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A Comprehensive Review on Melatonin Compound and its Functions in Different Fungi and Plants

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Authors' contributions

This work was carried out in collaboration among all authors. All authors read and approved the final manuscript.

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Review Article

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ABSTRACT

This study summarizes the importance of melatonin in different plants and fungi. In this review, we discussed the biosynthetic pathway of melatonin, its metabolites, and its oxidative reduction. Melatonin is a molecule derived from tryptophan, with pleiotropic activity. It is present in nearly every organism. Its synthetic course depends on the organism in which it resides. The tryptophan to the melatonin pathway, for example, varies in plants and animals. It is thought that the synthetic mechanism for melatonin was inherited in eukaryotes from bacteria caused by endosymbiosis. Nevertheless, the synthetic pathways of melatonin in microorganisms are unknown. The metabolism of melatonin is exceptionally complex with these enzymatic processes developed out of cytochrome C. As well as the enzymatic degradation, melatonin is metabolized by interactive pseudoenzymes and free radicals processes.

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1. INTRODUCTION

Melatonin is a small compound that was first identified in the pineal glands of cows [1]. Its core seen task was to make amphibians skin lighter by causing granules of melanin compound granules inside dermal melanosomes to be aggregated in frogs around the nucleus of skin cells [2]. The identified molecule was therefore called melatonin because it forces dark pigment (melanin) to lighten in the skin and is often extracted out from serotonin. Due to that action, in certain patients with concentrated hyperpigmented skin, melatonin was once used to minimize pigmentation. This was found to be not successful without a skin lightening effect in human beings [3]. The point is that mammalian melanosomes are more or less like those found in amphibians dispersed indefinitely, and therefore, melatonin has no impact on its capacity to change pigment aggregation in mammalian Skin. Some of the most unusual characteristics of melatonin in vertebrates are its circadian cycle, including its secretory night peak, and low daytime levels. It makes melatonin an effective signaling agent to inform internal organs of photoperiodic changes to the environment. At the end of melatonin in vertebrate blood, melatonin often correlates with the dark period of the light/night cycle, referred to as dim chemical expression [4]. The normal circadian melatonin rhythm in vertebrates is created solely by melatonin excreted from the pineal gland, after either pineal ectomy vanishes this pattern in the blood [5], or growing its intensity varies significantly [6]. The master clock, the pineal gland, and the suprachiasmatic nucleus (SCN) interact with one another, consist of key bio-clock elements that synchronize the physiological activities of organisms, most importantly in vertebrates with predominant light/dark cycle [7, 8]. SCN relays details concerning photoperiods using the sympathetic nervous system to the pineal gland and relies on the details received by the SCN, the pineal gland regulates the production of melatonin either up- or down-. Because the melatonin function is changing. When it is discharged, it affects the functioning of SCN [9, 10]. Receptors of melatonin, most importantly MT1, are appeared in SCN. Melatonin receptors, especially MT1, are expressed in the SCN [11, 12] and are densely populated. The interactions have been between SCN, sympathetic nervous system, pineal gland [13–15]. Changes in the levels of melatonin due to diurnal are apparent in photosynthetic primitive bacteria [16, 17] in which they are identical to those found in vertebrate species; but, these diurnal changes can occur be passive, that is, the low melatonin levels in bacteria during photo phase may not be the result from a reduced synthesis of this indole but also oxidation as a consequence of its application. It is being hypothesized that more melatonin in photosynthetic organisms is metabolized during the day because of its reactive oxygen species interaction (ROS). This is because bacteria are photosynthetic, photosynthesis is maximum during the day, and produces large amounts of ROS through this process. Moreover, the diurnal modification of melatonin in prokaryotes does not have a direct effect on the role of their bio-clock, but the shifts are simply a result of their irregular metabolism that happens before and throughout the day [18]. We had a clear one diel melatonin rhythm in a single-celled organism, Symbiodinium genus dinoflagellate. Throughout this sense species, the peak of melatonin occurred in the dark with low daytime levels. These changes are disappeared when the organism is placed in the dark. Based on modifications to the production of oxygen during the light/dark cycle resulting from photosynthesis in this organism, the researchers finally concluded that fluctuating pattern in symbiodinium was not induced by endogenous circadian synthesis, however, also shifts in its application owing to the regular photocycle. The rhythm was attributable to pathways involving increased light-utilization of melatonin through the use of free radicals in the morning. The evident circadian melatonin rhythm of vertebrates probably evolved during evolution from the passive improvements in the development of melatonin in bacteria; the rhythm then evolved to influence the bio-clock of Superior organisms [19]. For example, circadian melatonin rhythm relating to the sleep cycle is platynereis dumerilii, already observed in early marine zooplankton [20]. It could be that organism, the first animal in which melatonin acted as a quiescent signal molecule. Disorders in the circadian cycle of melatonin result in chronodisruption that is consistent with many health conditions, including neurodegenerative diseases, heart disease, high blood pressure, and cancer. For example, shift workers, notably nurses, aircraft crews, and miners, have a higher breast and prostate cancer

