

# Chapter 4

## Photoprotective Compounds: Diversity, Biosynthetic Pathway and Genetic Regulation



Saumi Pandey and Vinod K. Kannaujiya

**Abstract** The rapid increment in atmospheric pollution causes loss of stratospheric ozone which enhances the exposure of harmful ultraviolet radiation (UV) on the earth's surface. The detrimental impact of UV-A and UV-B causes photodamage, alteration in normal physiological processes of aquatic and terrestrial organisms. However, certain inbuilt existence of photoprotective compounds makes organisms to counteract with harmful UV radiations. Most of the groups of organisms such as cyanobacteria, algae, lichens, fungi, bryophytes, higher plants, and certain animals have unique photoprotective strategies for survivability under harsh radiation. Various types of secondary metabolites such as mycosporine-like amino acids (MAAs), mycosporine, scytonemin, lycopodine, carotenoids, and melanin are inherently synthesized in most of the organisms for protection from deleterious ultraviolet radiation. In the last few decades, most of the genetic and metabolomics pathways for synthesis of photoprotective compounds have been well established. However, industrial-scale production is still undeveloped due to limited knowledge of gene expression and cost-effective rapid production in various group of organisms. This chapter briefly describes the presence of different photoprotective compounds in various taxa of organisms. This chapter also deals with the biosynthetic pathways and genetic regulation of certain compounds for production and commercial applications in various group of life sciences and cosmetic industries.

**Keywords** Cyanobacteria · Mycosporine-like amino acids · Pentose phosphate pathway · Photoprotection · Scytonemin · Shikimate pathway

---

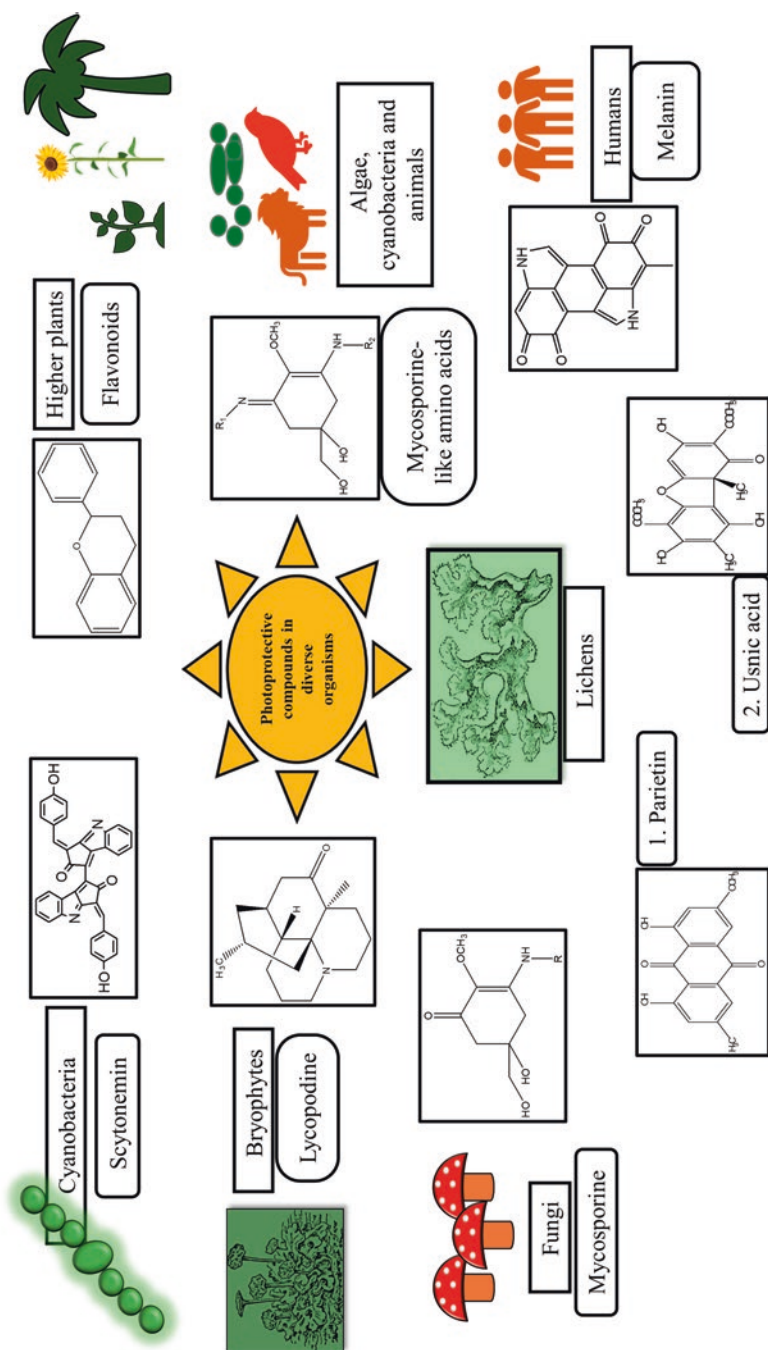
S. Pandey · V. K. Kannaujiya (✉)  
Department of Botany, MMV, Banaras Hindu University, Varanasi, India

© The Author(s), under exclusive license to Springer Nature Singapore Pte Ltd. 2023

V. K. Kannaujiya et al. (eds.), *Photoprotective Green Pharmacology: Challenges, Sources and Future Applications*,  
[https://doi.org/10.1007/978-981-99-0749-6\\_4](https://doi.org/10.1007/978-981-99-0749-6_4)

## 4.1 Introduction

The existence of different life forms on the earth's surface becomes possible due to obligate presence of solar energy. The solar spectrum mainly consists of photosynthetically active radiation (PAR) and ultraviolet radiation (UV). The UV (non-ionizing radiation) constitutes 8–9% of solar spectrum (Hollósy 2002). The visible range of solar spectrum drives the photosynthetic process whereas UV-A and UV-B cause several detrimental impacts on the survivability of organisms (Gao et al. 2007; Richa and Sinha 2013). The stratospheric ozone layer behaves as an umbrella to safeguard from biologically active harmful UV-B radiations coming from sun. Ozone harbors very high absorption coefficient but due to less amount (4  $\mu\text{m}$  thick layer) and thinning of ozone layer, UV-B radiation passes to the biosphere (Björn 2007). Scientific literature revealed that every 1% reduction in ozone thickness leads to the increment of UV-B radiation about 1.3–1.8% on the earth's surface (Hollósy 2002). The exposure of ultraviolet radiation significantly induces biochemical, physiological, and morphological changes in an organism which altered natural community and structure and function of ecosystem (Paul and Gwynn-Jones 2003; Wong et al. 2019). Moreover, UV-B radiation has directly affected nucleic acids (DNA and RNA) and induced formation of harmful DNA lesions such as cyclobutane pyrimidine dimer and 6–4 photoproducts (Singh et al. 2010a; Richa and Sinha 2013). In comparison to UV-B, UV-A has indirect effect which includes photosensitization of biological compounds and production of reactive oxygen species (Hargreaves et al. 2007). In addition, UV radiations (UV-A, UV-B) also affect cell differentiation, morphology, pigmentation, motility, phycobiliprotein composition, protein profile, nitrogen fixation and membrane lipid oxidation pathways (Lesser 2006, 2008; Gao et al. 2007). In humans, it causes skin inflammation, skin cancer, cutaneous photoaging and development of pigmentation disorder (Passeron et al. 2021). However, most of the microorganisms including plants, animals and humans have the ability to cope up with fluctuations occurring in the ambient environment (Hemm et al. 2001; Edreva 2005; Wong et al. 2019). They reside and adapt through the production of photoprotective compounds in adverse environmental conditions (Rastogi et al. 2010; Le Lann et al. 2016; Lalegerie et al. 2019). The number of photoprotective compounds is already described in certain group of organisms such as scytonemin, mycosporine-like amino acids, melanins, flavonoids and phenyl propanoids (Pallela et al. 2010; Kannaujiya et al. 2014) (Fig. 4.1). However, there are plenty of photoprotective compounds still to be discovered. The study of other stress factors besides UV radiation has not been well studied in correlation with production of photoprotective compounds (Sen and Mallick 2022). This chapter briefly describes the various kinds of photoprotective compounds found in various group of organisms. We also describe the various biosynthetic mechanisms and genetic regulation for synthesis of photoprotective compounds. In addition, this chapter also deals the current advancement in production technology of photoprotective compounds and commercial applications in biomedical and cosmetic industries.



