Mycosporine and mycosporine-like amino acids: A paramount tool against ultra violet irradiation

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ABSTRACT

Various facts demonstrated that UVB is harmful to organisms. Sunscreen compounds are usually used to prevent the excessive damage caused by UVB. However, certain photosynthetic organisms have evolved mechanisms to counteract the toxicity of ultraviolet radiation by synthesizing UV screening compounds such as mycosporine-like amino acids (MAAs). MAAs provide UV protection to primary and secondary consumers through food chain and to non-biological materials by photostabilizing action. Information related to the ecological consequence of MAAs and their spatial distribution from a wide range of organisms is accumulating. Hence, our studies seek a potent class of natural sun protective compounds to understand their relationship with environment and to develop a protocol for large-scale industrial production of these compounds so that they can find application as UV-protecting cosmetics.

Key words: Mycosporines, sunprotectants, ultraviolet rays, UV irradiation

INTRODUCTION

The environmental context

Here, we present a broader class of sun protective compounds which are obtained from various natural sources, and intending to compete with the existing sunscreen agents that are marketed. The article is based on the concept of how the defense mechanism of other kingdoms, e.g. algae (synthesize secondary metabolites for their own protection), against UV rays can be implemented in the development of sunscreen formulation against various mankind disorders (especially for skin protection). Keeping this in view, we have made an effort to fully cover the broad-spectrum photostable class of compounds known as "mycosporines", with all their reported descriptions.

Nowadays, consequences of UV rays on living beings have become an important issue. UV rays constitute different types of ranges, of which UVB is a minute but highly active and detrimental component.[1-4] Under stress caused by this range, marine organisms generate a multitude of sunscreening metabolites. Thus, before furnishing any formulation against UV, it is essential to understand which group on this earth is more resistant against them. There are hundreds of photoprotective compounds present in the market. Nevertheless, so far, no compound is proved to be versatile. Owing to the presence of certain UV resistant compounds marine algae show more resistance against UV than terrestrial plants.[5,6] The general name *mycosporine* is given to the fungal metabolites having absorption range at 310 or 320 nm and substituted with amino acid residues. Mycosporine-like amino acids (MAAs) are a family of intracellular compounds biosynthesized by shikimic acid pathway for the synthesis of aromatic amino acids involved in the protection of aquatic organisms against solar radiation. They are small (<400 Da), colorless and highly polar substances characterized by a cyclohexenone or cyclohexenimine chromophore,[7] conjugated with the nitrogen substituent of an amino acid or its imino alcohol, having absorption maxima ranging from 310 to 360 nm, with an average molecular weight of around 300 Da and were first discovered in some sporulating mycelia. In fact, these compounds accumulate within the spores of numerous and various fungi, especially those whose sporulating areas receive direct solar radiations.[8] Moreover, photostability in both distilled and sea water in the presence of photosensitizers and high resistance against physicochemical stressors like temperature, strong UVR, various solvents as well as pH make them successful photoprotectants in various

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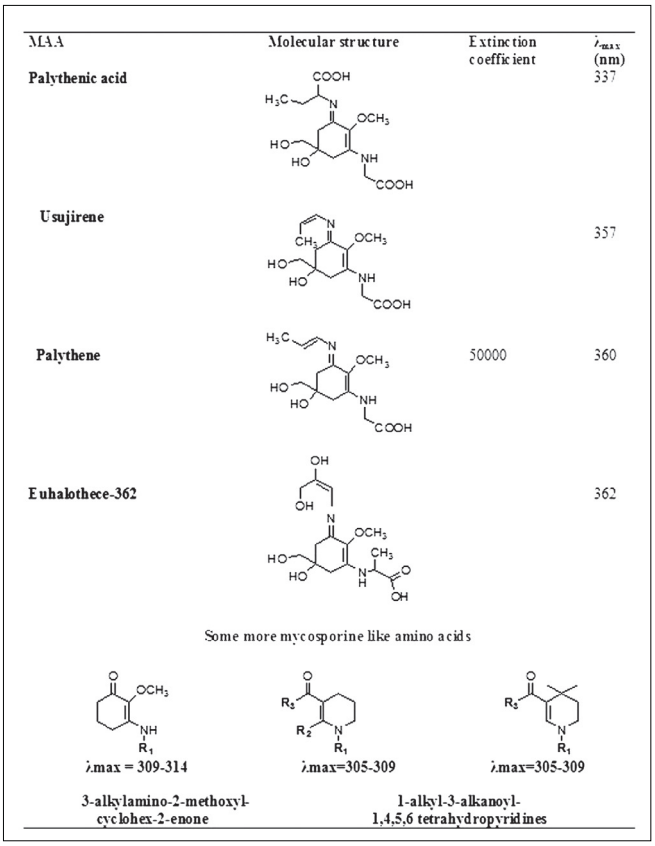
habitats and organisms.[9] Their cyclic structures vary essentially according to the substituents 2-OMe (mycosporine) or 2-OH (nor-mycosporine) [Graph 1] and the amino acid functionality.[7] Generally, the ring system of MAAs contains a glycine subunit at the third carbon atom, whereas some MAAs also contain sulfate esters or glycosidic linkages through the imine substituents.[7] Differences among the absorption spectra of MAAs are due to the variations in the side groups and nitrogen substituents.[7] Till now, the chemical structures of over 30 different mycosporines [Graph 1] have been elucidated including a number of glycosylated mycosporine derivatives and recently characterized mycosporine-glutamicol-glucoside and mycosporine-glutaminol-glucoside. As shown in Figure 1, almost all MAAs follow a common isolation procedure.[10] They have been identified in a number of taxonomically diverse organisms such as fungi, marine heterotrophic bacteria, cyanobacteria, eukaryotic marine invertebrates and a wide variety of other marine organisms.[11] Their highly photoprotective favorable properties such as high molar coefficients (ε = 28,100–50,000/M/cm), strong UV-absorption maxima and photostability,[9] and resistance to abiotic stressors increase their demand as effective sunscreening compounds. Their antioxidant nature increases the therapeutic effectiveness. Furthermore, the osmoregulation property make them an excellent example as a potent osmolyte.[12] However, in recent years, evidence is accumulating that mycosporines play additional roles such as protecting cells against salt stress, desiccation or thermal stress in certain organisms, serving as an intracellular nitrogen reservoir and their presence in fossils may be considered as potential probes to record past UV radiation (UVR) changes in the environment. So, currently, these natural amino agents are greatly experimented for their ecological and biological roles. Few reports are covered and few are in pipeline. Hence, this study focuses on several key issues concerning with the accepted roles of MAAs in environment, especially against harmful UV rays.