prevalence [21–23]. One possible mechanism is light exposure during the night (their operating hours) suppresses the melatonin levels [24]. Which is compatible with the statements in the animal in which human donors infuse tumor-bearing rats with melatonin-rich blood the development of the transplanted tumor (having nightly melatonin levels) was inhibited; however, if these rats were injected with equivalent daytime human blood deficient in melatonin, tumor development was released [25]. Therefore, as light exposure exaggerates tumor growth during the dark process. Melatonin production also exhibits seasonal changes as a signaling molecule. In the winter, the late peak period of melatonin is longer due to the longer nights, during the summer, the night-time high is shorter [26, 27]. Photoperiodic animals use this information to make adjustments to their reproductive behaviors during the correct season [28] and their hibernation behavior [29]. For example, without a proper melatonin message after pinealectomy, which through the blood melatonin rhythm, reproductive disturbances, and the hibernating photoperiodic cycle is noticeable [29–31]. The circadian rhythm of melatonin is neither as clear nor regular in plants as it is in animals. Only increased amounts of melatonin were observed during scotophase, and lower amounts during photophase chenopodium rubrum, in an evolutionarily ancient plant [32]. Indeed, multiple reports have shown that light-exposure induces the development of melatonin in plants [33–35]. If there is more sunlight, then there is more synthesis of melatonin molecules in a few plants. Photosynthesis is believed to produce significant amounts of ROS and plants; more melatonin is probably developed to defend against toxicity [36, 37]. Free radical scavenger and antioxidant are core functions of melatonin. While other melatonin functions have been acquired in all organisms in development [19, 38]. Because melatonin is among those products which are found naturally, so it is different in many ways from commonly found antioxidants. These involve melatonin cascade reaction with ROS and the possibility that its synthesis is inducible to high oxidizing stress in humans. These unique characteristics of melatonin make it bigger suitable for the defense of species from stressful conditions as an endogenous antioxidant.

2. BIOSYNTHETIC PATHWAY OF MELATONIN

The Source of melatonin in animals is the pineal gland. However, that organ does not exist in plants, and this discrepancy suggests that cell melatonin biosynthesis is somewhat different than in animals [39]. In plants, melatonin is found in different parts of plants like root, stem, and leaf, unlike in the animals. In plants, multiple factors may stimulate the biosynthesis of melatonin. Light is among the environmental factors which regulate melatonin biosynthesis [40]. There are more growth processes such as fruit ripening [41], plant development [42], and senescence [43], and climate stresses involved