**Fig. 4.1** Illustration of major photoprotective compounds found in different taxa with their molecular structures

## 4.2 Photoprotective Compounds and Their Role Against UV Radiation

### 4.2.1 *Mycosporine-Like Amino Acids*

Mycosporine-like amino acids (MAAs) belong to family of secondary metabolites, reported in many freshwater and marine organisms. They are water-soluble in nature with molecular weight >400 Da (Bhatia et al. 2011). They have absorption maxima from 310 to 360 nm, marked by the presence of cyclohexenimine or cyclohexenone chromophores (Häder et al. 2007; Bhatia et al. 2011; La Barre et al. 2014). They have been known for absorbing lethal UV radiations, act as cellular antioxidant and osmoprotectant in nature (Oren and Gunde-Cimerman 2007; La Barre et al. 2014). Corals predominantly exist in euphotic zone with endosymbiotic algal partners—*Symbiodinium* sp., zooxanthellae (Torregiani and Lesser 2007). Corals have sensitive MAAs which are inversely proportional to depth and also vary with season (Zeevi Ben-Yosef et al. 2006; Torregiani and Lesser 2007). Literature survey reveals that *Anabaena* sp. has produced a single kind of MAAs—shinorine ( $\lambda_{\max} = 334$  nm, Retention time (RT) = 2.3 min) (Sinha et al. 2007); however, other species of *Anabaena*, *Anabaena doliolum* possess different kinds of MAAs such as shinorine, porphyrin-334 ( $\lambda_{\max} = 334$  nm, RT = 3.5 min) and mycosporine-glycine ( $\lambda_{\max} = 310$  nm, RT = 4.1 min) (Singh et al. 2008a). Sunscreen factor was found to be 0.3 for MAAs in single cells (Garcia-Pichel et al. 1993). In the cyanobacterium *A. variabilis* PCC 7937, the biosynthesis of shinorine was recently discovered and also found that biosynthesis of shinorine not only depends on UV radiation but also on ammonium concentration, temperature and salt (Singh et al. 2008b, 2010b).

### 4.2.2 *Usnic Acid and Parietin*

Lichens thrive in sun-exposed habitats especially Arctic, alpine, arid and warm deserts (Gauslaa and Solhaug 2004). The bright and non-melanic lichens residing in open habitats produce photoprotective compounds, namely, usnic acid, parietin or atranorin (Solhaug and Gauslaa 2004). Lichens screen out harmful UV radiations by the process of absorption through melanin and parietin and reflectance mechanism through atranorin (Solhaug and Gauslaa 2012). However, usnic acid is commonly found in fungal Lecanorales order whereas parietin in Teloschistales order (Solhaug et al. 2003; Gauslaa and Solhaug 2004). Usnic acid is a dibenzofuran derived biologically active lipophilic based, yellow coloured compound which exhibits pronounced absorption in UV radiation (Huneck and Yoshimura 1996; Luzina and Salakhutdinov 2018). It is also well demarcated that usnic acid synthesis depends upon environmental habitats. The level of solar radiation and usnic acid content can be positively correlated (Bjerke et al. 2002). Sun-exposed lichens has more amount of usnic acid than shade habitats (Bjerke and Dahl 2002). Interestingly,

an enrichment of UV radiation in solar radiation is the primary cause of copious amount of usnic acid production in lichens (Bjerke and Dahl 2002). In addition, UV-B exposure of thalli of *Xanthoparmelia microspora* led to increase in usnic acid content from 1.9% to 4.16% (w/w) (Fernández et al. 2006). Recently, usnic acid has been compared with sunscreens available in the market along with some other chemical compounds such as Nivea sun spray LS 5 and 4-tert-butyl-4'-methoxy dibenzoylmethane (BM-DBM) (Rancan et al. 2002). The above results indicate that usnic acid can be used as ingredient for development of better UV filter as compared to Nivea sun spray LS-5 and BM-DBM (Rancan et al. 2002).

Parietin is an orange anthraquinone photoprotective compound (McEvoy et al. 2006). In literature, it is also mentioned that parietin functions as blue light screen filter rather than UV-B screen filter (Gauslaa and Ustvedt 2003). The parietin content is governed by habitat of lichens ranging from pale (closed forest) to orange colour (sea cliffs) (Solhaug and Gauslaa 2012). Interestingly, it was found that parietin content becomes double in mid-summer condition as compared in winter season (Gauslaa and McEvoy 2005). A study further confirms that parietin content in *Xanthoria parietina* was significantly higher in combined exposure of UV-A radiation and visible light than visible light alone (Solhaug et al. 2003).

### 4.2.3 *Lycopodine*

In *Lycopodium* (club moss), the various kinds of UV-absorbing compounds are present. The known compounds are lycopodine (alkaloid), flavonoids-luteonin and chrysoeriol. A lycopodine is a quinolizidine alkaloid and derivative of lycopodane hydrate. The confinement of flavonoids in reproductive parts like spores led to provide protection from UVR (Rozema et al. 2002). However, detailed study on lycopodine correlation with UV stress is not well explored.

### 4.2.4 *Melanin*

The skin colour of humans is governed by an amalgamation of oxyhemoglobin or deoxyhemoglobin, carotenoids and melanin. The types of melanin and its distribution in melanosomes plays an important role in skin pigmentation (Brenner and Hearing 2008). However, epidemiological data supported that skin colour and skin cancer are inversely correlated (Gilchrest et al. 1999). White skin has 70% more tendency to develop skin cancer than black skin (Halder and Bang 1988). The melanin provides shielding effect from ultraviolet radiation mainly eumelanin by two ways: firstly by scattering the UVR and secondly by acting as absorbent filter (Kaidbey et al. 1979; Brenner and Hearing 2008). In the skin melanin composition, eumelanin is better UV protectant than pheomelanin. The melanosomes of darker skin colour are very resistant to lysosomal enzymes and persist in epidermal layers

in the form of supranuclear caps in melanocytes and keratinocytes that help in protection from UV-induced damage whereas fair skin melanocytes degraded after exposure and existed in the form of melanin dust (Kobayashi et al. 1998). The degradation of melanocytes becomes causative factor for skin cancer (Bustamante et al. 1993).

