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# Exogenous Melatonin Enhances Cd Tolerance and Phytoremediation Efficiency by Ameliorating Cd-Induced Stress in Oilseed Crops: A Review

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## Abstract

Heavy metal pollution is of increasing global concern as it adversely impacts different spheres including pedosphere, hydrosphere, biosphere, and humansphere. Cadmium (Cd) contamination of agriculture soil has become a thoughtful challenge across the globe due to uncontrolled anthropogenic activities, limiting agricultural productivity and disturbing eco-environment sustainability. Sustainable mitigation strategies are, therefore, required for effective Cd decontamination. Biostimulation is a promising method to improve and stimulate life processes of plants in general and oilseed crops in particular, without posing threats to eco-environment sustainability and safer food production. Melatonin (*N*-acetyl-5-methoxytryptamine), a recognized pleiotropic molecule, has emerged as a research highlight regarding its role as an effective natural plant growth promoter, a broad spectrum antioxidant, and more specifically an efficient biostimulator to improve Cd-induced tolerance of plants for phytoremediation purposes and simultaneous biofuel production. This review provides a novel insight to understand the multifunctional role of melatonin in improving Cd phytoremediation capacity together with reducing phytotoxicity in oilseed crops, which was not previously assessed. Among oilseed crops, *Brassicaceae* spp. have unique stress adaptive mechanisms with exceptionally high Cd accumulating capabilities, apart from the diverse agri-horticultural importance. Interestingly, the discovery of dynamic approaches regarding melatonin application helped to better understand the basic mechanisms involved in melatonin-mediated responses against Cd stress in oilseed crops. Our review will provide a useful basis for the development of alternative strategies to genetically engineer low-Cd-content oilseed crops, with the aim of improving eco-friendly crop production and ensuring food safety. Furthermore, future researches will be supposed to provide more genetic evidences about Cd-induced melatonin regulation in higher plants.

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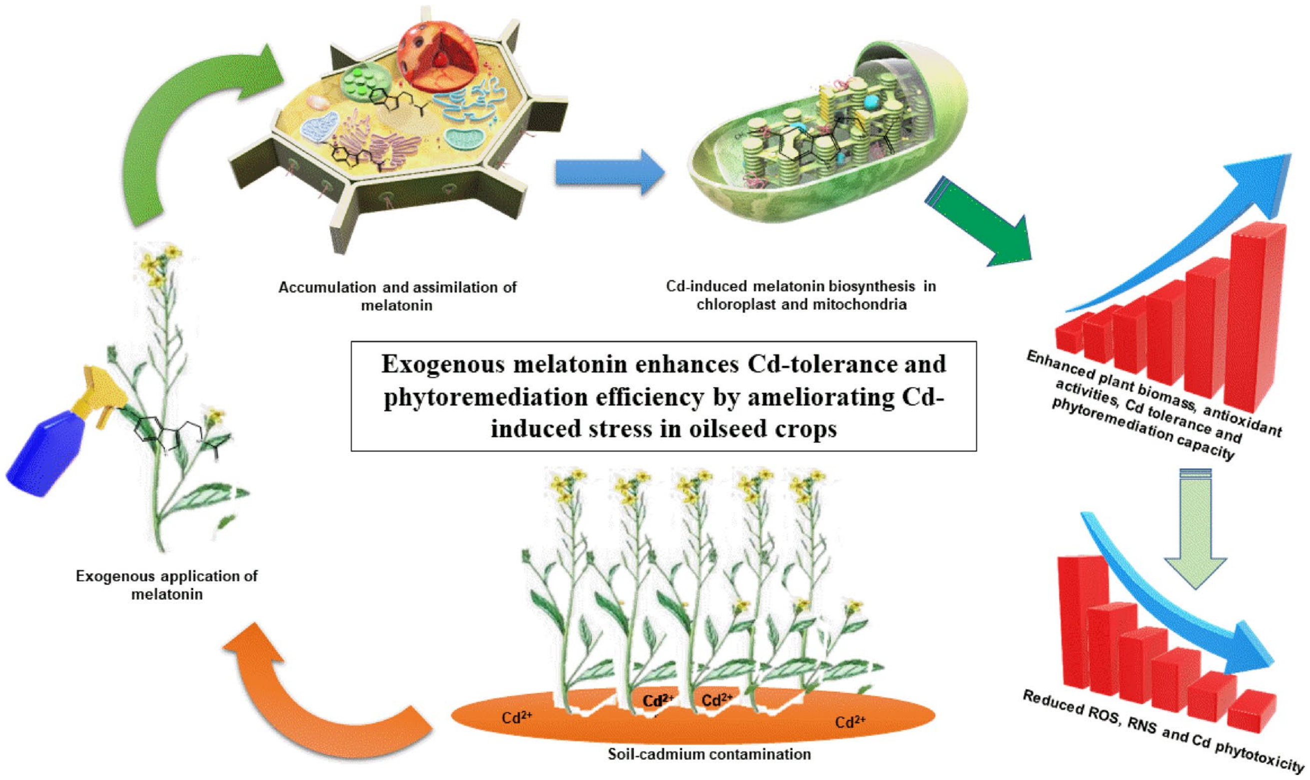
## Graphic Abstract



