohexenimine chromophore conjugated to an amino acid residue or its imino alcohol (28, 64).

Photoprotection by MAAs occurs because of their broadband absorption of UVR (86), a feature that has led to their commercial development in sunscreen products (16). MAAs have additional roles in organisms during exposure to stress where they play a role as antioxidants: quenching ROS and scavenging free radicals. Furthermore, MAAs are believed to be a source of intracellular nitrogen, in addition to playing a role in a variety of stress responses. They have also been profiled as potential light-harvesting pigments involved in photosynthesis (27, 66).

## BIOSYNTHESIS OF MAAs

The biosynthesis of MAAs is presumed to occur during the first part of the shikimate pathway (85, 87), where 4-deoxygadusol (4-DG), a strong antioxidant, is a direct precursor of MAAs (Fig. 2). According to the old assumptions (31, 72), the MAA core was derived from the 3-dehydroquinate (DHQ) intermediate in the main route of the shikimate pathway and then transformed, via a putative biosynthetic course, to 4-DG and the primary MAA (microsporine-glycine) followed by synthesis of a number of secondary MAAs (91). This proposed pathway for MAA biosynthesis was supported by the finding that in the reef-building coral *Stylophora pistillata*, MAA synthesis was blocked by the application of glyphosate, which is a

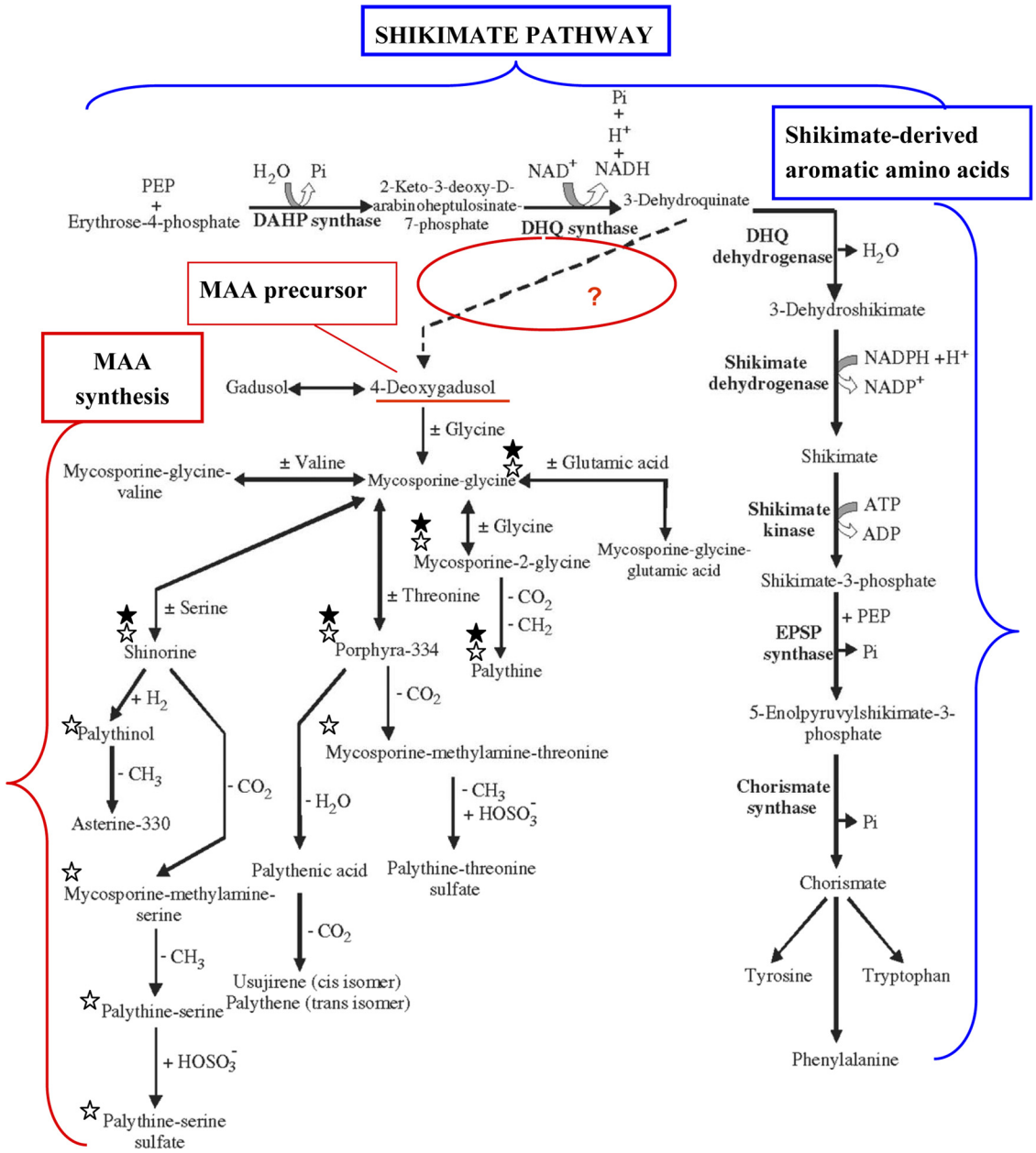