Graph 1: Different mycosprine amino acids with molecular structure, absorption maxima and extinction coefficient. [31, 40, 19, 17]

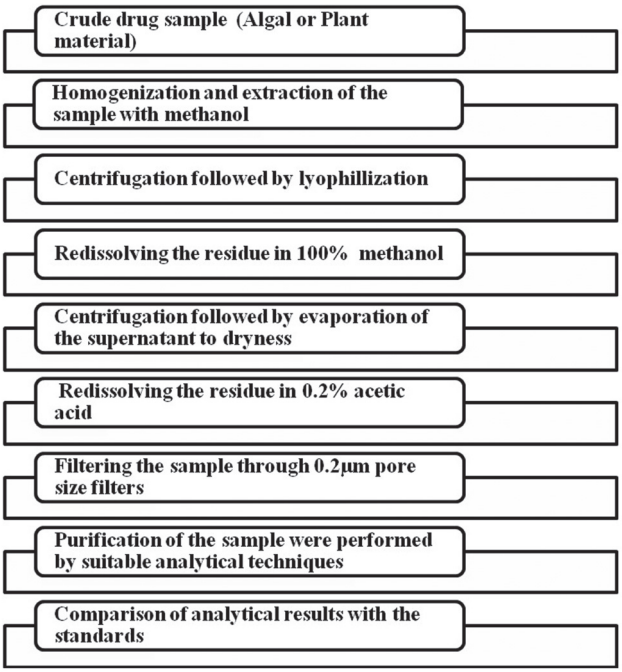


Figure 1: Protocol for isolation and purification for MAA

Impact of UV radiations on the environment

Year by year, the manmade progressive changes affect the stratospheric ozone layer, especially by promoting harmful zones of "UV irradiation", i.e. UVB irradiation (280–315 nm) and to some extent UVA (315–400 nm).[13-15] UVB and UVA radiation has to be considered unfavorable for the living matter and different protecting strategies have been developed to cope with their impact. Apart from a small portion near the UVA waveband,[1-3] UV irradiation is not photosynthetically active, whereas "UVC" (200–280 nm) is totally absorbed by the atmosphere and hence not of biological significance. Deep penetration of UVB radiation in the water column may affect the aquatic ecosystems. Therefore, marine organisms exhibit marvelous mechanisms to counteract the toxic effects of these rays.[6,16,17] UVB is a small but highly active component of the solar spectrum and causes wide range of harmful effects[13-14] on the environment due to which the whole productivity of ecosystems may be affected. Species differ greatly in their sensitivity to UVB. Five strategies have been identified that protect organisms against UV damage, namely, production of photoprotective compounds such as MAAs, escape from ultraviolet radiation by migration into habitats with reduced light exposure, production of quenching agents, repair mechanisms

and cyanobacterial chromatic adaptation. Mycosporine-glycine like compounds mainly show absorption in the UVB region,[18] but later on, as the oxygen level increases, the absorption of UVA becomes necessary because it mediates its effect through the formation of free radicals of oxygen. This change in the absorption spectrum can be achieved by replacing the ketone group with a nitrogen atom in UVB-absorbing compounds. This has a greater mesomeric effect on the benzene ring and absorbance is shifted into the UVA. A mutation in the proposed pathway of a UVB screening compound may also have caused a shift toward UVA absorption.[16,17,19]

Evolution of MAAs as UV-absorbing compounds

Solar light penetrates seawater with differential attenuation depending upon its wavelength. In clear tropical ocean waters, solar UV light can have a significant biological effect down to a depth of 20 m. Environmental UV light in the wavelength region 285–340 nm is damaging to biological tissues and can be physiologically detrimental or fatal to many marine forms of plant and animal life. From the earlier times, it has been known that widespread UV-absorbing compounds accumulated by extensive microorganisms play a vital role against the deleterious effects of UV irradiation.[1-3] During the early Proterozoic era, screening of harmful radiation was necessary to avoid the UV-induced destruction of complex organic molecules and this function might have been performed by organic molecules in the aqueous environment of the ancient earth. Plankton are often incapable of detecting UVB as they utilize UVA or visible light in photoreactivation [Figures 2 and 3].[20] In the present day, algal substances are promoted not only to develop a protective shield against UV irradiations but also for a better understanding of UV adaptation from these oldest oxygenic organisms. MAAs are found in many prokaryotes which are considered to be a source for understanding the UV effects of MAAs.[21] Mycosporines are widespread in the microbial world. For example, a survey of 152 species of marine microalgae showed that they all contained such UV-absorbing compounds.[22] The accumulation of large amounts of MAAs in cyanobacteria (*Microcoleus*) was first reported in 1969. The morphology, physiology and 16S rRNA gene sequence of 13 MAA-containing strains were studied and a common complement of MAAs was found among them. Archean earth's first specific UV-screening molecules are not well known but it is hypothesized that aromatic moiety reaction centers were some of the earliest UV screens that later started to perform a light-harvesting role in photosynthesis.[23] The evolutionary origins of UV-screening compounds are still unknown. It is presumed that many evolved to perform other physiological roles but later fulfilled a UV-screening function under selection pressure.[21] The MAAs in eukaryotic algae are thought to have been passed from cyanobacteria in the plastidic line. If green algae were the true origin of land plants, it may be speculated that early land plants initially were dependent on MAAs instead of flavonoids, as protectants from UV radiation.[1,161]