**Keywords** Melatonin · Biostimulant · Plant tolerance · Indole-3-acetic acid (IAA) · Antioxidant · Heavy metals

## Background

Plants in general and crops plants in particular are prone to a variety of stresses among which, environmental constraints such as drought, heavy metals, salinity, UV radiation, and intensive agricultural inputs (i.e., herbicides and pesticides) are potentially limiting the agricultural productivity and growth worldwide (Kalefetoğlu and Ekmekci 2005; Arnao and Hernández-Ruiz 2014; Hasan et al. 2015; Ni et al. 2018; Sami et al. 2020). Heavy metal pollution is commonly associated with natural as well as anthropogenic activities such as rapid industrialization, urbanization, mining and vice versa, which consequently disturb eco-environment sustainability and reduce global plant productivity (Rubio et al. 1994; Tan et al. 2007b). Among the heavy metals, cadmium (Cd) is considered as one of the major non-biodegradable, non-essential, and widespread environmental pollutant, owing to its detrimental effects on different spheres (Fig. 1) including pedosphere, hydrosphere, biosphere, and humansphere (Bundschuh et al. 2017; Ni et al. 2018; Sami et al. 2020; Shah et al. 2020; Xu et al. 2020). Cd level tends to increase continuously in different environmental matrices (soil and water) due to uncontrolled anthropogenic activities such as mining and intensive use of pesticide and phosphate fertilizers (Tang et al. 2018; Wang et al. 2019; Nabaei and Amooaghaie 2019; Shah et al. 2020). Soil is an important growth medium for plants and beneficial microbes; however, Cd contamination of agricultural soil has become a thoughtful challenge for safer food production in developing countries (Clemens et al. 2013; Lin et al. 2018; Wang et al. 2019; Sabir et al. 2020; Xu et al. 2020). According to the statistical analysis, the estimated area of Cd pollution in China has reached $1.3 \times 10^4$ $hm^2$ (Ma et al. 2013; Lin et al. 2018).

Elevated levels of Cd in agricultural soil could bring about diverse anatomical, biochemical, physiological, metabolic, and morphological anomalies in plants (Li et al. 2016; Ni et al. 2018), which eventually leads to the