FIG. 2. Proposed biosynthesis of MAAs via the shikimate pathway. The broken line represents the putative biosynthetic route of MAA synthesis, while 4-deoxygadusol (4-DG) acts as a direct MAA precursor (modified from references 91 and the 94 with permission of the publishers). Some MAAs (indicated by a black star) have been detected in symbiotic dinoflagellates (6), while more MAA products (indicated by white stars) have been found in reef-building corals such as *Stylophora pistillata* (17). PEP, phosphoenolpyruvate; DAHP, 3-deoxy-D-arabino-heptulosonate-7-phosphate; EPSP, 5-enolpyruvylshikimate-3-phosphate; ± Glycine, in the presence or absence of glycine.

specific shikimate pathway inhibitor (87). Recently, two genes from cyanobacteria, YP_324358 (predicted DHQ synthase) and YP_324357 (*O*-methyltransferase [*O*-MT]), were proposed to be involved in the biosynthesis of MAAs (90). New findings by Balskus and Walsh (5) suggest that the MAAs originate from the sedoheptulose 7-phosphate (SH 7-P) intermediate produced from the pentose phosphate pathway and an ATP-dependent enzymatic imine formed in a four-enzyme pathway (Fig. 3). In the cyanobacterium *Anabaena variabilis*, the proposed 6.5-kb shinorine biosynthetic gene cluster includes four open reading frames (ORF): (i) dehydroquinate synthase (DHQS) homolog Ava_3858, (ii) *O*-methyltransferase Ava_3857, (iii) ATP-grasp Ava_3856, and (iv) nonribosomal peptide synthetase (NRPS) homolog Ava_3855 (Fig. 3A). It has been proposed that the DHQS and *O*-MT enzymes assemble 4-deoxygadusol, while ATP-grasp and the NRPS homolog attach glycine and serine to 4-deoxygadusol, respectively (Fig. 3B). In addition, the putative shinorine biosynthetic pathway has been characterized *in vitro* using a bacterial expression system (5). The cyanobacterial shinorine gene cluster ho-

