

Chapter 1

Melatonin and the Metabolism of Reactive Oxygen Species (ROS) in Higher Plants



Jorge Taboada, Russel J. Reiter, José M. Palma, and Francisco J. Corpas 

Abstract Melatonin, designated in plants as phytomelatonin, is a key biomolecule in both animal and plant cells. This is because, in addition to the detoxifying capacity melatonin has against different reactive oxygen species (ROS), it also has signaling properties that boost certain metabolic pathways and trigger both enzymatic and non-enzymatic antioxidant systems. This review aims to give a wide perspective of melatonin biosynthesis in plant cells and the relevance of this molecule to palliate certain environmental stresses, many of which have been accompanied by oxidative stress. Likewise, it evaluates the data which documents the beneficial effects of melatonin when it is applied exogenously.

Keywords Antioxidant · Abiotic stress · Phytohormone · Nitric oxide · Melatonin · Oxidative stress

1.1 Introduction

Since its identification in plants in 1995 (Dubbels et al. 1995; Hattori et al. 1995), the indoleamine melatonin (N-acetyl-5-methoxytryptamine) has attracted the attention of many research groups working in highly diverse aspects of animal and plant systems. This interesting and promising biomolecule derived from tryptophan (Palego et al. 2016), whose chemical structure is the result of serotonin

J. Taboada · J. M. Palma · F. J. Corpas (✉)
Group of Antioxidants, Free Radicals and Nitric Oxide in Biotechnology, Food and Agriculture, Estación Experimental del Zaidín (Spanish National Research Council, CSIC), Granada, Spain
e-mail: javier.corpas@eez.csic.es

R. J. Reiter
Department of Cell Systems and Anatomy, UT Health San Antonio, Long School of Medicine, San Antonio, TX, USA

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(5-hydroxytryptamine) acetylation (Lerner et al. 1959a), is known in plants as phyto-melatonin (Blask et al. 2004; Zhao et al. 2021).

The discovery and isolation of melatonin in animals initially took place in 1958, more specifically in the pineal gland of cows (Lerner et al. 1958). A year later, it was discovered in humans (Lerner et al. 1959b). In animal systems, numerous physiological roles of melatonin have been documented, including the modulation of circadian rhythms (Vadnie and McClung 2017; Zisapel 2018; Stein et al. 2020), sleep regulation (Zisapel 2018; Stein et al. 2020), control of autophagy (Pan et al. 2018; Xiao et al. 2019), buffering the immune system (Carrillo-Vico et al. 2013) and prevention of oxidative stress (Reiter et al. 2016; Shen et al. 2018; Reiter et al. 2013; Hardeland 2013) and avoiding inflammatory response (Mannino et al. 2019). In addition, melatonin is currently used for the treatment of jet lag (Herxheimer 2005) and its therapeutic effectiveness is being evaluated both in Alzheimer's and Parkinson's disease and in many types of cancer and in recent times in diabetes and SARS-COV-2 (Di Bella et al. 2013; Xie et al. 2017; Alghamdi 2018; Blume et al. 2019; Pandi-Perumal et al. 2020; Okeke et al. 2022; Yiang et al. 2023; Wang et al. 2023a).

Melatonin is essential for cellular redox homeostasis in animal and plant systems since it works as a scavenger of different free radicals and therefore it is considered a potent endogenous cellular antioxidant effects (Reiter et al. 2016; Arnao et al. 2022). Due to its amphiphilicity and the presence of transporters, melatonin easily passes through the cell membrane and distributes in the cytoplasm from where it enters the nucleus and mitochondria to exert its antioxidant capacity (Reiter et al. 1997). Melatonin defends against oxidative stress and free radicals due to its direct capacity of scavenging reactive oxygen species (ROS) and reactive nitrogen species (RNS), but also it functions as a signaling molecule to enhance the activities of antioxidant enzymes and related enzymes, such as catalase (CAT), superoxide dismutases (SOD) isozymes, ascorbate peroxidases (APX), glutathione S-transferases (GST) and pathogenesis-related proteins (PR), as well as antioxidant molecules including glutathione and ascorbate (Khan et al. 2020; Sun et al. 2020a, b; Siddiqui et al. 2020; Ahmad et al. 2020), and maintaining mitochondrial homeostasis (Zhang and Zhang 2014; Wang et al. 2018). Furthermore, the discovery of the first melatonin receptor in *Arabidopsis thaliana* in 2018, designated candidate G-protein-coupled receptor 2/phyto-melatonin receptor (CAND2/PMTR1) (Wei et al. 2018), prompted many workers to identify melatonin as a plant hormone (Hardeland 2014; Ludwig-Müller and Lüthen 2015). PMTR1 has the capacity to specifically bind melatonin and interact with the G protein α subunit 1 (GPA1). GPA1 mediates the production of H_2O_2 and the influx of calcium ions (Ca^{2+}), resulting in stomatal closure (Wei et al. 2018). Recently it has been questioned whether the CAND2 receptor is located in the plasma membrane or in the cytosol. Also, using mutants deficient in the CAND 2 receptor, the stimulation of mitogen-activated protein kinase (MAPK) mediated by melatonin was not suppressed (Back and Lee 2020). Thus, it is an open question whether the CAND 2 receptor is valid and, if it is, the signaling processes remain unknown. Recently, new data provide evidence that PMTR1

mediates in the stomata closure induced by melatonin through the control of ROS and nitric oxide generation (Wang et al. 2022a, 2023b).