#### **4.2.5 Phenylpropanoids**

Plants being sessile in nature respond to abiotic changes by modulating their cellular chemistry or physiology (Escobar-Bravo et al. 2017). Plants have specific UV-B photoreceptor-UVR8 (UV-resistant locus) (Rizzini et al. 2011) which regulates photomorphogenic responses as well as modulates expression of genes associated with DNA repair, inhibition of hypocotyl elongation, antioxidative defence and phenolic compounds production (Escobar-Bravo et al. 2017). In order to cut off harmful effect of UV radiations, plants accumulate phenylpropanoids and flavonoids in leaf epidermis as well as spongy and palisade mesophyll tissue (Agati et al. 2013). Phenylpropanoids belong to large class of secondary metabolites synthesized from aromatic amino acids such as tyrosine and phenylalanine in plants. These are produced through sequential enzymatic biosynthetic pathway (Deng and Lu 2017). The phenylpropanoid has been classified into five categories: (1) Monolignols, (2) Flavonoids, (3) Coumarins, (4) Stilbenes and (5) Phenolic acids. However, most common occurrence in plants are monolignols, flavonoids and phenolic acids (Noel et al. 2005; Liu et al. 2015). Coumarins are restricted to families Asteraceae, Apiaceae, Nyctaginaceae, Oleaceae, Fabaceae, Caprifoliaceae, Guttiferae, Rutaceae and Moraceae (Venugopala et al. 2013; Deng and Lu 2017). Stilbenes are confined to Myrtaceae, Polygonaceae, Poaceae, Vitaceae, and Gnetaceae (Kiselev et al. 2016). Phenylpropanoid biosynthetic enzymes are encoded by gene superfamilies such as NADPH-dependent reductase family, 2-oxoglutarate-dependent dioxygenase (2-ODD), type III polyketide synthase (PKS III), P450 gene family (Turnbull et al. 2004; Tohge et al. 2013; Deng and Lu 2017).

#### **4.2.6 Flavonoids**

Flavonoids have played an evolutionary role for establishment of plants from aquatic to land habitat (Frohnmeier and Staiger 2003). Flavonoids are secondary metabolites, low molecular weight compounds and classified into different subclasses such as flavanones, flavones, flavonols, proanthocyanidins, anthocyanins, phlobaphenes and isoflavonoids (Liu et al. 2015). They are present in nucleus, cell vacuoles and chloroplast of mesophyll cells (Agati et al. 2013) and have an important biological function such as providing aroma and colour to flowers to attract pollinators for seed dispersion and germination, development and growth of seedlings.

Ultraviolet radiations have shown detrimental effect on plant growth, DNA content, protein and lipids (Deng and Lu 2017). Plants have well-defined photoproducts to counterfeit harmful effects of UV radiations namely flavonoids including flavones, anthocyanin, flavonol glycosides and phenylpropanoids such as coumarins, stilbenes, sinapate esters. These compounds act as ROS attenuator to inhibit deleterious effects of radiation (Heijde and Ulm 2012; Vidović et al. 2015). Thus, they act as strong UV-filter (Samanta et al. 2011). In addition, these compounds also protect plants from nutrient deficiency (low iron/nitrogen/phosphate), pathogen infection, herbivore attack, drought and low temperature (Simmonds 2003; Treutter 2005).

### 4.2.7 *Scytonemin*

Scytonemin is a natural compound present in cyanobacteria and has played an indispensable role in photoprotection from UV radiations since the origin of life (Rastogi and Sinha 2009). It is synthesized in extremophilic cyanobacteria of different groups (Garcia-Pichel and Castenholz 1991). It is small, hydrophobic, lipid-soluble yellow-brown to mahogany or dark red pigment molecules produced in extracellular sheath of approximately 300 species of cyanobacteria (Sinha and Häder 2008; Rastogi and Sinha 2009). The maximum UV absorption spectra of purified scytonemin is found at  $386 \pm 2$  nm (Rastogi et al. 2013). Scytonemin is a dimer of phenolic and indolic subunits with molecular weight of 544 Da. (Rastogi et al. 2010). Scytonemin acts as natural sunscreen found in cyanobacteria (Proteau et al. 1993; Rastogi et al. 2010). Scytonemin also acts as a natural ROS scavenger (Takamatsu et al. 2003; Matsui et al. 2012). Moreover, scytonemin has also reduced thymine dimer formation and ROS generation in *Rivularia* sp. HKAR-4 under UV stress condition (Rastogi et al. 2015).

## 4.3 Biosynthetic Pathway

### 4.3.1 *Shikimate Pathway*

In the total UV radiation, mainly UV-B plays a keen role in the induction of biosynthetic pathways in photosynthetic species (Bhatia et al. 2011). MAAs biosynthesis occurs in most of prokaryotes including bacteria, blue-green algae (cyanobacteria), macroalgae and phytoplankton but not synthesized in animals due to absence of shikimate pathway (Fig. 4.2). In animal system, MAAs are transferred through diet, bacterial or symbiotic associations (Sinha et al. 2007; Bhatia et al. 2011). It was believed that MAAs biosynthesis occurred via first part of shikimate pathway but still strong proofs needed for validation (Sinha et al. 2007; Sinha and Häder 2008). The precursor molecule 3-dehydroquinate synthesizes fungal mycosporines and MAAs synthesized through gadusols (Bandaranayake 1998; Shick and Dunlap 2002).