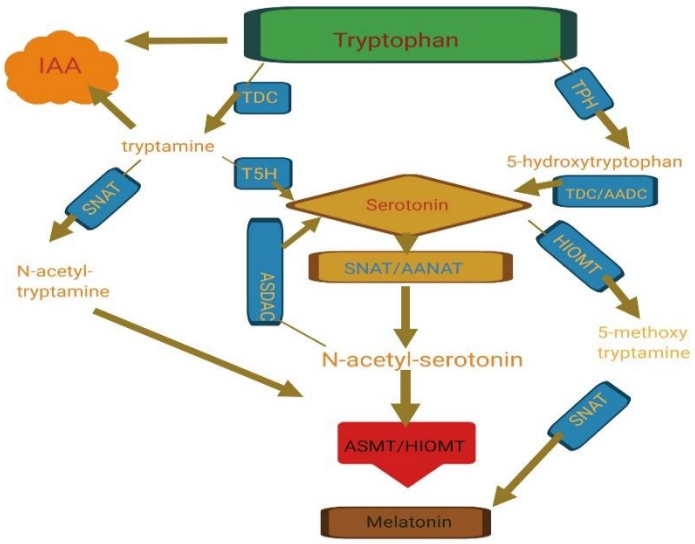

Fig. 1. The biosynthetic pathway of melatonin in plants

include Ultraviolet-B (UV-B) radiation [44], drought, cold [45] and heat [46] that stimulate melatonin biosynthesis. Melatonin biosynthesis begins in a wide array of plant species through tryptophan. Tryptophan decarboxylase (TDC) is catalyzed and transformed to tryptamine,as shown in Fig. 1; next, tryptamine 5-hydroxylase (T5H) catalyzes tryptamine in serotonin, which is transformed by two steps to melatonin [47]. Among certain other species, tryptophan, such as Hypericum perforatum, is catalyzed by tryptophan 5-hydroxylase (TPH) in 5-hydroxytophan, and then TDC / AADC (Decarboxylase, Aromatic-L-amino acid) transforms 5-hydroxytryptophan to serotonin [48]. This path is the same true of animals. The serotonin is converted to N-acetyl-serotonin in the next two steps using serotonin N-acetyltransferase (SNAT)/arylalkylamine N-acetyltransferase (AANAT), and then catalysis of n-acetyl-serotonin methyltransferase (ASMT)/hydroxyindole-O-methyltransferase (HIOMT) N-acetyl-serotonin comes in melatonin. Additionally, SNAT can be catalyzed from tryptamine into N-acetyl-tryptamine, which T5H [49] does not further convert into N-acetyl-serotonin. This is difficult to determine whether a pathway for converting N-acetyl-tryptamine to N-acetyl-serotonin exists. The other route is by HIOMT to transform serotonin into 5-methoxy-tryptamine and eventually catalysis of 5-methoxy-tryptamine by SNAT into melatonin [50, 51]. A reverse melatonin pathway was recently discovered. Reported, in which N-acetyl-serotonin is converted by N-acetyl-serotonin deacetylase into serotonin [52]. Tryptophan is not only a provider of melatonin but also an indole-3-acetic precursor acid (IAA), perhaps implying melatonin multifunctional role in plants.

3. METABOLISM OF MELATONIN

Melatonin oxidation is less well understood than melatonin synthesis. For several decades, the only significant metabolite was 6-hydroxymelatonin and, therefore, several studies centered on it. Melatonin synthesis is a full cycle, and 6-hydroxymelatonin is one of its metabolites. Melatonin metabolizes through enzymatic mechanisms, pseudo enzymatic mechanisms, or encounters with ROS and NOS. Melatonin is found in primary photosynthetic bacteria like the prokaryote rhodospirillum rubrum, cyanobacteria [53]. The former is the parent to mitochondria, occurring in nearly all cells, is the possible source to chloroplasts seen in green plants. There is not that much research on the metabolism of melatonin. Nonetheless, melatonin synthesis in mitochondria is established. In mitochondria, melatonin is degraded through the pseudo-enzymatic method. Cytochrome C acts as an enzyme to eliminate melatonin in N1-acetyl-N2-formyl-5-methoxykynuramine.

Cytochrome C potent independent protein, even in bacteria [54]. Therefore, we believe the bacteria will even use melatonin-metabolizing cytochrome C. Cytochrome C may be the first degrading protein degrading melatonin, and AFMK may be the first pseudo enzymatic result of the melatonin metabolism process. Method. The cytochrome C catalytic core for melatonin metabolism can be in its molecule of a single iron atom.