Phytomelatonin can also act as an essential regulator in the mechanism of response to both abiotic and biotic adverse factors (Arnao and Hernández-Ruiz 2019). Regarding the defensive function of melatonin against abiotic stresses, relevant studies show that it protects against cold (Li et al. 2019), heat (Jahan et al. 2019), high salinity (Zhan et al. 2019; Zhang et al. 2022a, b; Zhu et al. 2022), drought (Zhang et al. 2013; Li et al. 2019; Jensen et al. 2023), heavy metals (Xu et al. 2020; Ou et al. 2023; Yang et al. 2023) global warming (Back et al. 2021), and bright light (Lee and Back 2018). Moreover, studies on the beneficial role of melatonin against biotic stresses have been published (Zeng et al. 2022; Sharif et al. 2018; Moustafa-Farag et al. 2019; Zhao et al. 2021; Tiwari et al. 2021; Reiter et al. 2015; Yin et al. 2013; Lee et al. 2015; Hernández-Ruiz et al. 2023; Li et al. 2023); however, the mechanism of action is not yet clearly elucidated.

Phytomelatonin, as in animals a product of tryptophan metabolism, acts coordinately with other phytohormones and plays a pivotal role in regulating plant growth and development (Liu et al. 2022), being involved in different physiological processes such as promoting germination, seedling growth, root development, product yield, stomatal movements, circadian rhythm regulation, deferring leaf senescence, flowering and regulating fruit ripening (Corpas et al. 2021; Lee et al. 2022; Wang et al. 2018; Erdal 2019; Arnao and Hernández-Ruiz 2020; Hong et al. 2018; Arnao and Hernández-Ruiz 2021; Abbas et al. 2021).

This chapter provides an overview of the interaction of ROS with melatonin in various physiological processes, e.g., photosynthesis, stomatal aperture, etc., protection against abiotic and biotic adverse conditions, as well as the role of the various Zhang's phytomelatonin-derived hydroxy metabolites present in plants and their possible future application to the industry for developments in horticulture, agriculture and to obtain greater agro-economic benefits.

1.2 Biosynthesis of Melatonin

The animal pathway of the biosynthesis of melatonin has been widely studied and described (Axelrod and Weissbach 1960; Champney et al. 1984), but with some unexpected variations (Tan et al. 2016; Mannino et al. 2021; Tan and Hardeland 2021). In higher plants as revealed using biochemical, molecular biology, and genetic approaches it has been shown that the melatonin biosynthetic pathway is more complex than that in animals since it contains diverse routes and reversible processes that have not been well described in many plant species (Tan and Reiter 2020). Melatonin biosynthesis starts with tryptophan (Trp), an aromatic amino acid produced through the chloroplastic shikimate pathway (Schmid and Amrhein 1995); it is generally agreed upon that the synthesis of melatonin involves four main steps catalyzed by at least six enzymes (Sun et al. 2021). Figure 1.1 shows a simple