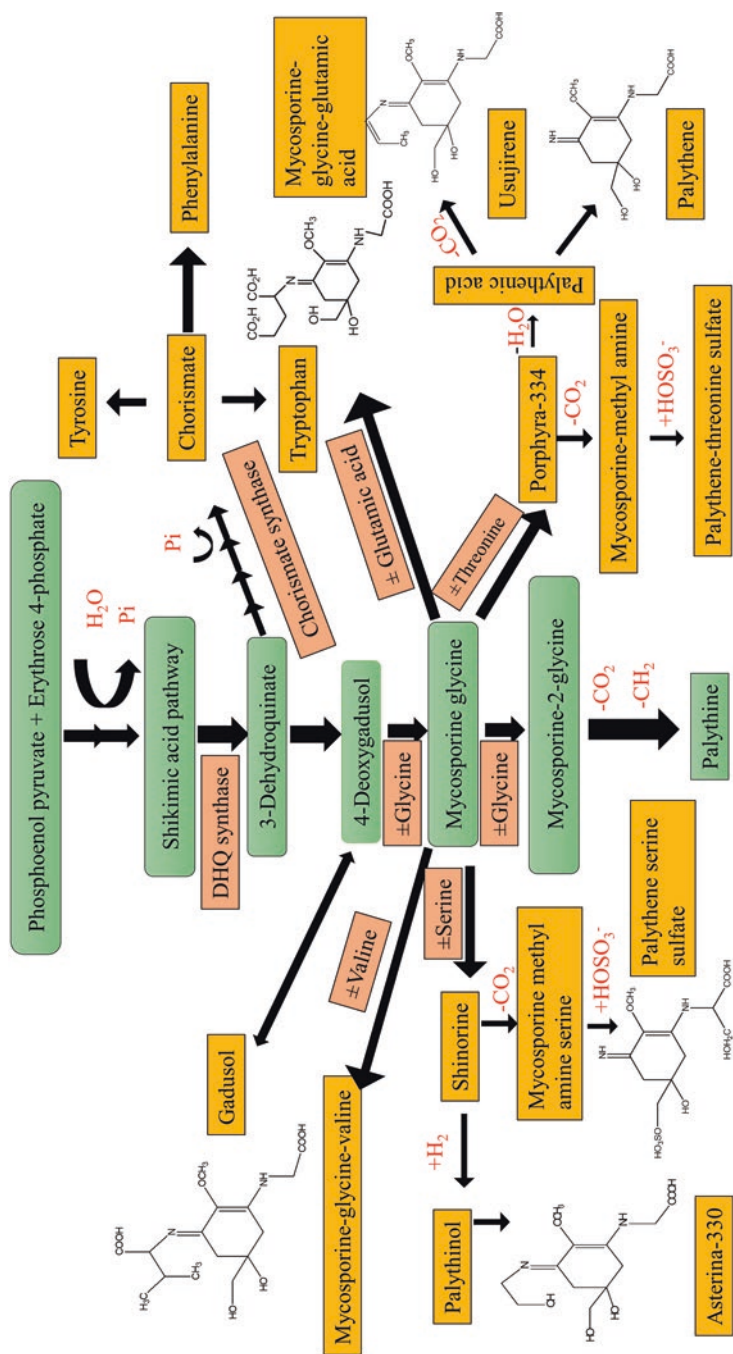


Fig. 4.2 Biosynthesis of different MAAs via shikimate pathway



### 4.3.2 *Pentose Phosphate Pathway*

Biosynthesis of MAAs is also carried out through pentose phosphate pathway. The core structure of MAAs is 4-deoxygadusol which is formed through intermediate sedoheptulose-7-phosphate by the enzymes O-methyltransferase (OMT) and 2-epi-5-epivaliolone synthase (EVS) in cyanobacteria (Pope et al. 2015; Jain et al. 2017). In literature survey, it was reported that deletion of EVS gene in *A. variabilis* ATCC 29413 has very little effect on MAAs biosynthesis which indicates pentose phosphate pathway is not sole pathway for biosynthesis (Jain et al. 2017). The genome mining also reveals EVS enzyme to be crucial for the synthesis of MAAs (Spence et al. 2012). A contradictory observation in relation to MAAs biosynthesis was elucidated in *Synechocystis* sp. PCC6803 in the absence of EVS enzyme; it synthesizes three novel mycosporine-like amino acids- M-tau, M-343 and dehydroxylusujirene (Spence et al. 2012; Zhang et al. 2007).

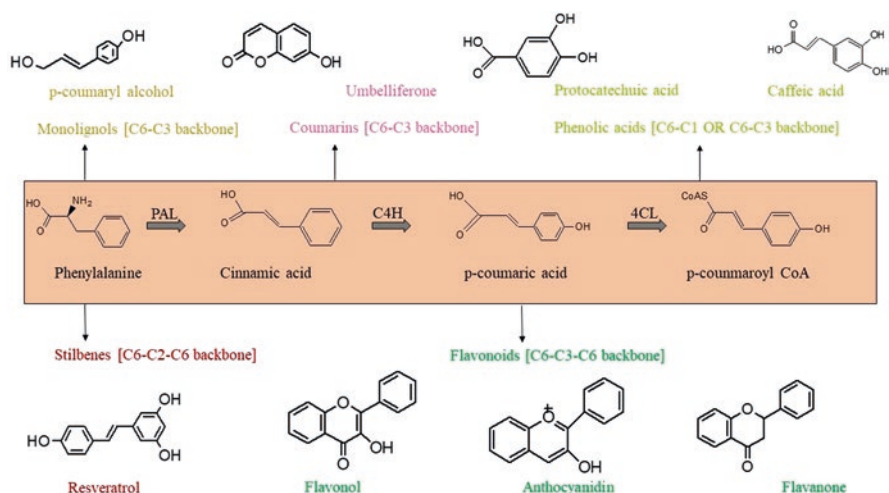
### 4.3.3 *Phenylpropanoid Pathway*

The pathway starts from phenylalanine precursor molecule to synthesize products through shikimate pathway. However, certain organisms of fungi, bacteria and monocots are used as tyrosine precursor to start the biosynthetic pathway (Deng and Lu 2017). The pathway starts from deamination of phenylalanine by PAL for conversion into cinnamic acid. The second enzymatic step involves hydroxylation of cinnamic acid to p-coumaric acid via C4H enzyme. In certain bacterial, monocots and fungal species, TAL—tyrosine ammonia lyase or PTAL—bifunctional ammonia lyase bypass the second enzymatic step; hence, tyrosine directly converts into p-coumaric acid (Watts et al. 2004). It is well documented that some enzymes of this pathway are UV light-inducible particularly phenylalanine ammonia lyase (PAL), chalcone reductase (CHR), cinnamic acid 4-hydroxylase (C4H), and flavanone 3-hydroxylase (F3H) (Meyer et al. 2021). The pathway is diagrammatically represented in Fig. 4.3.

## 4.4 Genetic Regulation

### 4.4.1 *Scytonemin*

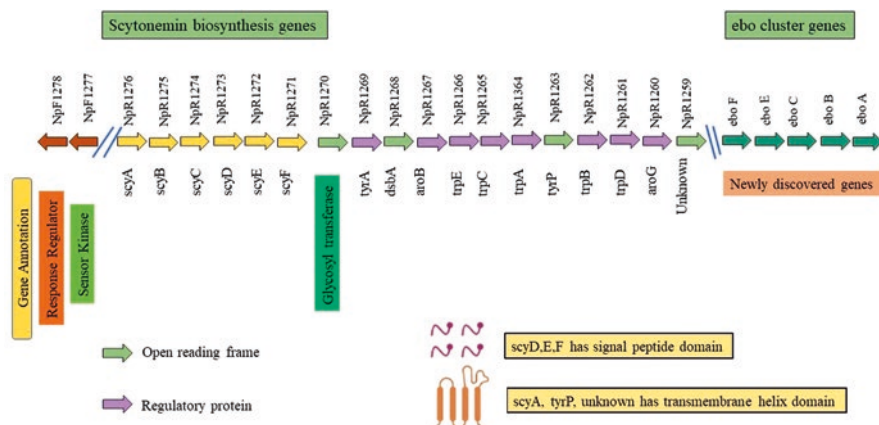
Biosynthesis of scytonemin at genetic level has been well studied in cyanobacterium *N. punctiforme* ATCC 29133 through random transposon insertion mutagenesis (Soule et al. 2007). In the genome of *N. punctiforme* ATCC 29133, an 18-gene cluster (Npun\_R1276 to Npun\_R1259) was found linked with the scytonemin biosynthesis (Pathak et al. 2019). Moreover, it was also found that tyrosine and



**Fig. 4.3** General phenylpropanoid pathway found in plants. PAL phenylalanine ammonia lyase, C4H cinnamic acid 4-hydroxylase, 4-CL 4-coumaroyl CoA ligase

tryptophan play as precursor molecules for synthesis of molecular structure of scytonemin (Proteau et al. 1993; Pathak et al. 2019). Certain identified gene clusters also play important role in encoding proteins for shikimic acid pathway such as tryptophan (TrpA, TrpB, TrpC, TrpD and TrpE) and tyrosine (TyrP) biosynthesis (Soule et al. 2007, 2009). Genomic analysis further validates the presence of additional copy of genes encoding for AroG, AroB, TrpA, TrpB, TrpC, TrpD and TyrP proteins present at another place in the genome of *Nostoc punctiforme* (Pathak et al. 2019). Scytonemin biosynthetic genes are also present in other cyanobacteria *Nodularia* sp. CCY 9414, *Chlorogloeopsis* sp. CCME5 5094, *Anabaena* sp. PCC 7120 and *Lyngbya* sp. PCC 8106 (Pathak et al. 2019, 2020). Interestingly, heterologous expression in *E. coli* of three *N. punctiforme* genes, particularly *scyABC*, culminated into scytonemin monomer moiety upon supplementation of 1 mM of tyrosine and tryptophan (Malla and Sommer 2014). The above experiment elucidates ScyA, ScyB, and ScyC genes are solely responsible for scytonemin biosynthesis (Malla and Sommer 2014; Pathak et al. 2019). The comparative genomic analysis reveals that cyanobacterium *Nostoc punctiforme* ATCC 29133 has two-component regulatory system of proteins Npun\_F1278 and Npun\_F1277 upregulated in response to UV-A radiation (Naurin et al. 2016; Janssen and Soule 2016).