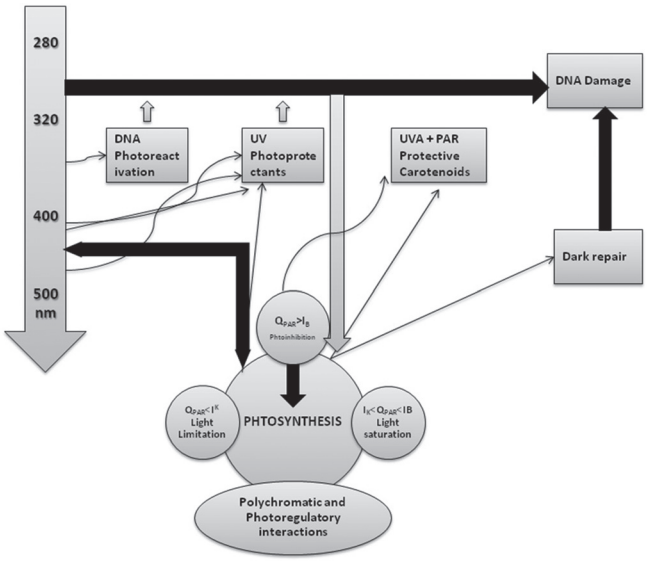


Figure 2: Polychromatic and photoregulatory interactions of QUVB (230–320 nm), QUVA (320–400 nm), and QPAR (400–700 nm) on primary production and DNA integrity in phytoplankton. IK is the minimum QPAR requirement to saturate rates of photosynthesis; IB is the minimum QPAR light requirement to photoinhibit rates of photosynthesis

Structure and biosynthesis of MAAs

Despite various progresses in synthetic chemistry, algae still constitute an important source of pharmaceuticals and other compounds of economic importance.[21] MAAs are found in various organisms from tropical to polar regions. The biosynthesis of MAAs has been suggested to occur via the first part of the shikimate pathway in both cyanobacteria and fungi. Biosynthetic pathways producing these compounds are not only species-specific, but also depend on various environmental factors. UV rays, particularly UVB exposure (UVB band, 280–315 nm), play an important role in the stimulation of biosynthetic pathways. Biosynthesis of MAAs occurs in bacteria, cyanobacteria, phytoplankton and macroalgae but not in animals due to the lack of the shikimate pathway in

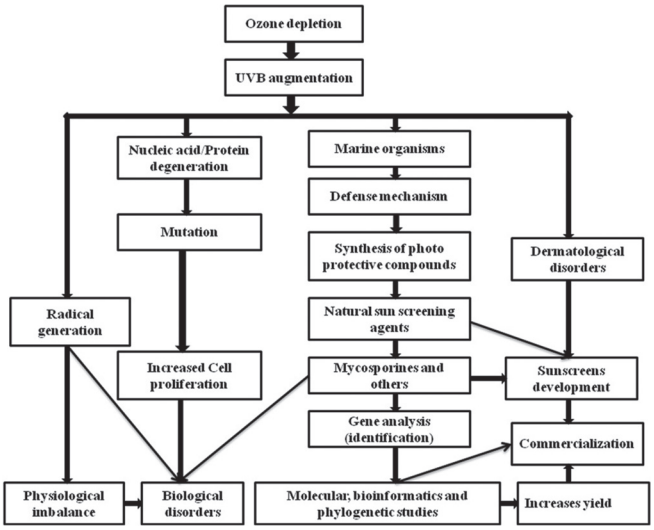


Figure 3: The persistent effect of UV rays on development in aquatic photosynthetic organism

them.[24-27] They acquire MAAs by diet transfer, symbiotic or bacterial associations. All 30 MAAs discovered [Graph 1] till now follow shikimate pathway for their biosynthesis, which reveals that 3-dehydroquinate (formed in the shikimate pathway) is the precursor for the synthesis of these fungal mycosporines and MAAs via gadusols[28] [Figure 4]. Various stimulating factors of MAA synthesis such as effect of season, development period of an organism and UV rays were noticed widely.[29] The primary MAA, mycosporine-glycine, [Graph 1] synthesized by the shikimate pathway is then transformed by chemical and/or biochemical conversions into other MAAs. Recently, this view has been challenged by the report of genes encoding the enzymes of the shikimate pathway in the genome of a marine animal.[6,15] Prior phylogenetic analysis and genomic mining has given the evidence for the set of genes responsible for the biosynthesis of MAAs. Out of the investigated species, PCC 7937 was able to synthesize MAA [YP_324358 (predicted dehydroquinate (DHQ) synthase) and YP_324357 (O-methyltransferase)]. Identification of these genes widens the field of research for molecular, bioinformatics and phylogenetic analysis of these evolutionary and industrially important compounds.[30,31]

MAAs as versatile elements

- *MAAs as photoprotectants:* Site-dependent protection is afforded by MAAs in the cells by absorbing lethal doses of highly energetic UVR and then dissipating this energy in the form of harmless heat radiation to their surroundings.[32] In water, they absorb at wavelengths that penetrate relatively deeply in the water; wavelengths below 300 nm are more damaging to DNA and other cellular components.[16] Out of 10 photons, these compounds prevent 3 from striking cytoplasmic targets in cyanobacteria.[33] Under aerobic conditions, light converts mycosporine glutamine into aminocyclohexenone and 2-hydroxy glutaric acid, which is temperature-dependent photolysis. On the other side, photolysis is also observed when other photosensitizers, which are carriers of singlet oxygen, replace flavins.[34]

- *MAAs as possible sunscreening compounds:* MAAs "nature's sunscreen compounds" are actively excreted and accumulated at the epidermis where they show sunscreening effect.[32] Studies on the photodegradation and photophysical characteristics have shown that MAAs are stable and effective sunscreen compounds. Recently introduced porphyra-334 isolate from Indian species of *Porphyra vietnamensis* has given excellent sunprotective effects against widely used *Aloe vera* gel.[35] However MAAs has low photodynamic reactivity when compared with several commercially available sunscreens [Graph 1]. Diverse synthetic analogues of MAAs have been developed for commercial purposes. Analogues of mycosporine-glycine (3-alkylamino-2-methoxycyclohex-2-enones) [Graph 1] and tetrahydropyridine (1-alkyl-3-alkanoyl-1,4,5,6-tetrahydropyridines) were developed though they suffer some stability related problems. After a large evaluation, a product called Helioguard® 365 from the red alga, *Porphyra umbilicalis*, has been commercialized successfully. In addition to their sun protection in smaller organisms,[35] MAAs are also of immense importance for