Such iron-containing hemoproteins such as AFMK and other metabolites associated with melatonin [55]. In this cycle, melatonin is oxidized and cleaned to form AFMK by oxoferryl-hemoprotein [56]. Many enzymatic pathways involved in melatonin synthesis during development. Most enzymes responsible for melatonin synthesis have a specific feature: iron-containing cytochrome-like hemoproteins. Namely cytochrome P450 (CP450), indole amine 2,3-IDO, horseradish peroxidase (HRP), myeloperoxidase (MPO), and eosinophilic peroxidase. Every enzyme will break melatonin into AFMK. CP450 is the animal's main enzyme for melatonin synthesis. It is primarily in the liver, but often present in many tissues. CP450 primarily generates 6-hydroxymelatonin, and its small product is AFMK. In the brain, the primary enzyme for melatonin synthesis is ID with its product AFMK. MPO and EPO are responsible for melatonin synthesis at inflammatory sites. HRP exists in plants and can engage in plant melatonin metabolism.

AFMK line, plants identified. Cyclic melatonin (unlike cyclic-3-hydroxymelatonin) and β-hydroxy melatonin were detected in plants as shown in Fig. 2.

Dominant melatonin in plants (24 species) metabolite is 2-hydroxymelatonin and is known as melatonin-2-hydroxylases [57]. When melatonin is made, it rapidly becomes 2-hydroxymelatonin. In the plants examined, the normal ratio of melatonin to 2-hydroxymelatonin was 1:368. If the ratio is verified according to others, melatonin synthetic ability in plants is much more effective than past aspirations. Interestingly, a non-enzymatic mechanism may also metabolize melatonin. Melatonin complex

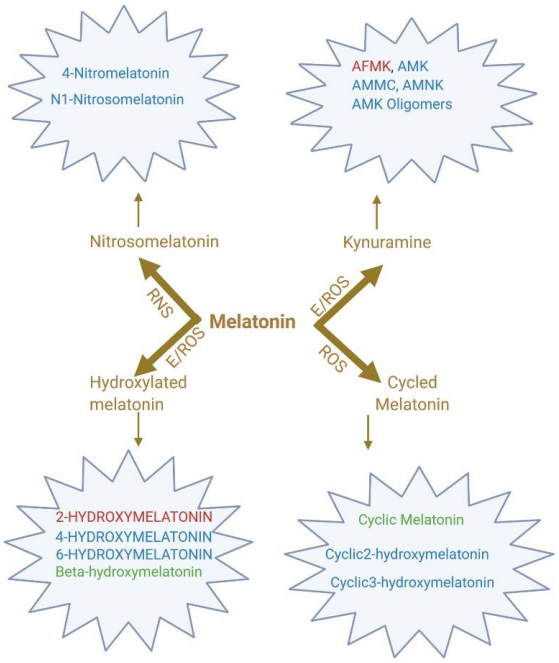

Fig. 2. Metabolites of melatonin; blue metabolites are found only in animals, green are found in plants and red are found in both animals and plants

interactions with ROS and NOS produce different metabolites. These contain 3-hydroxymelatonin, 2-Hydroxymelatonin, N-nitrosomelatonin, N-(1-formyl-5-methoxy-3-oxo-2,3- Dihydro-1H-indol-2) acetamide, AFMK, and AMK [58]. Enzyme-related metabolites, pseudo enzymatic processes, and ROS interaction pathways are common.

Furthermore, it is complicated to determine through the metabolic cycle that dominates in vivo conditions. In extreme oxidation stress, however, it is believed that ROS interactions metabolize most melatonin because of oxidative stressors dramatically lower overall organism melatonin rates. The melatonin synthesis nature faces problems for researchers. None is known to date. There is almost little research about melatonin synthesis in plant microorganisms. We assume in melatonin synthesis and several other pathways melatonin metabolites should be identified in the coming years [65].