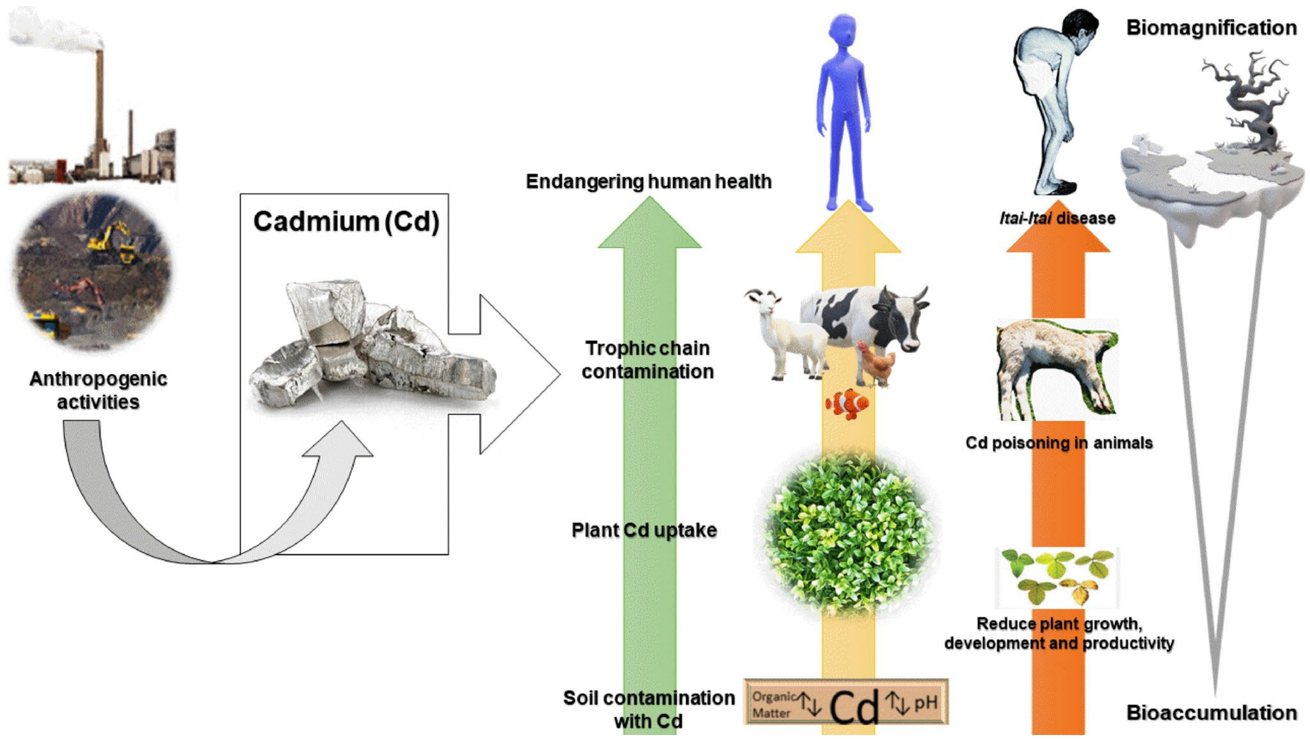


**Fig. 1** Impact of cadmium (Cd) on different spheres

production of reactive oxygen species (ROS) or reactive nitrogen species (RNS), plasma membrane damage, and $H^+$-ATPase inhibition, resulting in low biomass accumulation followed by reduced plant growth (Gupta et al. 2009; Janicka et al. 2012; Clemens et al. 2013; Mehmood et al. 2018; Nabaei and Amooaghaie 2019; Sabir et al. 2020). Additionally, Cd affects plant cell cycle and cell division, and causes chromosomal aberrations at cellular level, which ultimately result in malformed embryos (DalCorso et al. 2010; Hasan et al. 2015; Sami et al. 2020). Owing to high-water solubility, flexible specificity of ion channels and divalent Cd transporters, Cd is easily absorbed, accumulated, and thus assimilated in plant tissues (Liu et al. 2003; Hasan et al. 2015; Lin et al. 2018; Sabir et al. 2020). Cd as a toxic element (Fig. 1) is of increasing concern, not only because of its phytotoxic effects on crop production, but also due to potential human health hazards, including carcinogenicity, mutagenicity, and teratogenic effects associated with trophic chain contamination (Deng et al. 2010; Ajjimaporn et al. 2012; Kretsinger et al. 2013; Prasad and Strzalka 2013; Hasan et al. 2015; Lin et al. 2018).

Remediation of Cd-contaminated soil is, therefore, a global challenge for achieving sustainable development goals (SDGs). Conventional physicochemical remediation techniques are costly, deteriorating soil ecological balance (loss of soil nutrients) and causing secondary pollution (Liu et al. 2018; Nabaei and Amooaghaie 2019; Hayat et al. 2020a, b, c; Wang et al. 2020). Consequently, it is prime to find out economical, eco-friendly, and sustainable approaches for Cd decontamination in agricultural soils. Nonetheless, phytoremediation, an environment friendly, low-cost, and highly stable green technology for decontamination of Cd-contaminated soil or water has attracted the global attention of scientific community away from conventional physicochemical remediation technologies (Pulford and Watson 2003; Marques et al. 2009; Ali et al. 2013b; Ullah et al. 2015; Arnao and Hernández-Ruiz 2019d; Nabaei and Amooaghaie 2019; Hayat et al. 2020b; Wang et al. 2020; Xu et al. 2020; Yan et al. 2020). However, this biotic approach has certain limitations of its own e.g., low bioavailability of Cd in contaminated soils, slow growth rate, low biomass production, and limited number of Cd hyper-accumulator plants (Tang et al. 2018; Arnao and Hernández-Ruiz 2019d; Hayat et al. 2020b; Wang et al. 2020). Hyperaccumulators are plants that accumulate far exceeding levels of heavy metal in their aboveground tissues than non-accumulating plants (Ali et al. 2013b). Several studies have shown that most of the world's oilseed crops, including *Brassicaceae* species, cottonseed, groundnut, linseed, safflower, sesame seed, soybean, and sunflower, have rapid growth rates, high agro-economic value besides elevated Cd accumulation and tolerance capabilities (Arnao 2014; Mailer 2016; Arnao and Hernández-Ruiz 2019d). However, a marked slowdown in the expansion and/or production of oilseed crops was observed over the past two decades as a result of competing standard conventional crops, environmental constraints, and reduced surface of arable land (Mailer 2016).

Fortunately, with the increasing concern to expand oilseed production, people have become interested in the use of natural compounds and signal molecules, including plant growth promoters, biostimulators, and/or bioregulators. The role of auxin (indole-3-acetic acid; IAA), abscisic acid, brassinosteroids, ethylene, gibberellins, jasmonic acid, and salicylic acid to improve growth and Cd tolerance capability of edible crops are well documented in the literature (Masood et al. 2012; Ahammed et al. 2013; Stroiński et al. 2013; Meng et al. 2014; Arnao and Hernández-Ruiz 2019d). Biostimulation is one of the most promising methods to improve and stimulate life processes of ecological crops, without posing threats to eco-environment sustainability and safer food production (Janas and Posmyk 2013). Therefore, finding potential biostimulators and/or bioregulators is necessary to enhance Cd phytoremediation capacity together with growth attributes of oilseed crops. Melatonin (*N*-acetyl-5-methoxytryptamine) is a natural compound and signal molecule that can mediate plant defensive responses under Cd stress (Tan et al. 2007a; Nawaz et al. 2016; Kanwar et al. 2018; Arnao and Hernández-Ruiz 2019d; Tiwari et al. 2020), indicating its possible role in improving growth and phytoremediation potential of plants.