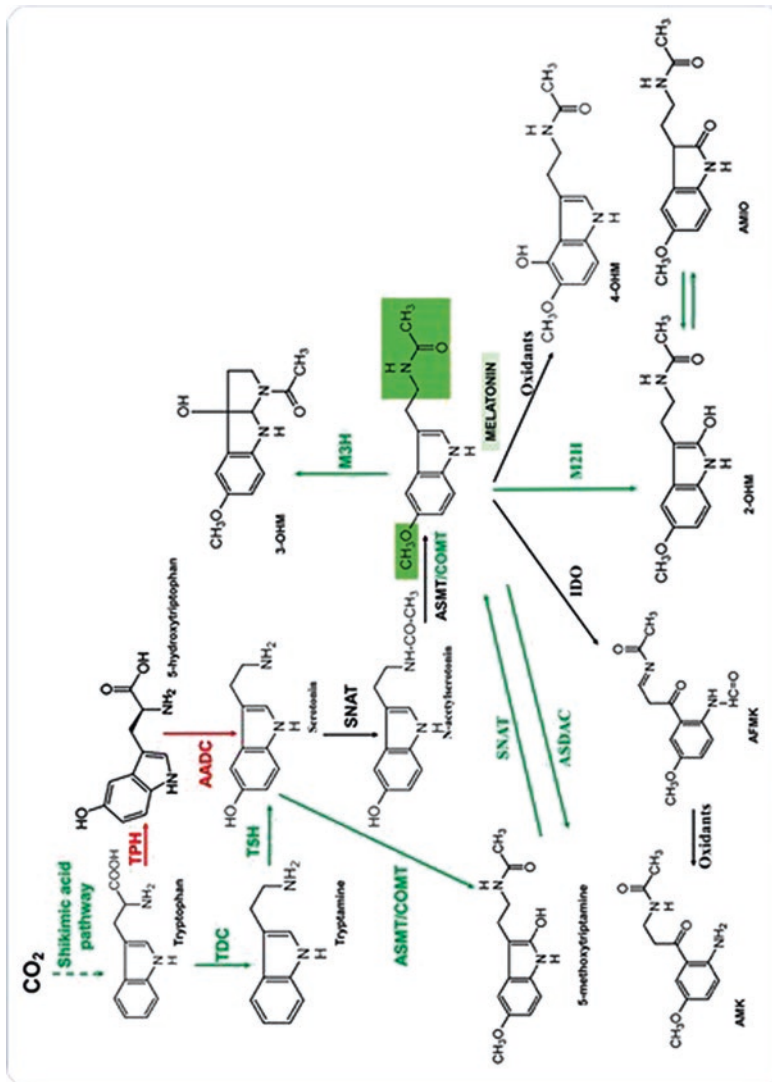


Fig. 1.1 Biosynthesis of melatonin in and formation of hydroxymelatonins. The main enzymes involved in the biosynthesis of melatonin are tryptophan decarboxylase (TDC), tryptamine 5-hydroxylase (TSH), serotonin N-acetyltransferase (SNAT), serotonin N-acetyltransferase (ASMT), N-acetylserotonin methyltransferase (ASMT), N-acetylserotonin decarboxylase (ASDAC), caffeic acid O-methyltransferase (COMT). Conversely, the enzyme melatonin 2-hydroxylase (M2H) and melatonin 3-hydroxylase (M3H) mediated the formation of (Lee et al. 2016) of 2-hydroxymelatonin (2-OHM), cyclic 3-hydroxymelatonin (3-OHM), respectively. The 2-OHM can be found in its tautomeric form, 2-acetamidodeethyl-5-methoxytryptamine-2-one (AMK). Additionally, indoleamine 2,3-dioxygenase (IDO) catalyzes the formation of N1-acetyl-5-methoxytryptamine (AMK) which can be oxidized to N-acetyl-5-methoxytryptamine (AMK)

scheme of the biosynthesis route of melatonin and some of the compounds derived from its oxidation. Tryptophan decarboxylase (TDC) catalyzes the first stage which involves the conversion of tryptophan to tryptamine (Noé et al. 1984; Méridon et al. 1986; Byeon et al. 2014a; Pang et al. 2018; Lee and Back 2019b; Taboada et al. 2023). In the next stage, tryptamine is converted to 5-hydroxytryptamine (serotonin) by tryptamine 5-hydroxylase (T5H), a cytochrome P450 enzyme found in the endoplasmic reticulum (Fujiwara et al. 2010; Park et al. 2013). The third stage involves the serotonin N-acetyltransferase (SNAT) that converts serotonin to N-acetylserotonin (NAS) in chloroplasts and mitochondria. Now, three *SNAT* genes that have a low sequence homology have been recognized in higher plants, *SNAT1*, *SNAT2*, and *SNAT3* (Kang et al. 2013; Byeon et al. 2016; Wang et al. 2017). The last stage is the conversion of NAS to melatonin by the enzyme N-acetylserotonin methyltransferase (ASMT) (Kang et al. 2011). In several plant species that lack ASMT homologs, the NAS is converted to melatonin by the action of caffeic acid O-methyltransferase (COMT) (Byeon et al. 2014b, 2015a; Lee et al. 2014). Furthermore, it has been reported a reverse pathway which involved the named enzyme N-acetylserotonin deacetylase (ASDAC), which catalyzes the conversion of NAS to serotonin; it is present in the chloroplast as is SNAT (Lee et al. 2018) and its overexpression leads to a lower endogenous melatonin content than that in the wild type (Back et al. 2020). In general, melatonin content in healthy plant tissues/organs range from picograms to nanograms per gram of fresh weight (Back 2021) but it could rise by several hundred-fold when plants are under diverse types of stresses (Lee et al. 2017).

Table 1.1 displays representative examples of the variability in melatonin content in diverse plant species and organs including fruits (climacteric and non-climacteric), leaves, stems, and different types of edible roots and seeds. This content can range from 10 to 5,300 pmol melatonin g⁻¹ fresh weight (FW). Although the values of melatonin are expressed in fresh weight, it should be noted that the data expressed by dry weight are more reliable since the water content of plant tissue varies widely and depends on many factors such as plant variety, organs (roots, stems, leaves or fruits), climatic conditions, the amount of water available in soils, ripening stage of the fruits, etc. (Riga et al. 2014).