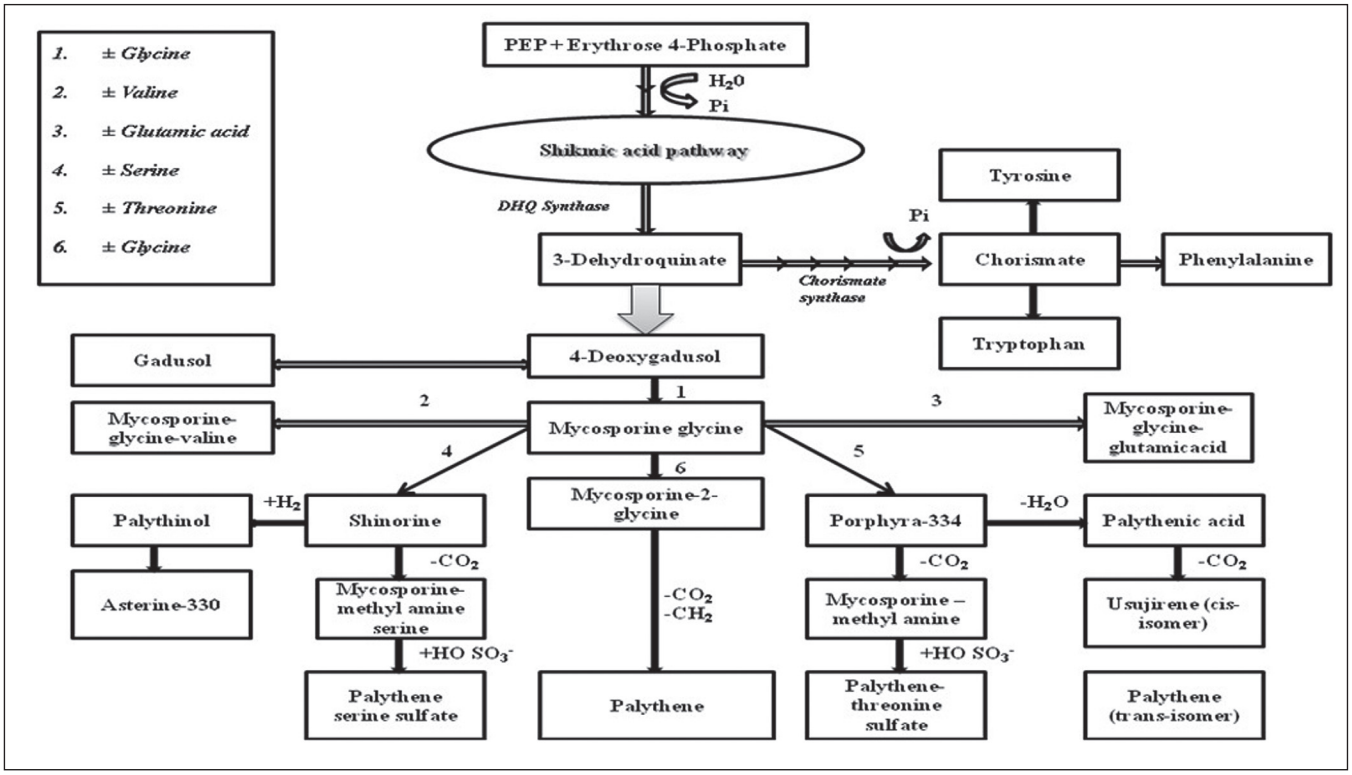


Figure 4: Conventional biosynthetic pathways for the formation of MAAs via the shikimate pathway.[24] Wide gray line represents the biosynthetic connection between dehydroquinate, gadusols and MAAs

humans as these compounds have been found to effectively block thymine dimer formation by UVR *in vitro* and were recently found to provide growth stimulation activity in human cells.[36-38] As a result, MAAs have varied ecological and therapeutic significance [Figure 5].

- *MAAs as antioxidant molecules:* The MAA, mycosporine-glycine, functions as a biological antioxidant as it was found to effectively suppress various detrimental effects of the type-II photosensitization and decreased the level of singlet oxygen generated by eosin Y or methylene blue.[39] In nature, most of the mycosoprines exhibit high antioxidant activity by scavenging large amounts of reactive oxygen generated by supersaturated oxygen in larger depth of the water, e.g. mycosporine-glycine was found in *Platygyra ryukyuensis*.[35] It has been reported that mycosporine-glycine has moderate antioxidant activity, whereas 4-deoxygadusol, a precursor of MAAs, has strong antioxidant properties and its retrobiosynthesis through bacterial conversion of algal MAAs has been performed for commercial applications. On the other hand, iminomycosporine-like amino acids shinorine, porphyra-334, palythine, asterina-330, and palythinol [Graph 1] were not oxidized and hence exhibit less or no activity. It was therefore concluded that at least certain MAAs may play a role in protection by probably, more importantly, scavenging O_2 produced by certain endogenous photosensitizers.[32,40,41]

- *MAAs and salt stress:* MAAs are highly resistant against abiotic stressors such as temperature, UV radiation, various solvents and pH.[12] They are uncharged low–molecular-weight organic substances which generally provide osmotic regulation to the cells where the surroundings of the cell is hypersaline. Freezing (binding of water into ice) and high salinity both lead to cellular dehydration and accumulation of free oxygen radicals, resulting in oxidative stress. To provide the necessary osmotic balance, most microorganisms accumulate, in the intracellular space of the cell, the so-called MAAs "osmotic solutes" or "compatible solutes", and therefore build osmotic pressure within the cell. In freshwater environments, MAAs accumulate in the cell by an osmotic mechanism in certain cyanobacteria. It is probably the highest MAA concentration ever reported; for comparison, values up to 0.8% of the cell dry weight were measured in the cyanobacterium *Gloeocapsa*.[12]

- *MAAs and desiccation stress:* Several experiments have proven that mycosporines contributed well to the drought resistance of the organisms. When microorganisms are exposed under simultaneous drought stress conditions, mycosporines, by various mechanisms (e.g. by formation of extracellular matrix or sheath around the microorganisms in which glycosylated MAAs are embedded), resist the desiccation related stress. However, it was reported in some cases that MAA containing cells are more resistant against combination of stresses then desiccation alone. Furthermore, it was also reported that MAA alone does not provide sufficient protection against this stress.[42]

- *MAAs and thermal stress:* Few evidences established a relationship between MAA formation and high-temperature stress, e.g. MAA content in the soft corals *Lobophytum compactum* and *Sinularia flexibilis* were upregulated under themal stress, and their concentrations were further enhanced during simultaneous exposure to UV.[43] On the other hand, neither increased temperature stress nor cold shock, nutrient limitation, or photooxidative stress induce MAA formation in the cyanobacterium *Chlorogloeopsis* PCC 6912.