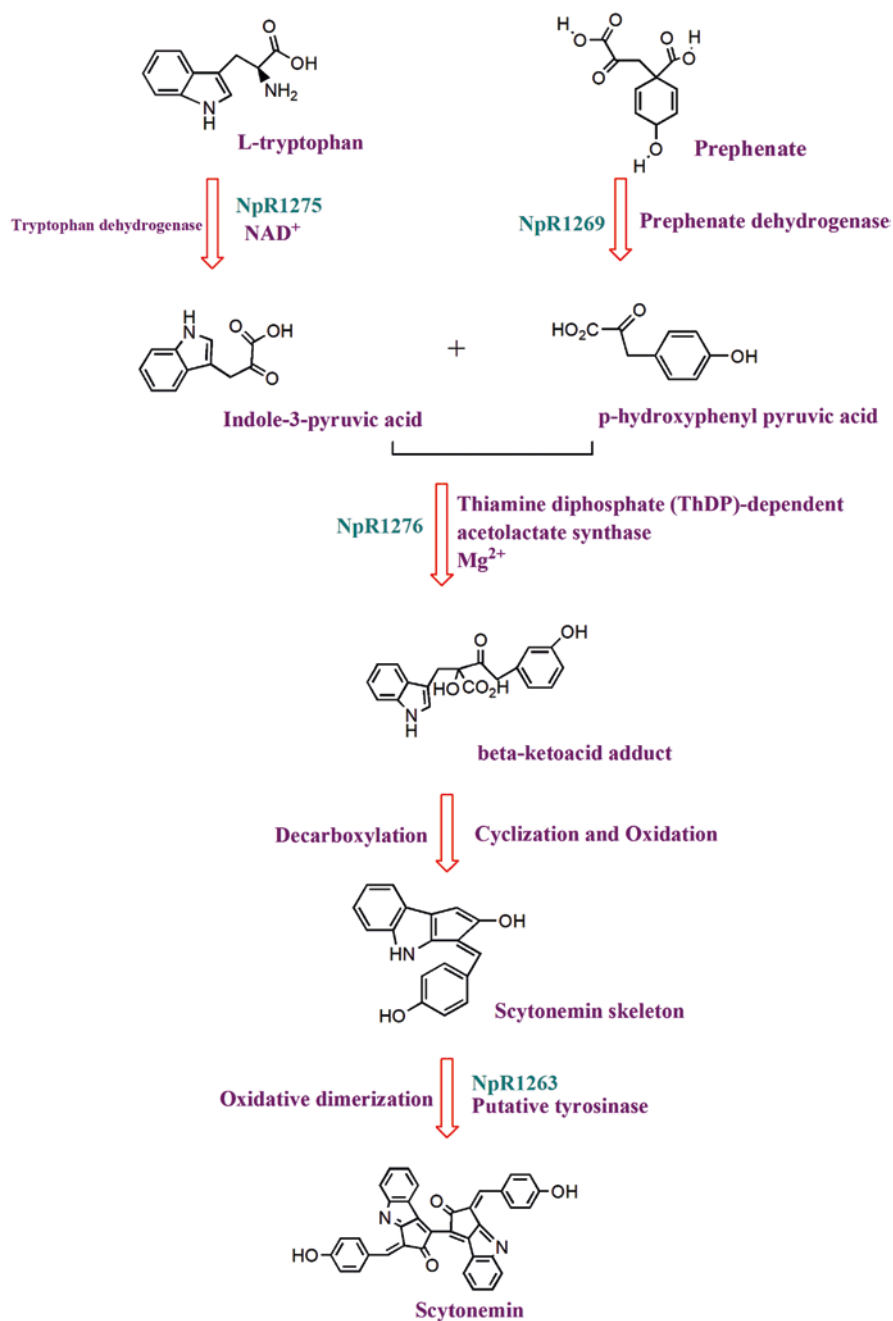
Scytonemin operon consists of five-gene cluster called as 'ebo' cluster, discovered through comparative genomic analysis widely conserved in algal and bacterial phyla (Pathak et al. 2019). The function of ebo cluster was validated through in-frame deletion method and their analysis proves 'ebo' cluster is responsible for scytonemin biosynthesis under UV-A exposure conditions (Klicki et al. 2018). Figures 4.4 and 4.5 depict scytonemin biosynthesis genes with annotations and scytonemin biosynthetic pathway, respectively.



**Fig. 4.4** Structure of gene cluster associated with scytonemin biosynthesis in *Nostoc punctiforme* ATCC 29133

#### 4.4.2 Mycosporine-Like Amino Acids

Cyanobacterial ancestors are served as starting point for MAAs biosynthetic enzymatic machinery. These are widespread among all taxa due to evolutionary endosymbiotic events and lateral gene transfer mechanism (Singh et al. 2012; Richa and Sinha 2013). Multiple studies have been performed which proves that MAAs biosynthesis occurs through the shikimic acid pathway (Pathak et al. 2019). It was found that *A. variabilis* PCC7937 has two gene locus YP\_324357 and YP\_324358 to carry biosynthesis of deoxygadusol for development of central core of mycosporine-like amino acids (Richa and Sinha 2013). The MAAs biosynthesis gets downregulated by exogenous supply of aromatic amino acids tyrosine at a concentration of 5 mM (Portwich and Garcia-Pichel 2003; Spence et al. 2012; Pathak et al. 2019). The cluster of four genes from *ava\_3855* to *ava\_3858* is responsible for the formation of shinorine in *Anabaena variabilis* ATCC 29413 (Singh et al. 2010b; Balskus and Walsh 2010). The shikimate and pentose phosphate pathways are completely linked for MAAs biosynthesis (Jain et al. 2017). The proteomic data clarifies shikimate pathway is predominant in UV-induced MAAs biosynthesis (Pope et al. 2015; Jain et al. 2017). The *ava\_3856* gene expression in *Anabaena variabilis* confirmed the conversion of 6-deoxygadusol and glycine into mycosporine-glycine in the presence of  $Mg^{2+}$  cofactors and ATP (Balskus and Walsh 2010). MAAs biosynthesis involves Npr5598-5600 homologous genes in both cyanobacterium *Nostoc punctiforme* ATCC 29133 and *A. variabilis* (Katoch et al. 2016). The interlinked convergent pathway for the synthesis of MAAs is shown in Fig. 4.6.