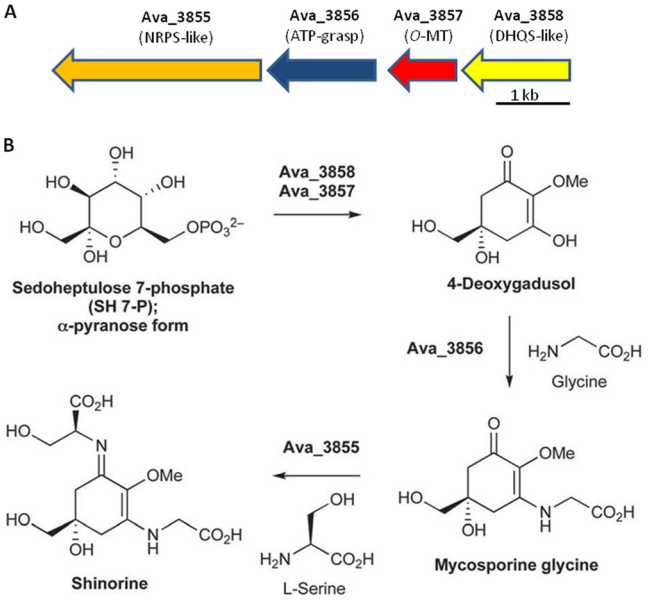


FIG. 3. Shinorine biosynthesis in the cyanobacterium *Anabaena variabilis* (modified from reference 5 with permission of the publisher). (A) The proposed 6.5-kb shinorine biosynthetic gene cluster consists of four open reading frames (ORF): (i) dehydroquinate synthase (DHQS) homolog Ava_3858, (ii) *O*-methyltransferase (*O*-MT) Ava_3857, (iii) ATP-grasp Ava_3856, and (iv) nonribosomal peptide synthetase (NRPS) homolog Ava_3855. (B) Biosynthesis of shinorine from sedoheptulose-7-phosphate.

mologs have been recovered from the genomes of other organisms such as dinoflagellates and fungi (5) and recently from coral and sea anemones (88). However, there are many uncertainties regarding the complete pathway for MAA synthesis, and this has, to some extent, impeded advancements in understanding the extent to which they are environmentally regulated.

Sequence and phylogenetic analyses of the genome of the basal metazoan *Nematostella vectensis* (sea anemone) has revealed that its genome contains some of the ancestral shikimate pathway genes from bacterial and/or dinoflagellate genomes (95). The shikimate pathway in eukaryotes has been proposed to evolve through a number of evolutionary processes, including horizontal gene transfer (HGT), gene fusion, and endosymbiotic replacement (77). The golden rule for identifying HGT is phylogenetic discrepancy between the gene and organism (48). A good indicator of potential horizontal gene transfer in eukaryotes is also the presence of transposable elements (TEs) associated with the targeted gene (78), although the identification and analyses of TEs could be challenging due to their large number and diversity (112). In addition, this method of exchange in genetic material is also supported by previous findings that nonzooxanthellate coral larvae exhibit increased MAA concentrations over time (115). Consequently, the possibility of horizontal transfer of genes involved in the shikimate pathway between symbiotic dinoflagellates and/or bacterial symbionts and the cnidarian (coral) host is an exciting option that requires further investigation.

## MAAs IN CORAL-ALGAL SYMBIOSIS

To date, more than 20 MAAs have been identified in aquatic organisms (60). Of these MAAs, 15 have been detected in all scleractinian corals (6, 17, 29, 32, 47, 84, 113), including the last MAA discovered, palythine-threonine (17). Up to 12 different MAA compounds have been found in a single coral species, *Stylophora pistillata* (17, 84, 87). However, a maximum of 5 different MAAs have been isolated from algal endosymbionts freshly isolated from a coral host or from cultures (Fig. 2 and 3). Most of these dinoflagellate compounds are the primary MAAs: mycosporine-glycine (maximum λ [$\lambda_{max}$] = 310 nm), shinorine ($\lambda_{max}$ = 334 nm), porphyra-334 ($\lambda_{max}$ = 334 nm), and mycosporine-2-glycine ($\lambda_{max}$ = 331 nm) (6, 7); palythine ($\lambda_{max}$ = 320 nm) was the only secondary MAA present within the alga. Positive effects of UVR on the synthesis of primary MAAs were reported for the coral *Stylophora pistillata*, but not for the synthesis of secondary MAAs, suggesting that UVR triggers enzyme activity at the beginning of the MAA biosynthetic pathway but was not necessary for downstream regulation of MAA synthesis and MAA conversion (84). Alternatively, much of the diversity in MAAs found in corals may be acquired through alternative avenues, such as diet, as seen in other heterotrophic organisms (29, 85).