4. ANTIOXIDANT ACTIVITY OF MELATONIN

While melatonin is found to be a decade earlier, a free radical scavenger [59], the data that recorded its function to conquer stress due to oxidative has accrued at an accelerated rate. The rate is now abundant [60-62]. Efficacy of melatonin for working throughout this power, it relates to its parent-free radical scavenging behavior, the capacity to improve the behaviors of several individuals. Antioxidant enzymes, it is a relaxing impact on the synthesis of another essential intracellular antioxidant, glutathione its effectiveness in the elimination of nucleus loss of the nuclear nucleus transport chain [63] and synergistic chain many antioxidant associations [64]. Moreover, it has been evident in recent years this is why melatonin scavenges radicals, related reactants, the products that are produced open radical scavengers, however, thereby massively exaggerating melatonin antioxidant potential [66]. Subsequent articles shall contain a summary of the melatonin-capable metabolites neutralizing free radicals and oxygen-dependent non-radicals the reagents [67].

4.1 Melatonin Reduces the Oxidative Stress Induced by Hydrogen Peroxide in *saccharomyces*

Melatonin (N-acetyl-5-methoxytryptamine) has a tryptophan synthesis cerevisiae and unusual yeast genus Saccharomyces. Properties of antioxidant the role of melatonin in an S. cerevisiae were suggested as possible wine strain. The possible effect on non-Saccharomyces species of antioxidants melatonin and other strains. It is necessary to

evaluate cerevisiae. The object of this analysis [68] was to determine the melatonin antioxidant capacity in 8 S. strains and cerevisiae four yeasts (*Torulaspora delbrueckii*, *Metschnikovia pulcherrima*, *Hanseniaspora uvarum*, and *Starmerella bacillaris*). The formation of ROS, therefore fat peroxidation, operation of catalase, fatty acids, and proliferation of peroxysomes, the inquiry has been completed. The tests indicated an improvement in melatonin peroxisome build-up, and the operation of the catalase decreases considerably. When rising cells oxidative stress induced by H2O2 was exposed to melatonin, all tested strains have observed lower ROS accumulation and lipid peroxidation [69]. The decreased development of catalysis, which was a consequence of oxidative stress, was less in melatonin presence. Also, MEL modulates cell presence composition of FA, increased oleic and palmitoleic acids, and increased UFA / SFA ratios previously associated with increased H2O2 tolerance. These discoveries prove that melatonin can act as an antioxidant in both S. cerevisiae and yeasts, which are non-Saccharomyces [70].

4.2 Growth of *Xanthomonas oryzae* PV. *oryzae* is Inhibited by Melatonin

Xanthomonas oryzae PV. oryzae (Xoo), one of the many severe and devastating diseases that exist in rice-growing regions around the world. Melatonin improves pathogenic tolerance by causing plant innate immunity, which has clear effect melatonin is little known on plant pathogenic bacteria. In the analysis [71], the immediate influence of melatonin on Xoo has been studied. Exogenous, 200 mg / mL melatonin, the Xoo proliferation was significantly impaired, and the mRNA production decreased by five genes active in separating cells [72]. This melatonin production also impaired motility; and Xoo Biofilm Formation. Melatonin was noteworthy for altering the length of Xoo cells. Provide more insight into the mechanisms that underlie this antibacterial activity. Also, we examined changes in global gene expression of Xoo strain PXO99 using RNA sequencing (RNA-Seq) for application of 200 mg / mL melatonin. Differential gene range (DGGs) related to catalytic activity and metal binding in response to the melatonin treatment, activity in Xoo cells was de-regulated [73]. Additionally, DEGs responsible for the metabolism of carbohydrates and amino acids were down-regulated too. Those results suggest melatonin inhibitory mechanism on Xoo proliferation; cell division can be controlled in conjunction with a reduction of the production or operation of metabolism enzymes [74].