**Fig. 4.5** Biosynthetic pathway of scytonemin biosynthesis in *Nostoc punctiforme* ATCC 29133

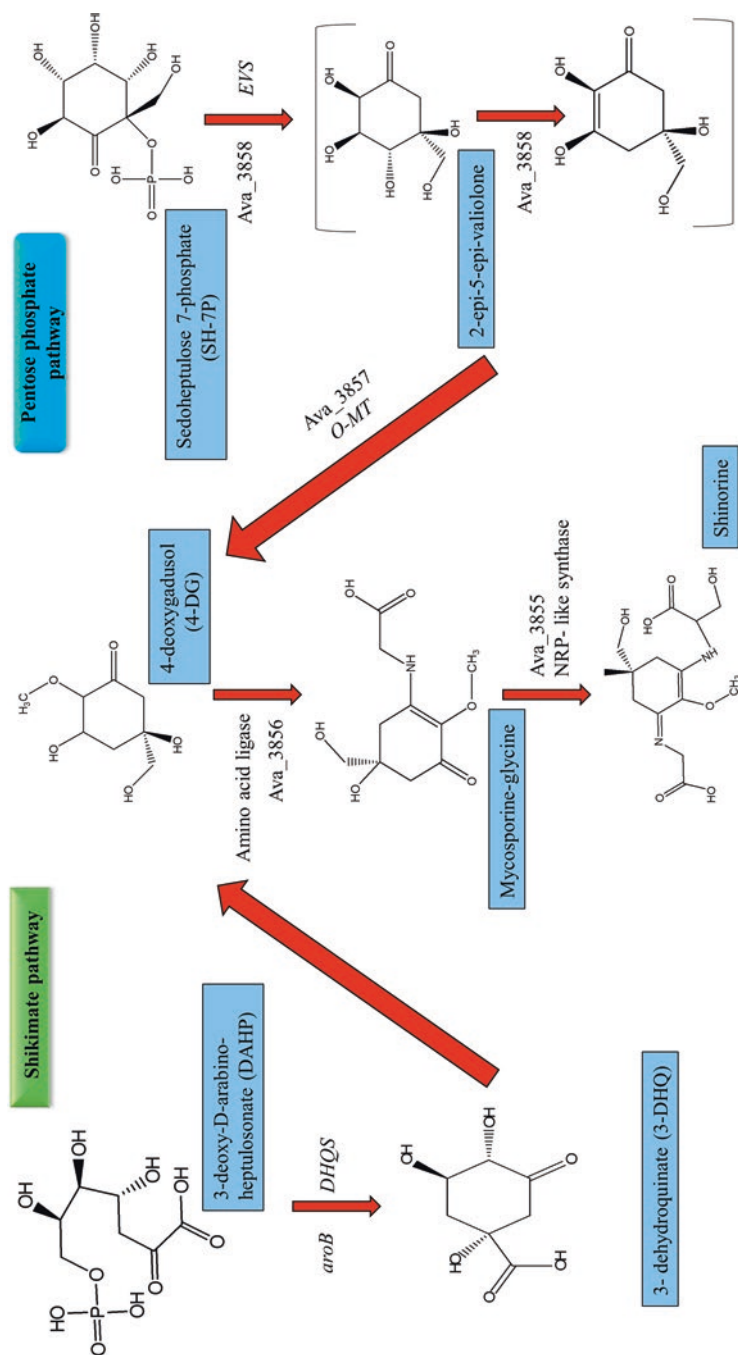


Fig. 4.6 Biosynthetic pathways involved in the synthesis of MAAs in cyanobacteria

## 4.5 Concluding Remarks

The organisms belonging to different taxa have unique kinds of photoprotective compounds. These photoprotective compounds have played an indispensable role in evolutionary context as well as for survival. Nowadays, extensive research work has been carried out in all species for the screening of valuable and stable photoprotective compounds to safeguard humans from the lethal effects of UV radiation. To complete studies on UV screening compounds, that is, genetic regulation and metabolomics, there is a current need for wide exploration of compounds diversity and the development of cost-effective strategies for commercial production and therapeutic applications for human welfare.

**Acknowledgements** Vinod K. Kannaujiya acknowledges IoE-Seed Grant, BHU, Varanasi (Scheme No. 6031) and Core Research Grant, DST-SERB, New Delhi (CRG/2020/001323) for financial support. Saumi is thankful to UGC and BHU for providing a research fellowship.

## References

- Agati G, Brunetti C, Di Ferdinando M, Ferrini F, Pollastri S, Tattini M (2013) Functional roles of flavonoids in photoprotection: new evidence, lessons from the past. *Plant Physiol Biochem* 72:35–45
- Balskus EP, Walsh CT (2010) The genetic and molecular basis for sunscreen biosynthesis in cyanobacteria. *Science* 329(5999):1653–1656
- Bandaranayake W (1998) Mycosporines: are they nature's sunscreens? *Nat Prod Rep* 15(2):159–172
- Bhatia S, Garg A, Sharma K, Kumar S, Sharma A, Purohit AP (2011) Mycosporine and mycosporine-like amino acids: a paramount tool against ultra violet irradiation. *Pharmacogn Rev* 5(10):138
- Bjerke JW, Dahl T (2002) Distribution patterns of usnic acid-producing lichens along local radiation gradients in West Greenland. *Nova Hedwigia* 75:487–506
- Bjerke JW, Lerfall K, Elvebakk A (2002) Effects of ultraviolet radiation and PAR on the content of usnic and divaricatic acids in two arctic-alpine lichens. *Photochem Photobiol Sci* 1(9):678–685
- Björn LO (2007) Stratospheric ozone, ultraviolet radiation, and cryptogams. *Biol Conserv* 135(3):326–333
- Brenner M, Hearing VJ (2008) The protective role of melanin against UV damage in human skin. *Photochem Photobiol* 84(3):539–549
- Bustamante J, Bredeston L, Malanga G, Mordoh J (1993) Role of melanin as a scavenger of active oxygen species. *Pigment Cell Res* 6(5):348–353
- Deng Y, Lu S (2017) Biosynthesis and regulation of phenylpropanoids in plants. *Crit Rev Plant Sci* 36(4):257–290
- Edreva A (2005) The importance of non-photosynthetic pigments and cinnamic acid derivatives in photoprotection. *Agric Ecosyst Environ* 106(2–3):135–146
- Escobar-Bravo R, Klinkhamer PG, Leiss KA (2017) Interactive effects of UV-B light with abiotic factors on plant growth and chemistry, and their consequences for defense against arthropod herbivores. *Front Plant Sci* 8:278
- Fernández E, Quilhot W, Rubio C, Hidalgo ME, Diaz R, Ojeda J (2006) Effects of UV radiation on usnic acid in *Xanthoparmelia microspora* (Müll. Arg. Hale). *Photochem Photobiol* 82(4):1065–1068

- Frohnmeier H, Staiger D (2003) Ultraviolet-B radiation-mediated responses in plants. Balancing damage and protection. *Plant Physiol* 133(4):1420–1428
- Gao K, Yu H, Brown MT (2007) Solar PAR and UV radiation affects the physiology and morphology of the cyanobacterium *Anabaena* sp. PCC 7120. *J Photochem Photobiol B Biol* 89(2–3):117–124
- García-Pichel F, Castenholz RW (1991) Characterization and biological implications of scytonemin, a cyanobacterial sheath pigment 1. *J Phycol* 27(3):395–409
- García-Pichel F, Wingard CE, Castenholz RW (1993) Evidence regarding the UV sunscreen role of a mycosporine-like compound in the cyanobacterium *Gloeocapsa* sp. *Appl Environ Microbiol* 59(1):170–176
- Gauslaa Y, McEvoy M (2005) Seasonal changes in solar radiation drive acclimation of the sun-screening compound parietin in the lichen *Xanthoria parietina*. *Basic Appl Ecol* 6(1):75–82
- Gauslaa Y, Solhaug KA (2004) Photoinhibition in lichens depends on cortical characteristics and hydration. *Lichenologist* 36(2):133–143
- Gauslaa Y, Ustvedt EM (2003) Is parietin a UV-B or a blue-light screening pigment in the lichen *Xanthoria parietina*? *Photochem Photobiol Sci* 2(4):424–432
- Geraldes V, Pinto E (2021) Mycosporine-like amino acids (MAAs): biology, chemistry and identification features. *Pharmaceuticals* 14(1):63
- Gilchrist BA, Eller MS, Geller AC, Yaar M (1999) The pathogenesis of melanoma induced by ultraviolet radiation. *N Engl J Med* 340(17):1341–1348
- Häder DP, Kumar HD, Smith RC, Worrest RC (2007) Effects of solar UV radiation on aquatic ecosystems and interactions with climate change. *Photochem Photobiol Sci* 6(3):267–285
- Halder RM, Bang KM (1988) Skin cancer in blacks in the United States. *Dermatol Clin* 6(3):397–405
- Hargreaves A, Taiwo FA, Duggan O, Kirk SH, Ahmad SI (2007) Near-ultraviolet photolysis of  $\beta$ -phenylpyruvic acid generates free radicals and results in DNA damage. *J Photochem Photobiol B Biol* 89(2–3):110–116
- Heijde M, Ulm R (2012) UV-B photoreceptor-mediated signalling in plants. *Trends Plant Sci* 17(4):230–237
- Hemm MR, Herrmann KM, Chapple C (2001) AtMYB4: a transcription factor general in the battle against UV. *Trends Plant Sci* 6(4):135–136
- Hollósy F (2002) Effects of ultraviolet radiation on plant cells. *Micron* 33(2):179–197
- Huneck S, Yoshimura I (1996) Identification of lichen substances. In: Identification of lichen substances. Springer, Berlin, pp 11–123
- Jain S, Prajapat G, Abrar M, Ledwani L, Singh A, Agrawal A (2017) Cyanobacteria as efficient producers of mycosporine-like amino acids. *J Basic Microbiol* 57(9):715–727
- Janssen J, Soule T (2016) Gene expression of a two-component regulatory system associated with sunscreen biosynthesis in the cyanobacterium *Nostoc punctiforme* ATCC 29133. *FEMS Microbiol Lett* 363(2):fnv235
- Kaidbey KH, Agin PP, Sayre RM, Kligman AM (1979) Photoprotection by melanin—a comparison of black and Caucasian skin. *J Am Acad Dermatol* 1(3):249–260
- Katoch M, Mazmouz R, Chau R, Pearson LA, Pickford R, Neilan BA (2016) Heterologous production of cyanobacterial mycosporine-like amino acids mycosporine-ornithine and mycosporine-lysine in *Escherichia coli*. *Appl Environ Microbiol* 82(20):6167–6173
- Kannaujiya VK, Richa and Sinha RP (2014) Peroxide scavenging potential of ultraviolet-B-absorbing mycosporine-like amino acids isolated from a marine red alga *Bryocladia* sp. *Front Environ Sci* 2: 26
- Kiselev KV, Grigorovich VP, Ogneva ZV, Suprun AR, Dubrovina AS (2016) Stilbene biosynthesis in the needles of spruce *Picea jezoensis*. *Phytochemistry* 131:57–67
- Klicki K, Ferreira D, Hamill D, Dirks B, Mitchell N, Garcia-Pichel F (2018) The widely conserved ebo cluster is involved in precursor transport to the periplasm during scytonemin synthesis in *Nostoc punctiforme*. *MBio* 9(6):e02266–e02218