The distribution and composition of MAAs in scleractinian corals in the Red Sea are affected by seasonal fluctuations (1). Also, in the shallow-water scleractinian corals, high solar irradiance not only induced MAA accumulation but also shifted the composition of MAAs during the day to enhance the photoprotective mechanisms of the coral against light stress (114). In isolated cultures of the coral endosymbionts from 5 clades (clades A, B, C, E, and F) exposed to UVR and photosynthetically active radiation (PAR) over a month, MAAs were produced only in one of the 5 clades (clade A) (6, 7). However, as MAAs were positively detected in extracts from the coral endosymbionts of all analyzed *Symbiodinium* clades that were isolated from their cnidarian host, the requirement of not only a high-light environment and UVR but also a regulation of MAA synthesis by host factors has been suggested (7).

"Coral holobiont" is a frequently used term that refers to reef-building corals where close partnerships occur between the cnidarian host, unicellular dinoflagellates, and also other organisms, such as fungi and bacteria (49, 68). Consequently, differences in MAA composition between a coral holobiont and symbiotic dinoflagellates in culture (7) might be due to the fact that MAAs found in reef-building corals originate from photosynthetic algal endosymbionts and/or associated cyanobacteria, but they may also be derived from the diet and processed by the coral host (84). Alternatively, there have been reports of the bidirectional transport of organic carbon between the host and symbiont (25, 106). Therefore, it is possible that host-synthesized MAAs or MAAs acquired from diet are translocated to the algal symbionts.

## DIVERSE FUNCTIONS OF MAAs

**(i) Sunscreen role of MAAs.** MAAs are efficient UV-absorbing compounds with absorption maxima within the UV range of 310 to 360 nm (18, 29). These secondary metabolites are capable of absorbing radiation energy without generating ROS

and are also suitable for a role in UV protection due to their uniform distribution in the cytoplasm of a cell (85). Because of their ability to absorb UVR, MAAs have been used commercially in sunscreen products such as Helioguard 365, which contains two imine-MAAs, shinorine and porphyra-334 isolated from the red alga *Porphyra umbilicalis* (5). These two MAAs also demonstrated a good photostability and efficiency as UV-absorbing compounds (111), capable of preventing sunburns *in vivo* (21). Although MAAs do not provide complete protection from damaging UVR, they do constitute an important means developed by marine organisms to diminish the damage produced by UVR (18, 29). In addition, UV-absorbing MAAs during the stress response may also be important due to their potential additional roles as antioxidants in organisms, as accessory light-harvesting pigments during photosynthesis, as intracellular nitrogen reservoirs, and in reproduction (66).

**(ii) Antioxidant role of MAAs.** Antioxidants from nature and synthetic antioxidants are commonly used in modern medicine as bioactive compounds due to their ability to decrease the amount of free radicals in cells and tissues (50). Beyond the well-recognized role of MAAs as natural sunscreens, some MAAs also demonstrate strong antioxidant capacity during photooxidative stress caused by ROS production. A number of *in vitro* studies indicated a role for MAAs as an antioxidant in scavenging ROS (30) and suppressing singlet oxygen-induced damage (22, 73, 97). Exposure to UVR has been shown to lead to DNA damage either directly or indirectly through ROS production, while UVR-induced DNA damage activates DNA repair enzymes or leads to apoptosis (10, 12, 42). However, large differences in antioxidative capacities for different MAAs have been observed. For example, imino-MAAs such as shinorine and porphyra-334 lack or have weak antioxidative activity, while mycosporine-glycine (Fig. 4) acts as an effective antioxidant protecting coral-algal symbiosis from oxidative stress (30). The most dominant MAA in the cnidarian host and in algal extract was mycosporine-glycine, suggesting the importance of this MAA compound in overall protection from damaging UV radiation, including its antioxidant capacities to scavenge free radicals and maintain the photosynthetic balance (6). In two thermally stressed scleractinian corals, *Platygyra ryukyuensis* and *Stylophora pistillata*, mycosporine-glycine expressly protected coral tissue and algal cells against oxidative stress even before antioxidative enzymes such as superoxide dismutase (SOD) and catalase (CAT) were induced (113). The MAA precursor 4-deoxygadusol (Fig. 4) also has a strong antioxidant activity (29). Interestingly, a dehydrated porphyra-334 produced after heat treatment (over 100°C) showed a huge boost in antioxidative activity over the antioxidative activity of the original porphyra-334 (117), opening another area with potential for future applications in biotechnology.