Melatonin, identified by Hattori et al. (1995) in *Pharbitis nil* plants (Japanese morning glories) and by Dubbels et al. (1995) both in 1995, is a tryptophan-derived ubiquitous and pleiotropic molecule, which improves plant stress tolerance through physiological, biochemical, and molecular actions (Arnao and Hernández-Ruiz 2007a, 2019c; d; Hasan et al. 2015; Tang et al. 2018; Nabaei and Amooaghaie 2019; Sami et al. 2020; Xu et al. 2020). There are various morpho-physiological and biochemical aspects that have been investigated in which melatonin exerts countless beneficial actions (Arnao and Hernández-Ruiz 2006). These include improvements in seed germination, seed and fruit development, plant growth and vegetative development, photosynthetic processes (such as pigment contents, photorespiration, stomatal conductance and water status), osmoregulation (including ion exchange, adjustments in osmotic and hydraulic potentials), regulation of the primary and secondary metabolic activities, and delaying leaf senescence (Hernández-Ruiz et al. 2005; Arnao and Hernández-Ruiz 2006, 2009; Buttar et al. 2020; Zhao et al. 2021). In the secondary metabolism, melatonin induces the biosynthesis of flavonoids, anthocyanins, and carotenoids, among others. Melatonin also promotes the development of primary, secondary, and adventitious roots (Arnao and Hernández-Ruiz 2017). In fruit postharvest, melatonin regulates the contents of ethylene and lycopene as well as cell wall-related enzymes. Moreover, it also induces parthenocarpy in fruit set in addition to delayed fruit senescence and flowering (Arnao and Hernández-Ruiz 2020b).

Furthermore, melatonin differentially influence microbial communities in agricultural soils under abiotic stress conditions, depending on various factors such as type of microbes, type of soil, and soil physicochemical characteristics (Madigan et al. 2019). Lastly, its role in combating bacterial, fungal, and viral pathogenic infections should be emphasized: Melatonin, as a signaling molecule, stimulates an effective defense mechanism against plant pathogens, known as “systemic acquired resistance (SAR), which contributes to plant protection and crop health (Moustafa-Farag et al. 2020a).

Most of the previously described actions in which melatonin plays an important role are also related to changes in the expression of a wide variety of genes (Zhang et al. 2015; Yu et al. 2018; Debnath et al. 2019). Numerous genes are up- and/or downregulated by melatonin under different conditions (Wei et al. 2016; Fan et al. 2018; Ahn et al. 2021). The role of melatonin as a modulating agent in the gene expression of diverse elements of plant hormones, regulating the hormonal homeostasis in several physiological and stressing conditions, is one of the most controversial actions melatonin takes part in and is currently the subject of numerous studies (Arnao and Hernández-Ruiz 2018a, b; Hernández-Ruiz and Arnao 2018; Moustafa-Farag et al. 2020b).

The first report on phytoremediation potential of melatonin was published by Tan et al. (2007a), who observed different melatonin levels in water hyacinth [*Eichhornia crassipes* (Mart) Solms] under natural photoperiod conditions, suggesting a possible mediating role of melatonin biosynthesis in plant tolerance. From this study, several heavy metals (and non-metals) have been analyzed to study the role of melatonin as a biostimulatory agent against these toxic elements (Tan et al. 2007a; Arnao and Hernández-Ruiz 2019d). Also, many studies on the protective role of melatonin in different environmental stress conditions such as drought, waterlogging, salinity, high and low temperatures, among others, have been conducted. Some relevant reviews of this thematic can be consulted (Arnao and Hernández-Ruiz 2015; Li et al. 2019; Moustafa-Farag et al. 2020b; Tan and Reiter 2020; Tiwari et al. 2020). This review mainly focuses on the multifunctional role of melatonin in improving phytoremediation capacity and stress-induced tolerance of oilseed crops (with particular emphasis on oilseed rape) in response to Cd stress, which has not yet been assessed previously. Additionally, it addresses Cd-induced biosynthetic pathways, molecular and mechanistic basis of stress-induced melatonin response, and possible effects of melatonin applications on stress-induced response to determine melatonin-mediated Cd homeostasis and detoxification mechanisms in plants. Moreover, our review shall provide a useful basis for the development of alternative strategies to genetically engineer low-Cd-content oilseed crops, with the aim of improving eco-friendly crop production and ensuring food safety.