1.3 Reactive Oxygen Species (ROS) and Reactive Nitrogen Species (RNS)

Aerobic life is inevitably associated with the generation of both ROS and RNS (del Río 2015; Kohli et al. 2019). Table 1.2 includes some of the main ROS and RNS. In addition, some of these molecules such as H₂O₂, NO, nitrosoglutathione (GSNO), or nitro-fatty acids (NO₂-FAs) have recognized signaling functions in plants in a wide variety of processes involving primary metabolism, growth, and development, response to biotic and abiotic stress, solute transport, autophagy, and programmed

Table 1.1 Melatonin concentration in different plant species and in the different organs, determined by radioimmunoassay. (Data extracted from Hattori et al. 1995). FW, fresh weight

Plant species	Melatonin content (pg g ⁻¹ FW)
Climacteric fruits	
Kiwi (<i>Actinidia chinensis</i>)	24.4
Tomato (<i>Solanum lycopersicum</i>)	32.2
Apple (<i>Malus domestica</i>)	47.6
Non- climacteric fruits	
Strawberry (<i>Fragaria magna</i>)	12.4
Cucumber (<i>Cucumis sativus</i>)	24.6
Pineapple (<i>Ananas comosus</i>)	36.2
Red chili pepper (<i>Capsicum annuum</i>)	1190–4480 ^a
Leaves	
Indian spinach (<i>Basella alba</i>)	38.7
Cabbage (<i>Brassica oleracea</i>)	107.4
Chungiku (<i>Chrysanthemum coronarium</i>)	416.8
Japanese ashitaba (<i>Angelica keiskei</i>)	623.9
Tall fescue (<i>Festuca arundinacea</i>)	5288.1
Stem	
Asparagus (<i>Asparagus officinalis</i>)	9.5
Welsh onion (<i>Allium fistulosum</i>)	85.7
Root	
Onion (<i>Allium cepa</i>) bulb	31.5
Carrot (<i>Daucus carota</i>) bulb	55.3
Ginger (<i>Zingiber officinale</i>) rhizome	583.7
Japanese radish (<i>Brassica campestris</i>)	657.2
Seed	
Barley (<i>Hordeum vulgare</i>)	378.1
Sweet corn (<i>Zea mays L.</i>)	1366.1
Rice (<i>Oryza sativa</i>)	1006.0
Oat (<i>Avena sativa</i>)	1796.1

^aData obtained from Riga et al. 2014

cell death (Corpas et al. 2013; Mata-Pérez et al. 2016, 2017; Turkan 2018; Foyer and Hanke 2022). Moreover, ROS and RNS are also involved in post-translational modification (PTMs) of proteins including S-sulfenylation, nitration, S-nitrosation, nitroalkylation or methylation of histones (Niu et al. 2015; Mengel et al. 2017; Aranda-Caño et al. 2019; Corpas et al. 2020a, 2022a).

ROS are primarily produced by two chemical routes. The primary way is the electron transfer (between one to three electrons) to oxygen, involving in the production of superoxide anion (O₂⁻), hydrogen peroxide (H₂O₂), or hydroxyl radical (*OH). The second of these processes is the transfer of energy to molecular oxygen (O₂), leading to the formation of singlet oxygen (¹O₂) (Halliwell and Gutteridge

Table 1.2 Main reactive oxygen and nitrogen species (ROS and RNS, respectively) containing inorganic and organic molecules

Nonradicals	Radicals
Inorganic molecules	
Hydrogen peroxide (H ₂ O ₂)	Superoxide anion (O ₂ ⁻)
Singlet oxygen (¹ O ₂)	Hydroxyl radical ([•] OH)
Nitroxyl anion (NO ⁻)	Hydroperoxyl radical ([•] OOH)
Nitrosonium cation (NO ⁺)	Nitric oxide ([•] NO)
Nitrous acid (HNO ₂)	Nitrogen dioxide ([•] NO ₂)
Dinitrogen trioxide (N ₂ O ₃)	
Dinitrogen tetroxide (N ₂ O ₄)	
Peroxynitrite (ONOO ⁻)	
Peroxynitrous acid (ONOOH)	
Organic molecules	
Nitrotyrosine (Tyr-NO ₂)	Lipid peroxyl radicals (LOO [•])
Nitrosoglutathione (GSNO)	
Nitrosothiols (SNOs)	
Nitro- γ -tocopherol	
Nitro-fatty acid (NO ₂ -FA)	

1999; Sánchez-Corrionero et al. 2017; Arnao and Hernández-Ruiz 2019; Lemke et al. 2021). Plant cells generate also reactive nitrogen species (RNS), but unlike ROS, for RNS the production mechanism is not fully resolved. Among the RNS, nitric oxide ([•]NO), nitrogen dioxide ([•]NO₂), and non-radical species peroxynitrite (ONOO⁻) and S-nitrosoglutathione (GSNO) are included (Halliwell and Gutteridge 1999; Kohli et al., 2019; Arnao and Hernández-Ruiz 2019).