- *MAAs as accessory pigments in photosynthesis:* Earlier, it was considered that MAAs are fluorescent compounds and may increase the photosynthetic efficiency. Following excitation in the UVA range, emission of fluorescence at wavelengths close to the absorbance of the Soret band of chlorophyll *a* was observed, so that theoretically, energy transfer from MAA to chlorophyll could be possible. However, MAAs are only weakly fluorescent, if at all, and MAAs are generally

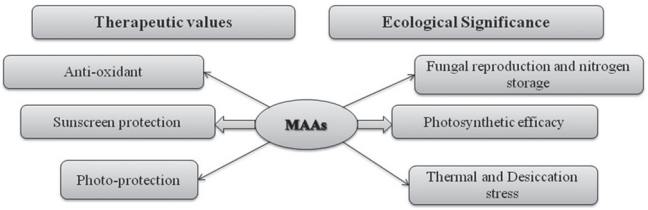


Figure 5: The most concerning usage of mycosporine amino acids

Table 1: Distribution of MAAs in some important marine organisms

Type of marine organism	Type of MAAs
Phytoplankton Alexandrium excavatum	Porphyra-334, palythene, shinorine. usujirene
Prorocenirum micans	Mycosporine-glycine, shinorine. porphyra-334, asterina-330
Prorocenirum minimum	Shinorine, palythene
Lingdodinium polyedra	Porphyra-334, mycosporine-glycine:valine, palythine,
Thalassiosira sp.	polythinol, palythene, Shinorine, porphyra-334
Macroalgae Chondrus crispus	Shinorine, palythine, palythene, palythinol
Curdlea racovixzae	Palythine, shinorine, palythinol
Iridaea chordare	Palythine, shinorine; palythinol, palythene
Liihotamnion aniarciicum	Shinorine, porphyra-334
Palnnria decipiens	Palythine, palythene, porphyra-334, palythinol, shinorine
Phyllophom antarctica	Shinorine, palythene
Plyllophom appenchculara	Shinorine
Porplnra umbilicalis	Shinorine, porphyra-334
Gracilaria cornea	Shinorine.porphyra-334
Gelidum sp.	Shinorine
Fucus spiralis	Shinorine

MAA: Mycosporine-like amino acids

most abundant in high light environments, in which light energy is not the factor for photosynthesis. So far, the early claim that MAAs may serve as accessory pigments in photosynthesis has never since been verified.[21,27,32]

- *MAAs in intracellular nitrogen storage:* In nature, MAAs acts as intracellular nitrogenous reservoir, storing two nitrogen atoms per molecule. Whenever required, it releases nitrogen by suitable mechanism.[32]

- *Mycosporines and fungal reproduction:* Mycosporines (not the direct photoproducts of fungi) were considered as biochemical markers for reproductive stages of fungi and have been related to sporulating mycelia. They are present in the mucilage that surrounds conidia of some fungi where they protect them from solar radiation. Mycosporines have also been located in the extracellular matrix and in the outer cell wall layers of microcolonial fungi. Nowadays, it is known that mycosporines are widespread among the fungal classes Zygomycetes, Deuteromycetes, Ascomycetes, and Basidiomycetes having absorption maxima at 310 nm and therefore called "P310".[15] The rate of their production varies with the wavelength of irradiation, period of irradiation, light intensity and nutritional conditions of the culture. Changes in irradiance induce a rapid response at high light intensity and short wavelengths. Nevertheless, radiance is essential only to initiate the process of mycosporine production, as its synthesis continues in the dark as well as in the light (except during sporogenesis).[8,44]

Environmental distribution of MAAs

Mycosporines are widely distributed in nature.[45] Usually in all life forms, cells do not contain more than 1% of their dry weight as MAA. These accumulated sunscreens can be effective only in cells larger than about 100 mm. As phenylproanoids and melanin protect higher plants and animals,[40] MAAs, by absorbing harmful UV radiations, play a similar role in lower organisms. Various evidences [Table 1] for their protective function in phytoplankton have been established where high amounts of intracellular MAAs diminish the inhibitory effect of UV radiation on photosynthesis. The accumulation of MAAs protects the microalgae from inhibition of motility by UVB radiation.[22,46] Many experimental evidences establish a relationship between MAAs and sunlight, e.g. exposure to sunlight leads to a strong increase of MAA content in *Alexandrium excavutum*.[31,44] Accumulation of MAAs has also been reported to depend on the spectral composition of the light; blue light is more effective than green and red light, and UVA radiation strongly enhances MAA accumulation. There are some reports on the decreasing contents of MAAs with increasing depth, but at the same time there are cases where no relationship was obvious. Most marine macroalgae inhabit coastal regions of the sea where they attach themselves to the ground.[47] In contrast to microalgae, sessile macroalgae are not able to avoid harmful irradiation by moving to deeper regions.[22,31,46,47] Therefore, they are supposed to have developed mechanisms to mitigate harmful UV radiation in their natural habitats. The highest absorption was found in red algae[5,18] with a tendency for decreasing contents of the compound with increasing depth. MAAs are found not only in phytoplankton, cyanobacteria and macroalgae[47] [Table 1] but also in many different marine organisms. MAAs provide protection from UV radiation not only to their producers but also to the primary and secondary consumers through the food chain or symbiotic association.[48] Rather, these organisms of high trophic levels ingest MAAs with their food and are able to accumulate them in specific tissues. Mycosporines are also found in the eye tissue of several tropical marine fish and other marine organisms to improve the optical contrast in the blue water environment by filtering UVB rays. Marine vertebrates, such as teleostean fish, are largely protected from environmental UV radiation by their external scales. Earlier reports substantiated the presence of MAAs in their ocular tissue and hence provide protection against UV damage. The use of DNA microarray technology and 2-D electrophoresis will probably help in understanding the adaptation of cyanobacteria to UV stress both at genome and proteome level.[30] Much information on MAAs and scytonemin from diverse organisms has been gathered over the past few decades. This has led to the development of a database on photoprotective compounds.[49] The lack of a taxonomic pattern in the distribution and the shikimate pathway [Figure 4] as a source for mycosporines leads to the conclusion that MAAs in animals are ingested with food and concentrated by marine organisms.[16,21,31]