## Biosynthetic Pathways of Melatonin Under Cd Stress Condition

Cadmium-induced tolerance capabilities of plants are closely related to regulation of melatonin biosynthesis through multiple endogenous pathways (Janas and Posmyk 2013; Lee and Back 2017b; Mir et al. 2020; Tan and Reiter 2020). However, with limited knowledge available so far about metabolic pathways and/or regulation of melatonin biosynthesis under Cd stress condition, researchers round the globe have focused their attention to fully understand all of the associated mechanisms. Nevertheless, multiple melatonin biosynthetic pathways (i.e., NM and MN) exist (see Fig. 2), and all of them involve tryptophan as a primary precursor and serotonin as an intermediate (Bandurski et al. 1995; Arnao and Hernández-Ruiz 2007b, c; Tan and Reiter 2020). The main melatonin biosynthetic pathway (as shown in Fig. 2a) in plants under normal growth conditions or low cellular serotonin levels, which is also known as "NM pathway" is: (i) tryptophan/tryptamine/5-hydroxytryptamine (serotonin)/*N*-acetyl serotonin/melatonin (Ye et al. 2019; Tan and Reiter 2020). The four major steps involved in NM pathway are; (1) decarboxylation of tryptophan to tryptamine by tryptophan decarboxylase (TDC); (2) amine hydroxylation of tryptamine to 5-hydroxytryptamine (serotonin) by tryptamine 5-hydroxylase (T5H); (3) N-acetylation through either direct transformation from tryptamine or indirectly from serotonin to *N*-acetyl serotonin by serotonin *N*-acetyltransferase (SNAT) enzyme; and (4) O-methylation of *N*-acetyl serotonin to melatonin through variable *N*-acetylserotonin methyltransferase (ASMT) or caffeic acid *O*-methyltransferase (COMT) enzymatic pathways (Hardeland 2014; Back et al. 2016; Cai et al. 2017; Tan and Reiter 2020).

Alternatively, the dominant pathway under Cd stress or large amounts of serotonin (Fig. 2b); also known as "MN pathway" is: tryptophan/tryptamine/5-hydroxytryptamine (serotonin)/5-methoxytryptamine/melatonin (Cai et al. 2017; Lee and Back 2017b; Ye et al. 2019). In addition to ASMT or COMT enzymatic pathways; Cd-induced chloroplast disruption also has a crucial role in mediating melatonin biosynthesis in plants including oilseed rape, rice and tomato (Byeon et al. 2015a, b; Back et al. 2016; Cai et al. 2017; Lee and Back 2017a; Sami et al. 2020). Melatonin intermediates are produced in different subcellular portions of plant including chloroplasts, cytoplasm, mitochondria and endoplasmic reticulum (Back et al. 2016; Tang et al. 2018; Tan and Reiter 2020). Depending on the biosynthetic pathway,