**(iii) Functions of MAAs during stress.** It has been suggested that MAAs may have a role in cell osmotic regulation as neutral, low-molecular-weight organic compounds that accumulate in cytoplasm (66). This feature is especially important for organisms living in environments characterized by high and variable salinities. In the cyanobacterium *Anabaena variabilis* (PCC 7937), an exposure to increased concentration of salt and ammonium positively affected the synthesis of MAA shinorine ($\lambda_{max}$ = 334 nm) even in the absence of UV exposure (89). In contrast, hypoosmotic conditions resulted in secretion of

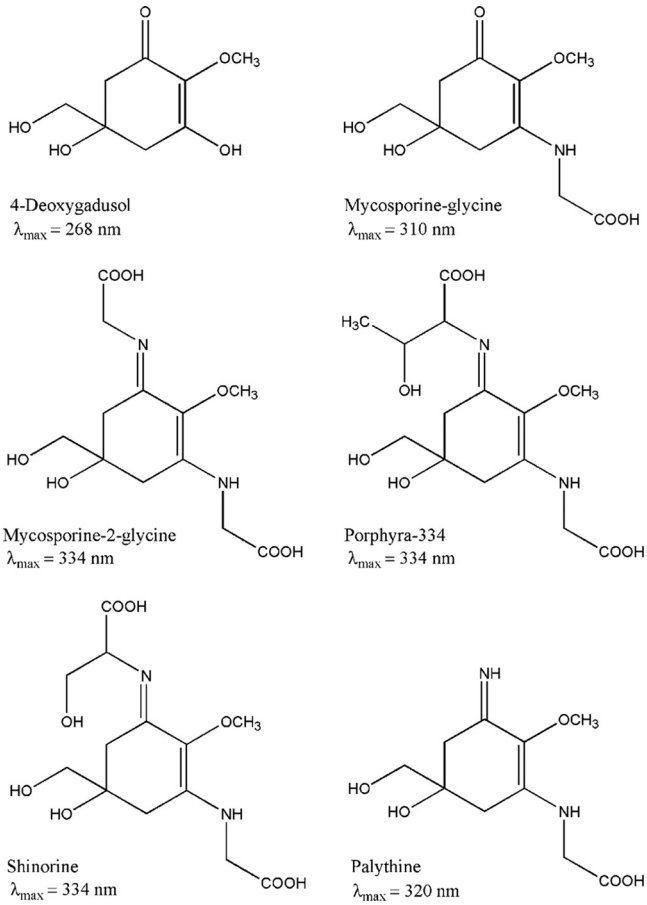


FIG. 4. Chemical structures of MAAs found in coral endosymbionts of *Symbiodinium* species and their absorption maxima.

MAAs to the medium in unicellular cyanobacteria living in a gypsum crust (65), indicating an additional role of these secondary metabolites in the organism exposed to osmotic changes (4).

Additionally, it has been proposed that MAAs are involved in the stress response during drought, as the production of photoprotective compounds such as MAAs, as well as carotenoids and some other UV-absorbing substances, was influenced by environmental stress, including desiccation (74). A study of cyanobacteria showed a positive correlation between MAA synthesis and exposure to drought and irradiation stress (101). However, in this case, high MAA concentrations were not sufficient to protect the organism from UVR-induced damage in the absence of a functional DNA repair mechanisms (37).