In higher plant cells, the central ROS sources are the electron transport chain present in chloroplasts and mitochondria (Kohli et al. 2019), but there are different enzymes present in the subcellular compartments which can generate ROS such as some metabolic pathways present in peroxisomes such as β -oxidation, photorespiration, purine metabolism, polyamine catabolism or sulfite detoxification pathway (Corpas et al. 2020a, b), the plasma membrane NADPH oxidase (NOX) is also known as a respiratory burst oxidase homolog (Rboh) (Torres and Dangl 2005; Liu et al. 2020) as well as the family of antioxidant superoxide dismutases (SODs) (del Río et al. 2018). Additionally, other subcellular places of ROS generation are cytosol, plasma membrane, and cell wall (Corpas et al. 2015; Podgórska et al. 2017; Kámán-Tóth et al. 2019). Although the primary enzymatic source of NO in plant cells is still an open question, there are two main candidates an L-arginine-dependent NO synthase-like activity and nitrate reductase (Mohn et al. 2019; Corpas et al. 2022a, b). In general, pathogen infections raise the endogenous content of H₂O₂ and NO, and these reactive species act upstream of melatonin and promote its synthesis (Shi et al. 2015; Lee and Back 2017), although the mechanism of how this is achieved remains unknown.

1.4 Interactions Between Phytomelatonin and ROS

As previously mentioned, phytomelatonin is a powerful antioxidant, which, due to its lipophilic nature, is capable of crossing biological membranes to act in the different cellular compartments (Reiter et al. 2001b; Sofic et al. 2005; Tan et al. 2007; Galano et al. 2013; Zhang and Zhang 2014). Melatonin can directly scavenge $\cdot\text{OH}$, H_2O_2 , $^1\text{O}_2$, NO , ONOO^- , and other free radicals (Reiter et al. 2001a; Reiter and Tan 2002; Galano and Reiter 2018). Thus, one molecule of melatonin has the capacity to scavenge two $\cdot\text{OH}$ molecules and four H_2O_2 molecules (Pieri et al. 1995; Reiter et al. 2000; Allegra et al. 2003).

In animal systems, it is well-documented that melatonin is converted to 6-hydroxymelatonin (6-OHM) by P_{450} enzymes and further conjugated by sulfation into 6-sulfatoxymelatonin (Ma et al. 2005; Hardeland 2017). Also, while some hydroxymetabolites such as N^1 -acetyl- N^2 -formyl-5-methoxykynuramine (AFMK) are generated from melatonin by the achievement of several enzymes such as indoleamine 2,3-dioxygenase (IDO) (Hirata et al. 1974; Tan et al. 2001) and cytochrome c (Semak et al. 2005), other derivative metabolites of melatonin such as N-acetyl-5-methoxykynuramine (AMK), AFMK, 2-hydroxymelatonin (2-OHM), cyclic 3-hydroxymelatonin (3-OHM) and 4-hydroxymelatonin (4-OHM) are generated non-enzymatically by interaction with different oxidants, including ROS and RNS (Hardeland 2017) with all of them exhibiting high antioxidant activity (Reiter et al. 2016) (Fig. 1.1).

Melatonin seems not to be an end product in plant cells, however, and the phytomelatonin-derived hydroxymetabolites are not simple oxidation products of reactions between melatonin and ROS as observed in animals (Mannino et al. 2021). In plant cells, these compounds constitute the main forms of phytomelatonin in terms of endogenous levels (Lee et al. 2016) highlighting the 3-OHM and 2-OHM catalyzed by the enzymatic reactions of melatonin 3-hydroxylase (M3H) (Lee et al. 2016) and melatonin 2-hydroxylase (M2H) (Byeon and Back 2015), respectively. Both M2H and M3H belong to the 2-oxoglutarate-dependent dioxygenase (2-ODD) family proteins (Bugg 2003; Kawai et al. 2014) that are only present in land plants (Lee and Back 2019a) (Fig. 1.1).