- Kobayashi N, Nakagawa A, Muramatsu T, Yamashina Y, Shirai T, Hashimoto MW, Ishigaki Y, Ohnishi T, Mori T (1998) Supranuclear melanin caps reduce ultraviolet induced DNA photo-products in human epidermis. *J Invest Dermatol* 110(5):806–810
- La Barre S, Roullier C, Boustie J (2014) Mycosporine-like amino acids (MAAs) in biological photosystems. In: Outstanding marine molecules, pp 333–360
- Lalegerie F, Lajili S, Bedoux G, Taupin L, Stiger-Pouvreau V, Connan S (2019) Photo-protective compounds in red macroalgae from Brittany: considerable diversity in mycosporine-like amino acids (MAAs). *Mar Environ Res* 147:37–48
- Le Lann K, Surget G, Couteau C, Coiffard L, Cérantola S, Gaillard F, Larnicol M, Zubia M, Guérand F, Poupart N, Stiger-Pouvreau V (2016) Sunscreen, antioxidant, and bactericide capacities of phlorotannins from the brown macroalga *Halidrys siliquosa*. *J Appl Phycol* 28(6):3547–3559
- Lesser MP (2006) Oxidative stress in marine environments: biochemistry and physiological ecology. *Annu Rev Physiol* 68:253–278
- Lesser MP (2008) Effects of ultraviolet radiation on productivity and nitrogen fixation in the cyanobacterium, *Anabaena* sp. (Newton's strain). *Hydrobiologia* 598(1):1–9
- Liu J, Osbourn A, Ma P (2015) MYB transcription factors as regulators of phenylpropanoid metabolism in plants. *Mol Plant* 8(5):689–708
- Luzina OA, Salakhutdinov NF (2018) Usnic acid and its derivatives for pharmaceutical use: A patent review (2000–2017). *Expert Opinion on Therapeutic Patents*, 28(6):477–491
- Malla S, Sommer MO (2014) A sustainable route to produce the scytonemin precursor using *Escherichia coli*. *Green Chem* 16(6):3255–3265
- Matsui K, Nazifi E, Hirai Y, Wada N, Matsugo S, Sakamoto T (2012) The cyanobacterial UV-absorbing pigment scytonemin displays radical-scavenging activity. *J Gen Appl Microbiol* 58(2):137–144
- McEvoy M, Nybakken L, Solhaug KA, Gauslaa Y (2006) UV triggers the synthesis of the widely distributed secondary lichen compound usnic acid. *Mycol Prog* 5(4):221–229
- Meyer P, Van de Poel B, De Coninck B (2021) UV-B light and its application potential to reduce disease and pest incidence in crops. *Hortic Res* 8(1):194
- Naurin S, Bennett J, Videau P, Philmus B, Soule T (2016) The response regulator Npun\_F1278 is essential for scytonemin biosynthesis in the cyanobacterium *Nostoc punctiforme* ATCC 29133. *J Phycol* 52(4):564–571
- Noel JP, Austin MB, Bomati EK (2005) Structure–function relationships in plant phenylpropanoid biosynthesis. *Curr Opin Plant Biol* 8(3):249–253
- Oren A, Gunde-Cimerman N (2007) Mycosporines and mycosporine-like amino acids: UV protectants or multipurpose secondary metabolites? *FEMS Microbiol Lett* 269(1):1–10
- Pallela R, Na-Young Y, Kim SK (2010) Anti-photoaging and photoprotective compounds derived from marine organisms. *Mar Drugs* 8(4):1189–1202
- Passeron T, Lim HW, Goh CL, Kang HY, Ly F, Morita A et al (2021) Photoprotection according to skin phototype and dermatoses: practical recommendations from an expert panel. *J Eur Acad Dermatol Venereol* 35(7):1460–1469
- Pathak J, Ahmed H, Singh SP, Häder DP, Sinha RP (2019) Genetic regulation of scytonemin and mycosporine-like amino acids (MAAs) biosynthesis in cyanobacteria. *Plant Gene* 17:100172
- Pathak J, Pandey A, Maurya PK, Rajneesh R, Sinha RP, Singh SP (2020) Cyanobacterial secondary metabolite scytonemin: a potential photoprotective and pharmaceutical compound. *Proc Natl Acad Sci India Sect B Biol Sci* 90(3):467–481
- Paul ND, Gwynn-Jones D (2003) Ecological roles of solar UV radiation: towards an integrated approach. *Trends Ecol Evol* 18(1):48–55
- Pope MA, Spence E, Seralvo V, Gacesa R, Heidelberger S, Weston AJ, Dunlap WC, Shick JM, Long PF (2015) O-Methyltransferase is shared between the pentose phosphate and shikimate pathways and is essential for mycosporine-like amino acid biosynthesis in *Anabaena variabilis* ATCC 29413. *ChemBiochem* 16(2):320–327
- Portwich A, Garcia-Pichel F (2003) Biosynthetic pathway of mycosporines (mycosporine-like amino acids) in the cyanobacterium *Chlorogloeopsis* sp. strain PCC 6912. *Phycologia* 42(4):384–392