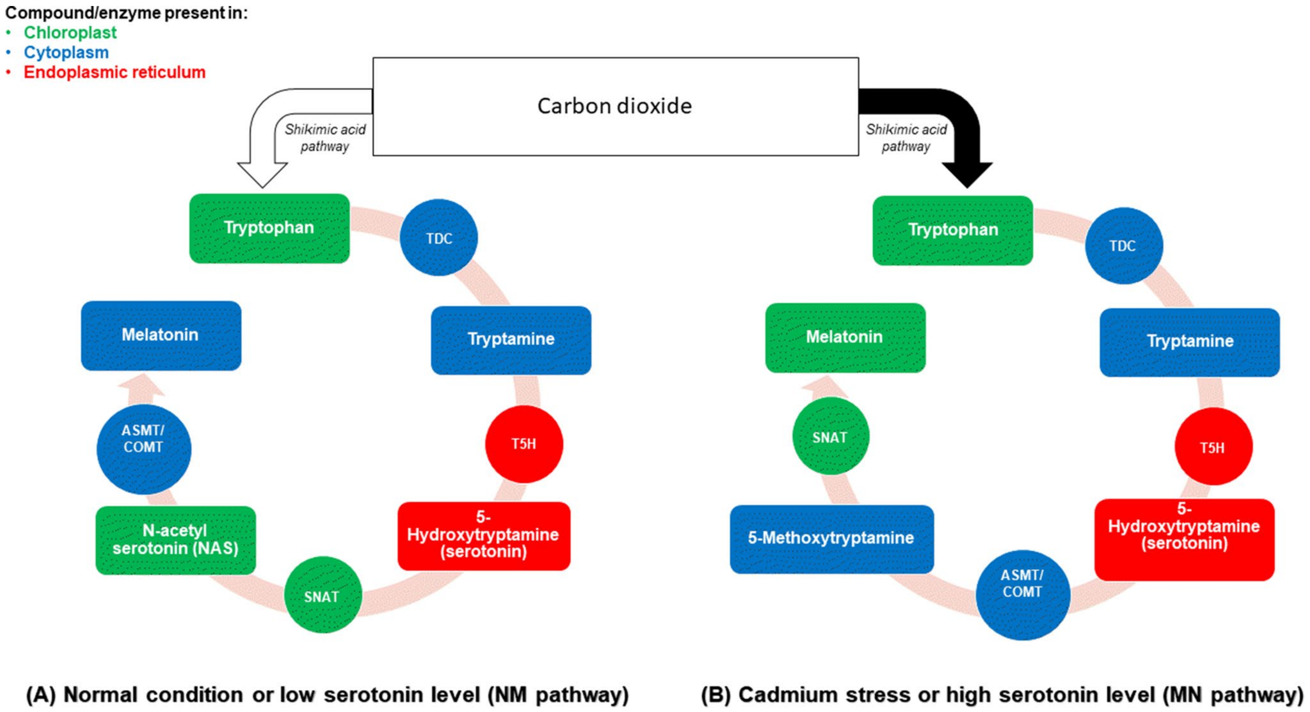


**Fig. 2** Generalized diagram of biosynthetic pathways of melatonin under **a** normal condition and **b** Cd stress in a plant with distinction to organelles. *TDC* tryptophan decarboxylase; *T5H* tryptophan hydrolase; *SNAT* serotonin *N*-acetyltransferase; *ASMT N*-acetyl serotonin *O*-methyltransferase; *COMT* caffeic acid *O*-methyltransferase

the final subcellular portion of melatonin biosynthesis can be either chloroplasts or mitochondria (Fig. 2), which are associated with different melatonin-induced stress responses in plants (Back et al. 2016; Mir et al. 2020; Tan and Reiter 2020).

## Molecular Basis of Melatonin Mediated Cd Stress Responses and Signal Transduction Pathways in Plants

Melatonin acts as a biostimulator and/or plant master regulator, which is capable of orchestrating many responses related to the redox network. The first molecular basis to elucidate melatonin-mediated stress response was demonstrated through transgenic induction in tomato and tobacco plants (Okazaki et al. 2009; Wang et al. 2009). Thereafter, an array of transgenic plants mainly upregulating or overexpressing (known as transgenic induction) melatonin-mediated genes including *RsMT1* (*Metallothionein 1*), miR166, serotonin *N*-acetyltransferase 1 (*OsSNAT1*), heat shock factor A1a (*HsfA1a*), caffeic acid *O*-methyltransferase 1 (*COMT1*), tryptophan decarboxylase 2 (*MeTDC2*)-interacting proteins, *N*-acetylserotonin *O*-methyltransferase 2 (*MeASMT2*) interacting proteins, and N-acetylserotonin *O*-methyltransferase 3 (*MeASMT3*) were generated to enhance Cd tolerance and uncover molecular basis of melatonin-mediated Cd stress response (Cai et al. 2017; Lee and Back 2017b; Nabaei and Amooaghaie 2019; Xu et al. 2020). However, little information is available about the stress-induced melatonin synthetic gene expression, genome-wide characterization of melatonin-induced miRNAome and transcriptome analysis under Cd stress. Moreover, molecular basis of Cd-induced melatonin response still remains obscure in oilseed and root vegetable crops.

Regarding stress-induced response, melatonin confers Cd tolerance by modulating critical heavy metal chelators including phytochelatines, glutathione and metallothionein; regulatory or signaling pathways i.e., salicylic acid, gibberellic acid, abscisic acid-dependent pathways and nitric oxide signaling cascade; transporters (such as ATP-binding cassette, heavy metal ATPase 4 (HMA4), natural resistance– associated macrophage protein (Nramp), pleiotropic drug resistance 8 (PDR8) and P1B ATPases); and generally mediating changes in gene such as FaHSFA3, FaAWPM, FaCYTC2, SAD, CAT, APX, MAPK, bZIP60, BIP2, BIP3, CNX1, CDPK1, MAPK1, TSPMS, ERF4, HSP80 and ERD15 expression (Arnao and Hernández-Ruiz 2019d; Debnath et al. 2020; Mir et al. 2020; Tiwari et al. 2020; Xu et al. 2020). Most of the previously described actions in which melatonin play a multifunctional role are related to changes in the expression of a wide variety of melatonin biosynthetic genes. Seemingly, five genes namely TDC, T5H, SNAT, ASMT, and COMT have been involved in Cd-induced melatonin biosynthesis (Fig. 2), that improve stress tolerance in plants (Back et al. 2016; Lee and Back 2017a; Lee et al. 2017; Ni et al. 2018). Overexpression of these genes enhances Cd-induced positive melatonin response, while suppression of these genes inhibit stress-induced melatonin response (Byeon et al. 2015b). In addition, the self-activation of COMT is a beneficial approach to enhance melatonin accumulation and thus mitigate heavy metal stress in higher plants (Sami et al. 2020). For example, in *B. napus* treated with Cd, the expression of caffeic acid *O*-methyltransferase (BnCOMT) genes including BnCOMT-1, BnCOMT-5 and BnCOMT-8 is upregulated with an increase in melatonin level, suggesting a possible link between phytomelatonin and COMT in augmenting stress tolerance in oilseed crops (Sami et al. 2020). Likewise, the *Arabidopsis thaliana* gene for caffeic acid *O*-methyltransferase (AtCOMT) is responsible for catalyzing the conversion of *N*-acetylserotonin into melatonin (Byeon et al. 2014a, b, c, 2015a).