5. ROLE OF MELATONIN IN PLANTS

Melatonin production has already been seen in a variety of plants, and [75] were regularly checked. Given the vast number of exhibitions, the awareness remarkably low on bodily roles; this was primarily because scholars became less involved in plant physiology with also to include medical or therapeutic goods many advantageous acts are ascribed to indole amine origins. A more Chrono biological function was pursued or little to no avail [76]. Chenopodium rubrum is an excellent research organism that was defined as a nocturnal peak circadian rhythm [77], but a photoperiodic short day presence response [78] remains vague. Same like, no short day in certain Lemnaceans and Kalanchoë responses were found [79] Tubiflora. For some other plants, the rhythms recorded in tomatoes such as these have not been authenticated, but instead changes during ripening of fruits [80]. A pattern well marked the *Eichhornia crassipes*, mentioned in the water hyacinth [81]. In this species, at the end of the photo phase, the limit was achieved, and followed by the periodicity of melatonin by another solid metabolite pattern AFMK. All have identified an auxin-like growth stimulus in a lupine, dicot [82], also in monocots. Stimulating progress in coleoptiles of many poacemen was related to another auxin-like operation, suppression of root growth [83-91]. Whether or not these results are essential in physiology and whether melatonin it can include metabolites, it is an interesting problem to address in the future. Particular involvement of high levels of melatonin in fruits, and especially oily seeds possible function in process separation and maintenance, maybe of dormancy, coupled with antioxidant dry seed defense, in which the enzymatic pathways cannot act [92]. In Eichhornia, particularly the high levels of AFMK which reached a limit at the end was detected photophase, i.e., a period at which light-induced harm photosystems and secondary pathways to recover are the best shapes, and hence oxidizing [93-99]. This may mean in the process of moderate incremental degradation of melatonin free radicals process, singlet oxygen, late photocatalytic hemoproteins, peroxidases, and other chemicals. On the other side, specific melatonin-consuming reactions can be deemed to be contributions to photoprotection. None, the function of melatonin in photoprotection, was thought to be one of the

animal tissue types, such as organs high in porphyrins photo catalytically healthy, like rodents harderian gland, certain mollusks in photoreceptors and crustaceans, and even in numerous macro- and microalgae [100]. This can extend similarly to higher plants [83], as shown in a variety of comments: I light-dependent melatonin recycling, (ii) UV-induced increases, and (iii) significantly; higher amounts of melatonin contained in exposed plants about a significant degree of natural radiation, for example in the Alps, the Mediterranean, and subtropical areas, along with the same ecosystem elsewhere or, in [84-87] greenhouses.

5.1 Melatonin Induces Heat Tolerance in *Arabidopsis*

Melatonin (N-acetyl-5-methoxytryptamine) is an essential part of the signal molecule in the process of plant development and multiple abiotic stress reactions. Melatonin involvement in thermos tolerance, however, in Arabidopsis, the fundamental molecular process was mainly not known. Shi [88] reported that the endogenous level of melatonin coupled with heat stress treatment induced *Arabidopsis* leaves significantly, and exogenous melatonin treatment enhanced thermos tolerance in *Arabidopsis*, which is [89]. The class A1 heat-shock factor transcript levels (HSFA1s), which act as master heat stress response regulators, have been essential, and in Arabidopsis, heat stress and exogenous melatonin treatment are upregulated. Of particular note, exogenous thermos tolerance enhanced by melatonin was enhanced mainly in HSFA1 quadruple knockout (QK) mutants, and HSFA1 activated heat-responsive gene transcripts (HSFA2), heat-induced stress response can be 32 (HSA32), 90 (HSP90) and 101 (HSP101) heat-shock protein has led to thermos tolerance regulated by melatonin [90, 91]. Some research provided a direct connection between melatonin and heat tolerance and demonstrated the engagement of heat-response genes activated by HSFA1s in thermos tolerance mediated with melatonin in *Arabidopsis* [101-103].