**(iv) Other functions of MAAs.** It has also been proposed that MAAs are intracellular nitrogen reservoirs (66). In the red alga *Porphyra columbina*, an increase in MAA concentration was reported after exposure to ammonium treatment under UVR (69). It has been shown that during nitrogen (N) limited conditions, the sensitivity of the photosynthetic apparatus to damaging UVR was increased due to less-effective repair in two estuarine dinoflagellates (59) and in phytoplankton (56). Similarly, N limitation in the red alga decreased MAA synthesis, increased the vulnerability of photosynthetic apparatus to

UVR damage, and reduced the growth rate (118). In the dinoflagellate *Heterocapsa* sp., photoprotective capacity was also affected by both MAA accumulation and nitrogen availability (51). In the latter study, it was reported that exposure to a high N concentration together with UVR positively affected MAA synthesis and the accumulation of photosynthetic pigments. MAA involvement during photosynthetic processes as accessory light-harvesting pigments and in reproduction has also been proposed, but additional investigations are needed to reveal the exact mechanisms of these events (66).

## ENVIRONMENTAL STRESS AND MAA BIOSYNTHESIS IN CORAL-ALGAL SYMBIOSIS

Multiple stress factors, including increased temperature, UVR, cold shock, salinity changes, and pollution, are known to be involved in the bleaching process (8, 33, 61). In summer, corals are exposed to temperatures close to their thermal bleaching threshold, and therefore, the exposure to a temperature 1 to 2°C above average summer temperatures over several days can lead to coral bleaching (43, 46, 54). Reactive oxygen species (ROS) are produced by coral holobiont, especially algal endosymbionts when exposed to thermal and UVR stress, resulting in oxidative stress, and potentially leading to bleaching due to the breakdown of the coral-algal symbiosis (52, 54, 110). Changes at the cellular level leading to the breakdown of the coral-dinoflagellate symbiosis include damage to photosystem II (PSII), especially D1 protein (3, 53, 100, 108), causing inactivity of PSII and dysfunctional photosynthesis (19, 44). Also, a number of changes in gene expression profiles have been reported following the exposure of coral to elevated temperatures. Focusing on the host (*Acropora millepora*), a significant upregulation in the levels of transcripts of 4 antioxidant genes (heat shock protein 70 [HSP70], MnSOD, ferritin, and $Zn^{2+}$-metalloprotease), including a huge intercolony variation in their gene expression profiles, was reported (20). In the Caribbean coral *Montastraea faveolata* and their embryos, thermal stress resulted in gene expression changes altering cytoskeleton structure, decreasing the calcification rate, negatively affecting $Ca^{+2}$ homeostasis, and initiating cell death processes, such as apoptosis and necrosis (24, 107). In transcriptomics of coral endosymbionts, differential regulation by heat stress was reported for newly discovered cytochrome P450 genes (80) and then for HSP70 and HSP90 (79, 81), bringing new insights into the mechanisms of stress response. In corals exposed to environmental stressors, oxidative stress and the production of ROS such as superoxide and singlet oxygen, can damage proteins, lipids, and other cellular constituents (55), possibly resulting in the exclusion of the coral endosymbionts from the host tissues (38). Consequently, reef-building corals lose color by expelling their algal symbionts and/or by degradation of algal photosynthetic pigments, resulting in coral bleaching (26).

Photosynthetic machinery and especially PSII are primarily damaged by a UV component of sunlight that leads to photoinhibition (99). Impaired photosynthetic activity caused by photoinhibition may result in further decreases in plant productivity and growth (98). A number of mechanisms are involved in preventing damage produced by UVR to PSII (such as photoprotection) and repair of PSII (104). In plants, UV-screening phenolic compounds (e.g., antocyanins that also screen light from visible spectra) and nonphenolic compounds (e.g., carotenoids) are involved in minimizing UV-induced photodamage to PSII, as well as MAAs in algae (98).