Furthermore, generation of reactive oxygen species (ROS) and reactive nitrogen species (RNS) also induces the expression of the melatonin biosynthesis genes, which leads to increased melatonin level in the stressed tissues (Arnao and Hernández-Ruiz 2019a, c). As a result of the increase in endogenous melatonin through the induction of its biosynthesis genes, or as a result of the application of exogenous melatonin, a direct ROS/RNS antioxidant action by melatonin has been described in several studies (Tan et al. 2007b; Arnao and Hernández-Ruiz 2019a). Exogenous melatonin treatments also induced these melatonin biosynthesis transcripts, showing melatonin to be its own regulator. This gives an idea of the importance of this molecule as an anti-stress manager, which is why it has been called a plant master regulator (Arnao and Hernández-Ruiz 2020a). The role of melatonin as a modulating agent in the gene expression of diverse elements of plant hormones, regulating the hormonal homeostasis in several physiological and stressing conditions, is one of the most controversial actions melatonin takes part in and is currently the subject of numerous studies (Arnao and Hernández-Ruiz 2018a, b; Hernández-Ruiz and Arnao 2018; Moustafa-Farag et al. 2020b).

## The Mechanistic Basis of Melatonin Mediated Cd Stress Responses in Oilseed Crops

Plants have developed complex Cd detoxification and tolerance mechanisms, such as limiting Cd translocation to harvestable parts (or immobilization), binding Cd to the cell wall epidermis, Cd chelation by phytochelatins (PCs) and metallothioneins (MT), Cd compartmentalization in the vacuole, and activation of the antioxidant system to repair structural alteration in cell (Leitenmaier and Küpper 2013; Nabaei and Amooaghaie 2019). Of these, Cd-induced PCs synthesis is regarded as “first line of defense mechanism” against Cd stress, that involve Cd chelation by PC-Cd complex formation and its sequestration into the vacuole (Park et al. 2012; Hasan et al. 2015). Moreover, Cd has been considered as one of widely assayed heavy metals along with most efficient elicitor of melatonin induction and/or biosynthesis in a range of melatonin-treated plants including radish (Xu et al. 2020), rice (Byeon et al. 2015b; Lee and Back 2017a, b; Liu et al. 2016), tomato (Cai et al. 2017; Umapathi et al. 2018a, b) and wheat (Ni et al. 2018). Melatonin improves stress-induced osmotic tolerance capability in plants via regulation of root growth and development through cell elongation and cell division, as well as enhancing nutrients and water uptake. Melatonin was reported to enhance IAA contents along with associated root proliferation characteristic in *Brassica juncea* and *Lupinus albus* (Hernandez-Ruiz et al. 2004; Arnao and Hernández-Ruiz 2007a; Chen et al. 2009). Likewise, melatonin improves plant’s antioxidant capacity under Cd stress by acting as an intermediate in the redox cycle, thereby augmenting oxidative stress tolerance capability of plants (Reiter et al. 2001; Cai et al. 2017).

Moreover, Cd stress modulates melatonin biosynthetic pathway in plants, describing the mechanism of plant stress response by alleviating Cd-induced phytotoxic symptoms such as chloroplast disruption and ruptured mitochondria (Tal et al. 2011; Lee and Back 2017a). Exogenous application of melatonin via root system, in irrigation water, seed coating or by spraying leaves confers Cd tolerance in plants (Janas and Posmyk 2013; Arnao and Hernández-Ruiz 2014, 2019a; b, d; Cai et al. 2017; Tang et al. 2018). According to the previously reported literature, exogenously applied melatonin alleviated Cd stress by its well-documented plant growth and antioxidant activities (Arnao and Hernández-Ruiz 2019a; Mir et al. 2020). Additionally, melatonin contributes to the phenomenon of phytoremediation at the cellular level (as shown in Fig. 3) known as “melatonin-induced Cd tolerance responses”, which include increase in the antioxidant capacity, reduction of ROS and RNS (via ROS- melatonin redox network), the improvement in the battery of antioxidant enzymes (SOD, CAT, POX, GPX, etc.), improvement in the ASA-GSH cycle, osmoregulatory response (via proline, GABA accumulation), activation of N, P, S transporters in roots and activation of PCs (that results in Cd sequestration, transport and storage in vacuoles) (Arnao and Hernández-Ruiz 2009; Janas and Posmyk 2013; Hasan et al. 2015; Reiter et al. 2015; Cai et al. 2017; Zhang et al. 2017; Nawaz et al. 2018; Ni et al. 2018). Cd sequestration is considered to be one of the prime biostimulatory effects of melatonin on plants to improve plant tolerance against Cd stress (Arnao and Hernández-Ruiz 2019d). Strikingly, exogenous melatonin application alleviated Cd