In healthy leaves of rice, concentrations of $600 \text{ ng} \cdot \text{g}^{-1}$ fresh weight (FW) of serotonin, $0.3 \text{ ng} \cdot \text{g}^{-1}$ FW of melatonin, $100 \text{ ng} \cdot \text{g}^{-1}$ FW of 3-OHM and $40 \text{ ng} \cdot \text{g}^{-1}$ FW of 2-OHM have been obtained. However, higher levels of these hydroxymetabolites derived from phytomelatonin and serotonin are measured are in higher concentrations than phytomelatonin itself under cadmium stress and senescence (Lee et al. 2017; Choi and Back 2019a, 2019b). According to the example in rice, and taking into account that the catalytic efficiency of the M3H enzyme is 35 times higher than the M2H enzyme, 3-OHM is the most abundant hydroxymetabolite in plants, followed by 2-OHM and then AFMK and AMK (Byeon and Back 2015; Lee et al. 2016). Nevertheless, in plant species such as coffee (*Coffea arabica*), ginkgo (*Ginkgo biloba*), spinach (*Spinacia*

oleracea) and feverfew (*Tanacetum parthenium*), 2-OHM concentrations 368 times higher than phytomelatonin have been found, once again indicating its role as a precursor of these hydroxymetabolites (Byeon et al. 2015b).

1.4.1 The Function of 2-hydroxymelatonin (2-OHM)

As mentioned, 2-hydroxy melatonin is the product of the M2H enzyme and because it has a higher catalytic efficiency than SNAT and COMT enzymes (Back 2021), concentrations of 2-OHM are up to 100 times higher than phytomelatonin (Byeon et al. 2015b). Several plant studies show that 2-OHM participates in the induction of defense genes (Byeon et al. 2015c), tolerance against abiotic stress (Lee and Back 2019a), and cadmium (Shah et al. 2020). In addition, other studies document that 2-OHM can act as a senescence-inducing factor in *Arabidopsis thaliana* since it has pro-oxidative properties, capable of inducing the ROS production in a respiratory burst NADPH oxidase (RBOH)-dependent manner in senescent leaves (Lee and Back 2021a) and seeds (Lee and Back 2022a). In a recent study, the effects of 2-OHM and phytomelatonin on seed germination concerning ROS production were compared in *Arabidopsis thaliana* (Lee and Back 2022a). Thus, it was observed that the seed pretreatment with 20 μ M melatonin increased, by around 13%, the germination in both dormant and non-dormant seeds, while the treatment with 20 μ M 2-OHM increased the germination rate by 80% and 40% in non-dormant and dormant seeds, respectively. Furthermore, this concentration of 2-OHM enhanced the expression of acid gibberellic (GA) biosynthetic genes such as 3-oxidase 2 (*GA3ox2*) and ent-kaurene synthase (*KS*) compared with the control. Furthermore, when a GA synthesis inhibitor (paclobutrazol) was applied, the germination was fully abolished, indicating that both GA and 2-OHM are clearly associated with the seed germination. Likewise, genetic approaches using knock-out mutant or overexpression of M2H in embryo tissues during seed germination demonstrate that 2-OHM mediates ROS production in the germination of seeds (Lee and Back 2022a).

Similarly, 2-OHM acts rather as a signaling molecule capable of inducing ROS production both in leaf senescence and seed germination. Therefore, the balance between melatonin and 2-OHM is capable of regulating various physiological processes such as seed germination, senescence, and embryogenesis. It should be noted that 2-OHM is in equilibrium with its tautomeric form, 2-acetamidoethyl-5-methoxyindolin-2-one (AMIO) (Hardeland 2017, 2019), which in turn has a low antioxidant capacity (Pérez-González et al. 2017), making it difficult to eliminate, and although its exact distribution in plant cells is not known. AMIO is located in lipid droplets or compartments with many membranes such as chloroplasts or mitochondria. It is involved in the activation of MAP kinases against pathogens (Lee and Back 2016a) and protects against abiotic stresses such as low temperatures and drought (Lee and Back 2016b). Therefore, it is in turn an active biomolecule that complements the physiological effects of phytomelatonin.

1.4.2 Cyclic 3-hydroxymelatonin (3-OHM)

3-OHM is a hydroxy metabolite derived from phytomelatonin resulting from the action of M3H activity; it exhibits an antioxidant effect dealing with $\cdot\text{OH}$ and hydroperoxyl radical ($\cdot\text{OOH}$) (Tan et al. 2014; Galano et al. 2014). This cytoplasmic enzyme shares only a 2-ODD domain with M2H, but it shows a low M2H activity in rice. Owing to the catalytic efficiency of M3H being even higher than M2H, and the endogenous levels of 3-OHM are higher than 2-OHM; thus, phytomelatonin is rapidly transformed into 3-OHM (Lee et al. 2016).