MAAs over synthetic UV blockers

According to the previous researchers, ozone depletion is not the cause for the increase in skin cancers among the present generation. Chemical agents currently present in sunscreen formulations are proved to be more harmful then the effects of ozone depletion on the skin. Also, on the contrary, sunlight exposure may actually decrease human cancer rates and improve our health. The majority of sunscreens have highly efficient absorption or reflecting capabilities throughout the whole range of UV and, in some instances, infrared wavelengths. Though a successful UV-screening compound ultimately depends upon simple organic photochemistry, π-electron found in conjugated bond structure systems are a common theme in the function and characteristics of natural UV-screening molecules.[35,50] Due to less awareness about the dangers of constituents in chemical sunscreens, publically it is highly acceptable that application of additional chemical sunscreen to the skin before any exposure to sunlight would prevent skin cancer and protect our health. Recent researches have given the evidences of the harmful effects (radicals' generation, risks of skin cancer and estrogen like-effects) of the available chemical sunscreens in the market and their regular application to the skin. These chemical agents were proven as primary causative agents for increasing the cancer risk by virtue of their abundant free radical generating properties and estrogen-like effects. These effects are similar to many banned chemicals such as dichloro-diphenyl trichloroethane (DDT), dioxin, and polychlorinated biphenyls (PCBs), but they are still present in the market due to profit gaining purpose of the chemical industries. Most of the chemical sunscreens contain 2–5% of UVA and UVB blockers [Table 2]

Table 2: US FDA-approved sunscreen ingredients, 1997[52]

	Chemical blockers	Physical blockers
UV-1 blockers	UVB blockers	Zinc oxide
Benzophenones	PABA and its derivatives	Titanium dioxide
Oxybenzone	p-Amyldimethyl PABA (padimate A)	Iron oxide
Sulisobenone	Glyceryl PABA	Kaolin
Dioxybenzone	Octyldimethyl PABA (padimate O)	Ichthammol
Methyl anthranilate		Red petrolatum
Camphor analogues	Cinnamates	Talc (MgSiOx) Calamine
Terephtalylidene dicamphor-sulfonic acid	2-Ethoxyethyl-p-methoxycinnamate 2-Ethylhexyl p-methoxycinnamate	Microionized
4 methjibenzy-lidenecamphor		blockers
	Salicylates	Microtitanium
Dibenzoy-lmethanes Avobenzone	Homomenthyl salicylate Triethanolamine salicylate 2-Ethylhexyl salicylate	dioxide Oral agents
Butly methoxy-Dibenm-simethane	Acrylates	(Systemic photoprotection)
Triazines	2-Ethylhexyl 2-cyano-3,3-diphenylacrylate	PABA Antihistamines
Bisethlyhexy-loxyphenol -		Aspirin
methoxyphenyl	Others	Indomethacin
Triazene	Digalloyl trioleate	Retinol
Octly triazone	Ethyi 4-bishydroxpropyl	Ascorbic acid
	aminobenzoate Dihydroxyacetone 2-Phenylbenzimidazole-5-sulfonic acid	α-Tocopherols Corticosteroids Psoralens β-carotene Antimalarials

as the active ingredients . Most of these UV-blocker compounds are cancer causing elements, e.g. Benzophenone (and similar compounds) and Avobenzone (powerful free radical generators), Padimate-O or other *p*-aminobenzoic acid (PABA) derivatives (DNA damaging effects), and Triethanolamine (formation of cancer causing nitrosamines). Most of the sunscreen compounds are either UVA or UVB protective and are usually combined with other sunscreen chemicals to produce a "broad-spectrum" product. Furthermore, in sunlight, some show instability after a particular period of time. It clearly indicates the need of a potent, stable and broad-spectrum group of agents which are devoid of their hazardous effects to the skin. Here, mycosporine like amino acids stand as a good example due to their excellent antioxidant and sun protection activities without causing any harmful effects.[51]

Evaluation of mycosporine like amino agents

Over the last several years, more efficient sunscreening ingredients have been developed for improved skin protection [Table 2]. After the discovery of the first commercial sunscreen in 1928, till now, so many formulations have been developed, but unfortunately every formulation comes with certain demerits.[35] Moreover, almost all of the early agents were directed toward UVB not UVA [Table 2]. Thereafter, broad-spectrum MAAs were developed and there are so many techniques to assess the efficacy of these agents against sunburn, based on the determination of the sun protection factor (SPF), which is defined as the ratio of the time of UV exposure necessary to produce minimally detectable erythema in sunscreen-protected skin to that of the time taken to produce the same effect for unprotected skin.[20,35] Evaluation of the efficiency of sun care products has, for a long time, been assessed through the *in vivo* SPF test, which is performed on human volunteers. A high SPF normally leads to a greater uncertainty in the final *in vivo* result. For economical, practical and ethical reasons, a reliable *in vitro* measurement of the SPF seems particularly useful as a supplement to but not a replacement for the *in vivo* SPF. Moreover, SPF might be insufficient as an indicator of protection from UV-induced carcinogenesis. Currently, various modules have been used in the evaluation of these compounds such as the following: Evaluation of protection against UVA, Phototoxic protection factor, UVA erythema protection factor, Pigment-darkening protection factor and Immediate pigment darkening, *In vitro* transmission protection[36] factor, and substantively,[52] the most common method for detection and quantification of these compounds is high performance liquid chromatography (HPLC) based on their retention times and their absorption maxima or obtaining entire UV scans via diode-array detector (DAD). The electrospray ionization mass spectrometry coupled with liquid chromatography (LC-MS) has also been used to analyze the MAAs in several organisms.[53]