- Proteau PJ, Gerwick WH, Garcia-Pichel F, Castenholz R (1993) The structure of scytonemin, an ultraviolet sunscreen pigment from the sheaths of cyanobacteria. *Experientia* 49(9):825–829
- Rancan F, Rosan S, Boehm K, Fernández E, Hidalgo ME, Quihot W, Rubio C, Boehm F, Piazena H, Oltmanns U (2002) Protection against UVB irradiation by natural filters extracted from lichens. *J Photochem Photobiol B Biol* 68(2–3):133–139
- Rastogi RP, Sinha RP (2009) Biotechnological and industrial significance of cyanobacterial secondary metabolites. *Biotechnol Adv* 27(4):521–539
- Rastogi RP, Sinha RP, Singh SP, Häder DP (2010) Photoprotective compounds from marine organisms. *J Ind Microbiol Biotechnol* 37(6):537–558
- Rastogi RP, Sinha RP, Incharoensakdi A (2013) Partial characterization, UV-induction and photoprotective function of sunscreen pigment, scytonemin from *Rivularia* sp. HKAR-4. *Chemosphere* 93(9):1874–1878
- Rastogi RP, Sonani RR, Madamwar D (2015) Cyanobacterial sunscreen scytonemin: role in photoprotection and biomedical research. *Appl Biochem Biotechnol* 176(6):1551–1563
- Richa, Sinha RP (2013) Biomedical applications of mycosporine-like amino acids. In: Kim S-K (ed) *Marine microbiology in bioactive compounds and biotechnological applications*, pp 509–534
- Rizzini L, Favory JJ, Cloix C, Faggionato D, O'Hara A, Kaiserli E, Baumeister R, Schäfer E, Nagy F, Jenkins GI, Ulm R (2011) Perception of UV-B by the *Arabidopsis* UVR8 protein. *Science* 332(6025):103–106
- Rozema J, Björn LO, Bornman JF, Gaberščik A, Häder DP, Trošt T, Germ M, Klisch M, Gröniger A, Sinha RP, Lebert M (2002) The role of UV-B radiation in aquatic and terrestrial ecosystems—an experimental and functional analysis of the evolution of UV-absorbing compounds. *J Photochem Photobiol B Biol* 66(1):2–12
- Samanta A, Das G, Das SK (2011) Roles of flavonoids in plants. *Carbon* 100(6):12–35
- Sen S, Mallick N (2022) Scytonemin: unravelling major progress and prospects. *Algal Res* 64:102678
- Shick JM, Dunlap WC (2002) Mycosporine-like amino acids and related gadusols: biosynthesis, accumulation, and UV-protective functions in aquatic organisms. *Annu Rev Physiol* 64(1):223–262
- Simmonds MS (2003) Flavonoid–insect interactions: recent advances in our knowledge. *Phytochemistry* 64(1):21–30
- Singh SP, Sinha RP, Klisch M, Häder DP (2008a) Mycosporine-like amino acids (MAAs) profile of a rice-field cyanobacterium *Anabaena doliolum* as influenced by PAR and UVR. *Planta* 229(1):225–233
- Singh SP, Klisch M, Sinha RP, Häder DP (2008b) Effects of abiotic stressors on synthesis of the mycosporine-like amino acid shinorine in the cyanobacterium *Anabaena variabilis* PCC 7937. *Photochem Photobiol* 84(6):1500–1505
- Singh SP, Häder DP, Sinha RP (2010a) Cyanobacteria and ultraviolet radiation (UVR) stress: mitigation strategies. *Ageing Res Rev* 9(2):79–90
- Singh SP, Klisch M, Sinha RP, Häder DP (2010b) Genome mining of mycosporine-like amino acid (MAA) synthesizing and non-synthesizing cyanobacteria: a bioinformatics study. *Genomics* 95(2):120–128
- Singh SP, Häder DP, Sinha RP (2012) Bioinformatics evidence for the transfer of mycosporine-like amino acid core (4-deoxygadusol) synthesizing gene from cyanobacteria to dinoflagellates and an attempt to mutate the same gene (YP\_324358) in *Anabaena variabilis* PCC 7937. *Gene* 500(2):155–163
- Sinha RP, Häder DP (2008) UV-protectants in cyanobacteria. *Plant Sci* 174(3):278–289
- Sinha RP, Singh SP, Häder DP (2007) Database on mycosporines and mycosporine-like amino acids (MAAs) in fungi, cyanobacteria, macroalgae, phytoplankton and animals. *J Photochem Photobiol B Biol* 89(1):29–35
- Solhaug KA, Gauslaa Y (2004) Photosynthates stimulate the UV-B induced fungal anthraquinone synthesis in the foliose lichen *Xanthoria parietina*. *Plant Cell Environ* 27(2):167–176

- Solhaug KA, Gauslaa Y (2012) Secondary lichen compounds as protection against excess solar radiation and herbivores. In: Progress in botany, vol 73. Springer, Berlin, pp 283–304
- Solhaug KA, Gauslaa Y, Nybakken L, Bilger W (2003) UV-induction of sun-screening pigments in lichens. *New Phytol* 158(1):91–100
- Soule T, Stout V, Swingley WD, Meeks JC, Garcia-Pichel F (2007) Molecular genetics and genomic analysis of scytonemin biosynthesis in *Nostoc punctiforme* ATCC 29133. *J Bacteriol* 189(12):4465–4472
- Soule T, Garcia-Pichel F, Stout V (2009) Gene expression patterns associated with the biosynthesis of the sunscreen scytonemin in *Nostoc punctiforme* ATCC 29133 in response to UVA radiation. *J Bacteriol* 191(14):4639–4646
- Spence E, Dunlap WC, Shick JM, Long PF (2012) Redundant pathways of sunscreen biosynthesis in a cyanobacterium. *Chembiochem* 13(4):531–533
- Takamatsu S, Hodges TW, Rajbhandari I, Gerwick WH, Hamann MT, Nagle DG (2003) Marine natural products as novel antioxidant prototypes. *J Nat Prod* 66(5):605–608
- Tohge T, Watanabe M, Hoefgen R, Fernie AR (2013) Shikimate and phenylalanine biosynthesis in the green lineage. *Front Plant Sci* 4:62
- Torregiani JH, Lesser MP (2007) The effects of short-term exposures to ultraviolet radiation in the Hawaiian coral *Montipora verrucosa*. *J Exp Mar Biol Ecol* 340(2):194–203
- Treutter D (2005) Significance of flavonoids in plant resistance and enhancement of their biosynthesis. *Plant Biol* 7(06):581–591
- Turnbull JJ, Nakajima JI, Welford RW, Yamazaki M, Saito K, Schofield CJ (2004) Mechanistic studies on three 2-oxoglutarate-dependent oxygenases of flavonoid biosynthesis: anthocyanidin synthase, flavonol synthase, and flavanone 3 $\beta$ -hydroxylase. *J Biol Chem* 279(2):1206–1216
- Venugopala KN, Rashmi V, Odhav B (2013) Review on natural coumarin lead compounds for their pharmacological activity. *Biomed Res Int* 2013:963248
- Vidović M, Morina F, Milić S, Albert A, Zechmann B, Tosti T, Winkler JB, Jovanović SV (2015) Carbon allocation from source to sink leaf tissue in relation to flavonoid biosynthesis in variegated *Pelargonium zonale* under UV-B radiation and high PAR intensity. *Plant Physiol Biochem* 93:44–55
- Watts KT, Lee PC, Schmidt-Dannert C (2004) Exploring recombinant flavonoid biosynthesis in metabolically engineered *Escherichia coli*. *Chembiochem* 5(4):500–507
- Wong HJ, Mohamad-Fauzi N, Rizman-Idid M, Convey P, Alias SA (2019) Protective mechanisms and responses of micro-fungi towards ultraviolet-induced cellular damage. *Pol Sci* 20:19–34
- Zeevi Ben-Yosef D, Kashman Y, Benayahu Y (2006) Response of the soft coral *Heteroxenia fuscescens* to ultraviolet radiation regimes as reflected by mycosporine-like amino acid biosynthesis. *Mar Ecol* 27(3):219–228
- Zhang L, Li L, Wu Q (2007) Protective effects of mycosporine-like amino acids of *Synechocystis* sp. PCC 6803 and their partial characterization. *J Photochem Photobiol B Biol* 86(3):240–245