In addition, the 3-OHM levels are maximum at night and when overexpressed *M3H* mutants, the secondary tiller number is increased in rice (Choi and Back 2019a), whereas in *Arabidopsis thaliana*, M3H knockout (*m3h*) exhibited less growth and antioxidant activity resulting in a delayed flowering phenotype, due to the suppression of *Flowering Locus T* gene (*FT*), indicating that this hydroxymetabolite promotes plant growth and reproduction. Furthermore, *m3h* plants had lower total biomass per plant and are smaller than the wild-type, owing to a lower expression of *GA* genes, such as *KS*, *GA3ox1*, and *GA3ox2*. Also, since no differences were found in the length of the root in response to saline stress (100 mM NaCl for 3 weeks) or the pathogen (*Pseudomonas syringae* pv. Tomato DC3000) compared to wild-type, it was concluded that 3-OHM is not involved in the response to infections by pathogens or saline stress (Lee and Back 2022b)

1.5 Phytomelatonin and Antioxidant System Under Physiological and Stress Conditions

The exogenous application of melatonin has commonly been used at the experimental level due to its priming effects, protecting the plants against different types of environmental stresses, both of biotic and abiotic origin (Debnath et al. 2018, 2019; Dai et al. 2020; Mohamadi Esboei et al. 2022; Xie et al. 2022a, b). One of the most widespread aspects is that many types of stress lead to a marked increase in the generation of ROS, which usually triggers oxidative damage at the level of membranes as well as certain cellular components (nucleic acid, proteins, and lipids), affecting their functionality (Siddiqui et al. 2020; Ren et al. 2022). Table 1.3 contains some examples in which it is shown how melatonin applied in different ways and diverse plant species causes an increase in the main antioxidant systems, which makes it possible to control the exacerbated production of ROS and, therefore, alleviate its associated damage. Among the most studied are the enzymatic antioxidants including the peroxisomal catalase (CAT), the different superoxide dismutase (SOD) isozymes, components of the ascorbate-glutathione pathway including ascorbate peroxidase (APX), monodehydroascorbate peroxidase (MDAR), dehydroascorbate reductase (DHAR) and glutathione reductase (GR) as well as non-enzymatic antioxidant including ascorbate and glutathione (GSH) and the peroxidase

Table 1.3 Main effects of exogenous application of melatonin in different plant species

Plant species	mM MT	Method of application	Main effects of ROS metabolism	References
Peach (<i>Prunus persica</i> L.)	0.1	Immersion for 10 min	Increases of SOD and APX activities. Accumulation of ascorbate. Reduces the content of O ₂ ⁻ and H ₂ O ₂ . Delays postharvest senescence.	Gao et al. (2016)
Sweet cherry (<i>Prunus avium</i> L.)	0.1	Immersion for 5 min	Increases the activity of SOD, CAT, APX, and GR activity. Decreases the content of O ₂ ⁻ , H ₂ O ₂ and MDA. Reduces the electrolyte leakage and increases the membrane integrity.	Wang et al. (2019)
Mango (<i>Mangifera indica</i> L.)	0.2	Immersion for 30 min	Decreases H ₂ O ₂ and MDA contents in the exocarp of the fruit, delaying the ripening process	Dong et al. (2021)
Blueberry (<i>Vaccinium corymbosum</i> L.)	1.0	Immersion for 30 min	Improves antioxidant system in the fruits such as catalase, SOD, APX, AsA, polyphenols, flavonoids, and anthocyanins during cold storage and reduces qualitative decay	Magri and Petriccione (2022)
Apple (<i>Malus domestica</i> L. Borkh)	1.0	Spray	Increases the activity of catalase, SOD, and peroxidase. Reduces ethylene production Keeps apple quality during postharvest storage.	Onik et al. (2021)
Bermudagrass (<i>Cynodon dactylon</i> L. Pers)	0.02 and 0.1	Irrigated for 7 days	Significant improve of cold, drought and salt stress tolerance exhibiting higher chlorophyll content and survival rate, and lower electrolyte leakage	Shi et al. (2015)
Cucumber (<i>Cucumis sativus</i> L.)	0.05 and 0.5	Immersion for 5 days	Improves seed germination and viability against cold stress enhancing SOD and GR activity and show a lower H ₂ O ₂ content	Marta et al. (2015)
Cucumber (<i>Cucumis sativus</i> L. 'Jinyou 28')	0.1	Spray	Improves resistance against <i>Fusarium oxysporum</i> fungi disease decreasing H ₂ O ₂ and MDA content and electrolyte leakage	Ahammed et al. (2020)
Wheat (<i>Triticum aestivum</i>)	0.05 and 0.1	Immersion for 7 days	Alleviates the growth inhibition of wheat seedlings under cadmium stress (0.2 mM cadmium)	Ni et al. (2018)
Cotton (<i>Gossypium hirsutum</i> L.)	0.015	Added to the nutrient solution	Seed pre-treatment with melatonin protects cotton seedlings from cadmium-induced oxidative injury by increasing the activities of CAT, SOD, APX and POD.	Khan et al. (2022b)
Pigeon pea (<i>Cajanus cajan</i>)	0.050	Added to the nutrient solution	Under salt, drought, and heat stresses, melatonin treatment triggers the enrichment of flavonoids and mediates the reprogramming of biosynthetic pathway genes	Song et al. (2022)

APX ascorbate peroxidase, AsA ascorbate, CAT catalase, GR glutathione reductase, GSH reduced glutathione, MDA malondialdehyde, POD peroxidase, SOD superoxide dismutase

(POD) family (Mohamadi Esboei et al. 2022). Likewise, melatonin applies exogenously also triggers the biosynthesis of secondary metabolites which possess antioxidant capacities such as phenolic or terpene derivatives, for example, flavonoids, isoflavones, or carotenoids (Sun et al. 2020a, b; Jafari and Shahsavari 2021; Yin et al. 2022a, b; Corpas et al. 2023).