Worldwide market for sun screening agents and their economical effect

MAAs have been commercially explored as sun care products for the protection of skin and other non-biological materials. Diverse role and increased utilization of these amino acid constituted products are increasing their market demands day by day. An expanding market of these products is a fact and is facing a new challenge of growing algae to produce algal isolates constituting mycosporines on a large scale in aquaculture based industry. Total aquaculture production in 2000 was reported to be 45.71 mmt by weight, valued at US$ 56.47 billion, with the production going up by 6.3% by weight and 4.8% by value since 1999. Mycosporine based sunscreen use has significantly expanded in the last decades as a consequence of the perception that UVB ray is the main cause for the development of skin cancer and the photoaging process. On the other hand, recent reports have shown that in the last 20 years, the incidence of non-melanoma skin cancer (NMSC) has increased significantly. It has been suggested that the incidence of NMSC can be drastically reduced by using certain algal derived sun ray blockers.[20] Due to the increasing cosmetic market, this area is highly promising and the use of mycosporine-like amino acids as a highly efficient natural UV blocker in the sunscreen formulations is commercially attractive. To survive in a competitive environment, certain marine organisms have developed defense strategies that result in a significant level of

structural chemical diversity, from different metabolic pathways. The exploration of these organisms for pharmaceutical purposes has revealed important chemical prototypes for the discovery of new agents, stimulating the use of sophisticated physical techniques and new syntheses of compounds with biomedical application. Therefore, an increasing supply for algal extracts, fractions or pure compounds for the economical sector is needed.

CONCLUSION

Mycosporine is a common name used to describe a collective group of water soluble nitrogenous metabolites associated with light-stimulated sporulation in terrestrial fungi.[8] They have strong UV-absorption maxima at 310 nm and were chemically identified by Favre-Bonvin *et al*.[7] Most of the sunscreen products present in the market are primarily limited to UVB and short wavelength UVAII (315–340 nm). Only a few compounds are broad-spectrum UVA filters. However, some of these compounds are problematic in terms of photostability and cross stability with other sunscreen agents.[9] In view of the fact that the UVA band constitutes about 5% of the solar spectrum at the Earth's surface, whereas UVB only makes up to 0.5%, there is an urgent need of novel broad-spectrum and photo stable compound. Algal derived sunscreening compounds hold great promise for discovery and development of new pharmaceuticals. Algal biochemicals are gifts from nature as they are renewed each year through the energy from the sun. MAAs are typical representatives of these botanical gifts universally present in marine organisms. In addition to their biological functions in marine environment and, in some cases, to their esthetic value, these stable compounds give a new range of protection (broad spectrum) in sunscreen formulations against UV rays. Hence, they can be used in the development of artificial human sunscreens. However, discovery of these compounds is still incomplete, every month new structures are coming out and the dissection of their metabolic pathways is far from being complete. Taken together, it seems that these compounds provide sufficient therapeutic role in photoprotection, not only for algae but also for humans (via formulation).

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REFERENCES

1. McKenzie RL, Bjorn LO, Bais A, Ilyasd M. Changes in biologically active ultraviolet radiation reaching the Earth's surface. Photochem Photobiol Sci 2003;2:5-15.
2. Crutzen PJ. Ultraviolet on the increase. Nature 1992;356:104-5.
3. Marchant HJ. Impacts of ozone depletion on antarctic organisms. In: Battaglia B, Valenica J, Walton DW, editors. Antarctic communities: Species, structure, and survival. Cambridge: UK: Cambridge University Press; 1997. p. 367-74.
4. Castenholz RW, Pichel FG. Cyanobacterial responses to UV radiation. In: Whitton BA, Potts M, editors. The Ecology of Cyanobacteria. Dordrecht: Kluwer Academic Publishers; 2000. p. 591-611.
5. Yuan YV, Westcott ND, Hu C, Kitts DD. Mycosporine-like amino acid composition of the edible red alga, Palmaria palmata (dulse) harvested from the west and east coasts of Grand Manan Island, New Brunswick. Food Chem 2008;112:321-8.
6. Talarico L, Maranzana G. Light and adaptive responses in red macroalgae: An overview. J Photochem Photobiol Biol 2000;56:1-11.
7. Bonvin JF, Arpin N, Brevard C. Structure de la mycosporine (P310). Can J Chem 1976;54:1105-13.
8. Leach CM. Ultraviolet absorbing substances associated with light-induced sporulation in fungi. Can J Bot 1965;43:185-200.
9. Conde FR, Churio MS, Previtali CM. The photoprotector mechanism of mycosporine-like amino acids: Excited-state properties and photostability of Porphyra-334 in aqueous solution. J Photochem Photobiol Biol 2000;56:139-44.
10. Zhaohui Z, Xin GA, Tashiro Y, Matsukawa S, Ogawa H. The isolation of Porphyra-334 from marine algae and its UV-absorption behavior. Chinese J Oceanol Limnol 2005;23:400-5.
11. Sinha RP, Singh SP, Hader DP. Database on mycosporines and mycosporine-like amino acids (MAAs) in fungi, cyanobacteria, macroalgae, phytoplankton and animals. J Photochem Photobiol Biol 2007;89:29-35.
12. Kogej T, Gostincar C, Volkmann M, Gorbushina AA, Gunde-Cimerman N. Mycosporines in extremophilic fungi: Novel complementary osmolytes? Environ Chem 2006;3:105-10.
13. Sinha RP, Klisch M, Groniger A, Hader DP. Ultraviolet-absorbing/screening substances in cyanobacteria, phytoplankton and macroalgae. J Photochem Photobiol Biol 1998;47:83-94.
14. Sinha RP, Klisch M, Groniger A, Hader DP. Mycosporine-like amino acids in the marine red alga Gracilaria cornea: Effects of UV and heat. Environ Exp Botany 2000;43:33-43.
15. Sommaruga R. The role of solar UV radiation in the ecology of alpine lakes. J Photochem Photobiol Biol 2001;62:35-42.
16. Callone AI, Carignan M, Montoya NG, Carreto JI. Biotransformation of mycosporine like amino acids (MAAs) in the toxic dinoflagellate Alexandrium tamarense. J Photochem Photobiol Biol 2006;84:204-12.
17. Groniger A, Sinha RP, Klisch M, Hader DP. Photoprotective compounds in cyanobacteria, phytoplankton and macroalgae: A database. J Photochem Photobiol Biol 2000;58:115-22.
18. Whitehead K, Vernet M. Influence of mycosporine-like amino acids (MAAs) on UV absorption by particulate and dissolved organic matter in La Jolla Bay. Limnol Oceanogr 2000;45:1788-96.
19. Klisch M, Hader DP. Mycosporine-like amino acids and marine toxins: The common and the different. Mar Drugs 2008;6:147-63.
20. Bjorn LO, Widell S, Wang T. Evolution of UV-B regulation and protection in plants. Adv Space Res 2002;30:1557-62.
21. Cardozo HM, Guaratini T, Barros MP, Falcao VR, Tonon AP, Lopes NP, *et al*. Metabolites from algae with economical impact. Comp Biochem Physiol 2007;146:60-78.
22. Jefferey SW, Tavish HS, Dunlap WC, Vesk M, Groenewoud K. Occurrence of UVA- and UVB-absorbing compounds in 152 species (206 strains) of marine microalgae. Marine Ecol Progr Series 1999;189:35-51.
23. Lao K, Glazer AN. Ultraviolet-B Photo-destruction of a light harvesting complex. Proc Natl Acad Sci USA 1996;93:5258-63.
24. Holzinger A, Lutz C. Algae and UV irradiation: Effects on ultrastructure and related metabolic functions. Micron 2006;37:190-207.