5.2 Melatonin Induces Heat Tolerance in Tomato Plants

Melatonin is a pleiotropic molecule for physiological protection compared to various environmental stresses in plants. The mechanisms for melatonin driven thermotolerance are uncertain. [104] reported the number of endogenous melatonin increases as air temperature rises and that about 40 ° C. Optimal melatonin dose (10 μmol / L) foliar pretreatment or N-acetylserotonin over-expression effectively, DNA methyltransferase (ASMT) heat-induced change tomato photography and electrolyte leakage trees. Trees, [105]. Treatment of exogenous melatonin and manipulation of melatonin the levels of insoluble and ubicuous proteins decreased by over-expression of ASMT, but improved heat-shock expression HSPs for refolding denatured proteins and heat-stressed unfolded proteins [106]. Melatonin has also led to expression. Meanwhile, multiple ATG genes and autophagosome formation aggregated to degrade under the same stress, proteins. Analysis of the proteomic profile found that protein aggregates accumulated in the wild for a large number of biological processes trees. Trees, [107]. The treatment or overexpression of ASMT in exogenous melatonin, however, was reduced aggregated protein accumulation. Protein reactors such as aggregation preference were given to the accumulation and ubiquitisation of HSP70 and Rubisco activase type Wild heat stress plants, while melatonin reduces heat stress aggregated protein accumulation and ubiquitisation [108]. These findings show that the combination of HSPs and melatonin facilitates cellular protein defense and autophagy in tomato plants for refolding or degrading heat stress denatured proteins [109, 110].

5.3 Melatonin Induces Heat Tolerance in Maize Seedlings

Melatonin (MT) is a superb signaling molecule with multiple functions in plants and derived from tryptophan. Induced thermal stress (HS) a significant stress factor limiting plant metabolism, growth, development, and productivity is high temperature. MT could improve maize seedlings thermotolerance, and the underlying mechanisms are unknown. In research [111] reported, treatment of maize seedlings with MTE the survival percentage of maize seedlings under HS has been improved and the conditions mitigated malondialdehyde and electric leakage and improved tissue vitality in comparison with MDA (membrane lipid peroxidation) treatment control without MT indicates that the thermotolerance of maize seedlings could be enhanced by MT treatment [112]. To comprehend the mechanisms behind MT-enhanced antioxidant protection (guaiacol

peroxidase, GPX; GPX) maize seeding thermotolerance; catalase: CAT, ascorbic acid: ASA; and glutathione: GSS), detoxifying methylglyoxal (mg) (glyoxalase I: systems have been tests on Gly I; and Glyoxalase II: Gly II) and Osmoregulation (Proline: Pro; Trehalose, TSS) systems. The findings indicate that MT therapy promotes antioxidant (GPX, GR, CAT) and MG detoxification practices. Non-enzyme antioxidants (ASA and GSH) and osmolytes (Pro, Tre, and TSS) increased in enzymes (goly I and gly II), maize seedlings retained higher enzyme activity, and antioxidants under regular culture and the content of osmolyte is compared with the control under HS conditions. This study indicated that MT could improve the thermotolerance maize seedlings, MG detoxification, and Osmoregulation mechanisms through control of antioxidant response [113-117].

6. CONCLUSION

Melatonin has paramount importance in curbing the diseases caused by different fungi. Fungi cause most of the plant diseases, and recent researches has shown that melatonin has great importance in the prevention of fungal diseases in crop plants, and some of those researches are also discussed in this study. In recent years there has been a remarkable development in plant and melatonin research made. The improvement expands knowledge about the existence of melatonin, metabolism, and functions of seedlings. Melatonin is found in various types of organs and plants, as mentioned above, though precise concentrations are not stable in the various plants and organs. Biosynthetic pathway of melatonin is different in plants because there is no pineal gland in plants. The mechanism of melatonin synthesis in plants is similar to that of auxin mechanism in animals. Much researches have shown that melatonin has great importance in increasing resistance in plants against biotic and abiotic stresses. Endogenous concentrations in plants, melatonin rose under various stress conditions, from which we can conclude that melatonin is involved in enhancing tolerance in plants against different stresses. Different critical points related to melatonin like its metabolism pathway and its regulation because of the stress environment are still unknown.

COMPETING INTERESTS

Authors have declared that no competing interests exist.

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