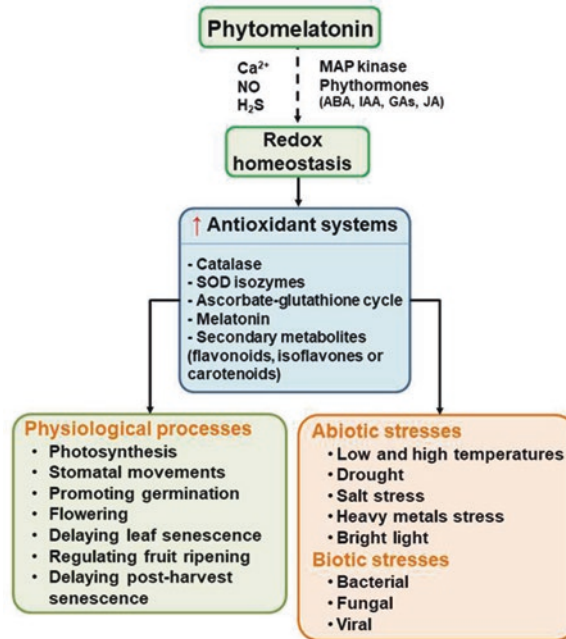
The cascade of signals which mediate how melatonin triggers these antioxidant systems including its own biosynthesis is still poorly understood (Khan et al. 2022a). At present, there is a battery of interactions among melatonin and other cellular components which seem to participate including calcium (Siddiqui et al. 2020; Tian et al. 2022), mitogen-activated protein kinase (MAPK) cascades (Lee and Back 2021b; Ma et al. 2022; Maity et al. 2022; Xie et al. 2022b), nitric oxide (Zhao et al. 2018; Feng et al. 2021; Imran et al. 2022; Yin et al. 2022a, b), hydrogen sulfide (Kaya et al. 2022; Wang et al. 2022a), phytohormones such as abscisic acid (Guo et al. 2022), indole-3-acetic acid (Zhang et al. 2022a, b), gibberellins (Arabia et al. 2022) or jasmonic acid (Ding et al. 2022; Wang et al. 2022a, b) as well as transcription factors. For example, melatonin treatment of pigeon pea triggers an increase in the expression of flavonoid 3' hydroxylase (*F3'H*) family which encodes for enzymes involved in the biosynthesis of luteolin; this may be a result of the transcription factor PhytoClock1 (PCL1) directly being bonded to the *F3'H-5* promoter to enhance its expression that finally promotes an increase resistant to different stresses (Song et al. 2022).

1.6 Concluding Remarks

At present, melatonin is recognized as a master molecule in animal and plant systems because in addition to its highly diverse antioxidant properties (Manchester et al. 2015; Reiter et al. 2016), it has signaling capacities to stimulate a variety of metabolic pathways (Back 2021). Among them, the main enzymatic and non-enzymatic antioxidant systems are highly implicated since they respond to melatonin allowing it to exert its beneficial effects to palliate the oxidative stress associated with different types of environmental stress. Therefore, melatonin initiates the cascade of signals and exerts its beneficial effects to counteract potential oxidative damage. Melatonin exhibits coordinated activities with a battery of other signaling molecules including calcium, MAP kinase, phytohormones, nitric oxide, or hydrogen sulfide. Figure 1.2 shows a working model where the main effects triggered by melatonin are summarized particularly where they relate to antioxidant systems; these systems have high relevance to the regulation of diverse physiological processes as well as to the mechanism of response to environmental stresses where oxidative metabolism usually is a significant feature. One aspect of melatonin that has attracted the attention of many plant researchers is its biotechnological potential, since the exogenous application of melatonin makes it possible to alleviate oxidative damage in the face of numerous types of stresses, but also due to its application in the horticultural industry since it is involved in maintaining the quality of horticultural products throughout their postharvest storage (Aghdam et al. 2023; Corpas et al. 2022a, b).

Fig. 1.2 Model of actions of melatonin

(phytomelatonin) in higher plants under physiological and stress conditions where the antioxidant systems play a key function. The mechanism of melatonin modulation of the different antioxidant systems seems to be mediated by different signaling molecules including calcium (Ca^{2+}), nitric oxide (NO), hydrogen sulfide (H_2S), mitogen-activated protein (MAP) kinase, and phytohormones such as abscisic acid (ABA), indole-3-acetic acid (IAA), gibberellins (GAs) or jasmonic acid (JA)



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