25. Davidson AT. The impact of UVB radiation on marine plankton. Mutat Res 1998;422:119-29.
26. Sinha RP, Hader DP. UV-protectants in cyanobacteria. Plant Sci 2008;174:278-89.
27. Sinha RP, Hader DP. Life under solar UV radiation in aquatic organisms. Adv Space Res 2002;30:1547-56.
28. Grant PT, Plack PA. Gadusol: A metabolite from fish eggs. Tetrahedron Lett 1980;21:4043-4.
29. Tartarotti B, Sommaruga R. Seasonal and ontogenetic changes of mycosporine-like amino acids in planktonic organisms from an alpine lake. Limnol Oceanogr 2006;51:1530-41.
30. Singh SP, Klisch M, Sinha RP, Hader DP. Genome mining of mycosporine-like amino acid (MAA) synthesizing and non-synthesizing cyanobacteria: A bioinformatics study. Genomics 2010;95:120-8.
31. Rastogi RP, Sinha RP. Biotechnological and industrial significance of cyanobacterial secondary metabolites. Biotechnol Adv 2009;27:521-39.
32. Oren A, Cimerman NG. Mycosporines and mycosporine-like amino acids: UV protectants or multipurpose secondary metabolites ? FEMS Microbiol Lett 2007;269:1-10.
33. Hoyer K, Karsten U, Sawall T, Wiencke C. Photoprotective substances in Antarctic macroalgae and their variation with respect to depth distribution, different tissues and developmental stages. Marine Ecol Progr Series 2001;211:117-29.
34. Bernillon J, Parussini E, Letoublon R, Bonvin JF, Arpin N. Flavin-mediated photolysis of mycosporines. Phytochemistry 1990;29:81-4.
35. Bhatia S, Sharma K, Namdeo AG, Chaugule BB, Kavale M, Nanda S. Broad-spectrum sun-protective action of Porphyra-334 derived from Porphyra vietnamensis. Pharmacog Res 2010;2:45-9.
36. Bandaranayake WM. Mycosporines: Are they nature's sunscreens? Nat Pro Rep 1998;15:159-72.
37. Schulz ME, Scherer S. UV protection in cyanobacteria. Eur J Phycol 1999;34:329-38.
38. Cockell CS, Knowland J. Ultraviolet radiation screening compounds. Biol Rev 1999;74:311-45.
39. Whitehead K, Hedges JI. Photodegradation and photosensitization of mycosporine-like amino acids. J Photochem Photobiol Biol 2005;80:115-21.
40. Dunlap WC, Yamamoto Y. Small-molecule antioxidants in marine organisms" antioxidant activity of mycosporine-glycine. Comp Biochem Physiol 1995;112:105-14.
41. Tao C, Sugawara T, Maeda S, Wang X, Hirata T. Antioxidative activities of a mycosporine-like amino acid, Porphyra-334. Fisheries Sci 2008;74:1166-72.
42. Singh SP, Hader DP, Sinha RP. Cyanobacteria and ultraviolet radiation (UVR) stress: Mitigation strategies. Ageing Res Rev 2009;9:79-90.
43. Shick JM, Walter CB, Chalker E, Banaszak AT, Osenzwei TK. Survey of ultraviolet radiation-absorbing mycosporine-like amino acids in organs of coral reef holothuroids. Mar Ecol Prog Ser 1992;90:139-48.
44. Quesadal A, Goff L, Karentz D. Effects of natural UV radiation on antarctic cyanobacterial mats. Proc NIPR Symp Polar Biol 1998;11:98-111.
45. Clintock JB, Karentz D. Mycosporine-like amino acids in 38 species of subtidal marine organisms from McMurdo Sound, Antarctica. Antarctic Sci 1997;9:392-498.
46. Xiong F, Kopecky J, Nedbal L. The occurrence of UV-B absorbing mycosporine-like amino acids in freshwater and terrestrial microalgae (Chlorophyta). Aquatic Botany 1999;63:37-49.
47. Makarov M. Influence of ultraviolet radiation on the growth of the dominant macro-algae of the Barents Sea. Chemosphere: Global Change Science 1999;1:146-7.
48. Sommaruga R, Whitehead K, Shick JM, Lobban CS. Mycosporine-like amino acids in the Zooxanthella-ciliate symbiosis Maristentor dinoferus. Protist 2006;157:185-91.
49. Dunlap WC, Williams DM, Chalker BE, Banaszak A. Biochemical photoadaptation in vision: UV-absorbing pigments in fish eye tissues. Comp Biochem Physiol 1989;93:601-7.
50. Torres A, Enk CD, Hochberg M, Srebnik M. Porphyra-334: A potential natural source for UV-A protective sunscreens. Photochem Photobiol Sci 2006;5:432-5.
51. Pickart L. The chemical sunscreen health disaster. Skin Biology, 4122 Factoria Boulevard - Suite 200, Bellevue, WA: 98006;2000.
52. Lowe NJ. An overview of ultraviolet radiation, sunscreens, and photo-induced dermatoses. Dermatol Clin 2006;24:9-17.
53. Whitehead K, Hedges JI. Analysis of mycosporine-like amino acids in plankton by liquid chromatography electrospray ionization mass spectrometry. Mar Chem 2002;80:27-39.

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