A positive effect of UVR on MAA synthesis has been revealed in a number of organisms as reviewed by Oren and Gunde-Cimerman (66). MAAs have been shown to be stable under extreme environmental conditions, including exposure to abiotic stressors such as temperature, UVR, and pH (41, 93). In the coral *Stylophora pistillata*, UVR induced ROS production, MAA synthesis, and conversion of MAAs (84). Thermal stress also resulted in increased MAA concentration in soft corals followed by a further increase when elevated temperatures were combined with UV exposure (85). In cultured *Symbiodinium* (clade A), UVR exposure increased MAA concentration (7, 9). The same effect was observed in the coral *Stylophora pistillata* exposed to UVR (84). Induction of MAA synthesis by UVR is seen in some corals when thermal stress and UVR occurs simultaneously (62, 85). Conversely, exposure to high solar radiation (PAR and UVR) and thermal stress had a negative effect on MAA synthesis in the Caribbean coral *Montastraea faveolata* (57), suggesting a complex regulation of MAA synthesis by environmental factors.

## CONCLUDING REMARKS

The marine environment is an amazing source of bioactive compounds and natural biomedicines for the treatment of various medical conditions, such as cancer and tuberculosis and is important in drug discovery due to the antitumor, anti-inflammatory, antiviral, and other pharmacological activities of the bioactive compounds and natural biomedicines (13, 14). In 2008 alone, 1,065 new compounds were isolated from a diversity of marine organisms, including bacteria, phytoplankton, algae, sponges, cnidarians, and other organisms (14). Focusing on preserving natural biodiversity and exploring natural marine products, a good deal of attention has been given to natural UV-absorbing compounds such as MAAs that have shown a wide distribution through a number of aquatic organisms from bacteria to metazoans (94). MAAs are found not only in corals but also in other animals, cyanobacteria, and algae. The presence of these secondary metabolites in so many species emphasizes their evolutionary importance (90). Animals cannot produce MAAs, as they lack the proposed MAA shikimate pathway and acquire MAAs from their diet or from symbiotic algae. However, recent molecular evidence confirms the presence of genes from the shikimate pathway in the sea anemone genome, indicating the possibility of horizontal transfer of ancestral genes from bacterial and dinoflagellate donors (95). This opens the possibility of animals obtaining the MAA biosynthetic capacities (e.g., for UV protection) from their symbiotic partners, which in the case of coral-algal symbiosis are not yet known and require further investigation. Conclusive evidence about MAA biosynthesis is also still missing and requires additional studies to confirm a long-standing assumption about MAAs originating from the shikimate pathway (31, 72) and/or potential origin from the pentose-phosphate pathway (5). Moreover, a gene cluster from a four-step pathway in cyanobacteria converting the pentose-phosphate products to MAAs has been recovered in the genomes of coral *Acropora*

*digitifera* and sea anemone *Nematostella vectensis*, potentially indicating metazoan capacities for MAA synthesis (88). From a biotechnological aspect, the use of MAAs as biological sunscreens and antioxidants has been already initiated in natural products such as Helioguard 365 (5, 16) and will open novel possibilities for innovative and natural approaches in generating organic cosmetics and therapeutics.

The importance of MAAs in protection from damaging UVR and other environmental stressors facing coral reefs and a wide range of other marine organisms is yet to be explored under different climate change scenarios. During the second half of the last century and the beginning of the 21st century, coral reefs have been facing a serious decline due to climate change and anthropogenic factors (45). Solar irradiance forms an important factor (43, 57) with both the visible and UV components accelerating the impact of heat stress. Declining water quality and overexploitation of fisheries have placed significant pressure on coral reefs, leading to their deterioration at the rate of 1 to 2% per year in most parts of the world (15). As a result of the degradation of coral reefs, hundreds of thousands of marine organisms reliant on this ecosystem are detrimentally affected. Additional studies are needed to understand the UVR-induced photoprotective mechanisms such as the one involving algal UV-absorbing MAA compounds as well as the ability of coral-algal cells to survive and protect their cellular structure from damaging UVR. Consequently, studying the pathways that underpin the ability of reef-building corals to avoid stress (such as the MAA biosynthetic pathway and MAA photoprotective role) is fundamentally important to developing our ability to understand growing global stress. Without a better grasp on the source of MAAs within corals and a more complete understanding of their biosynthetic pathway(s), we will struggle to make sense of their responses to climate change.

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