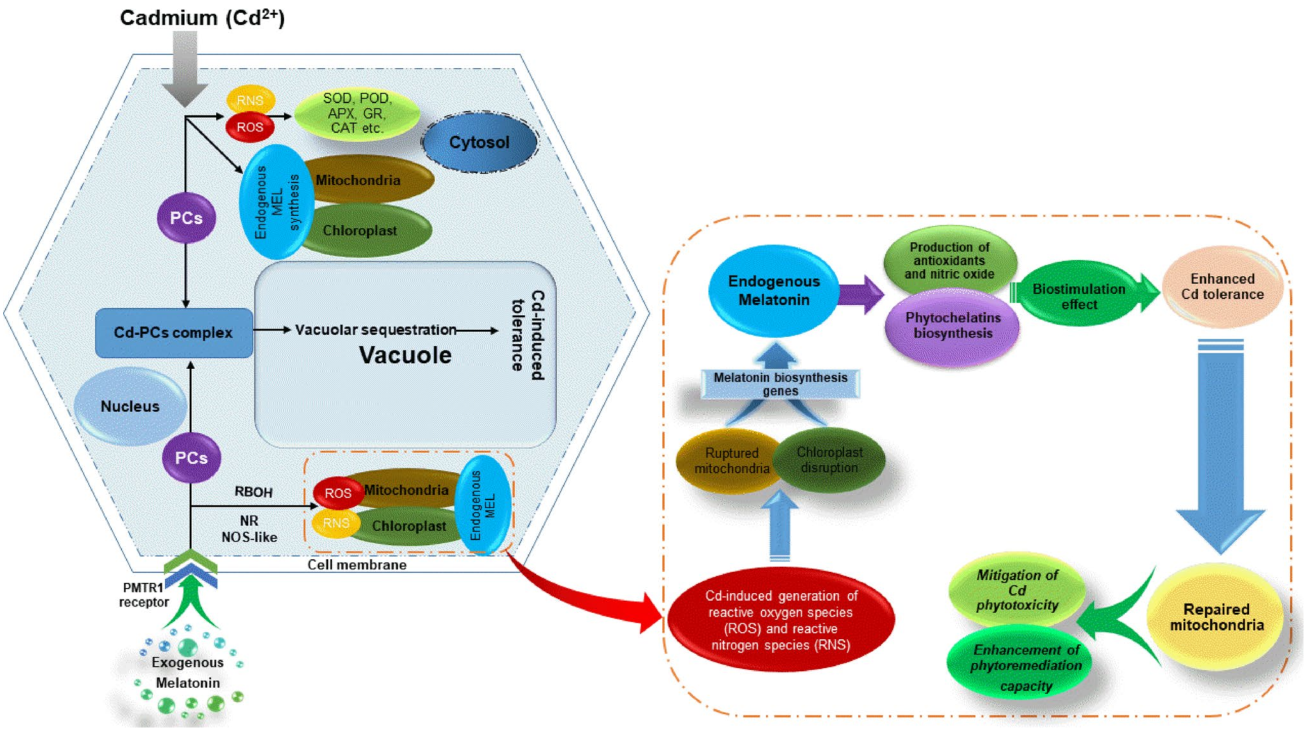


**Fig. 3** A detailed model of Cd-induced melatonin-positive responses and its impact on plant growth, tolerance capability, and phytoremediation capacity. *PMTR1* phytomelatonin receptor 1

phytotoxicity through modulation of vacuolar sequestration, antioxidant potential, and phytochelatins biosynthesis while demonstrating enhanced Cd tolerance capability in alfalfa, *Cyphomandra betacea*, tomato, and wheat against Cd stress (Hasan et al. 2015; Tang et al. 2018; Arnao and Hernández-Ruiz 2019a). In addition, exogenous melatonin treatments enhanced stress tolerance capability of Bermuda grass under a range of abiotic stresses including cold, drought and NaCl (Shi et al. 2014).

The development of excellent strategies for phytoremediation purposes contributed to the insight into melatonin-induced Cd tolerance mechanisms. These strategies include exogenous melatonin application, inducing melatonin biosynthesis endogenously via environmental elicitors, mediating the absorption and metabolism of nutrients (i.e., N, P, and S), unraveling biostimulatory effect of melatonin and using transgenic plants that over-accumulate melatonin (Arnao and Hernández-Ruiz 2019d). Nevertheless, information about the impact of melatonin on enhancing melatonin-induced PC biosynthesis, Cd accumulation and/or Cd tolerance in higher plants still remains elusive due to lack of genetic evidences. It is worth nothing that Hasan et al. (2019) provided genetic evidences for melatonin-induced Cd tolerance in *Solanum lycopersicum*, that might be associated with the efficient regulation of sulfur metabolism, redox homeostasis, and Cd translocation. Several authors (Liu et al. 2017; Lin et al. 2018; Tang et al. 2018; Umapathi et al. 2018a, b; Nabaei and Amooaghaie 2019; Bose and Prianka 2020; Mir et al. 2020; Tiwari et al. 2020) demonstrated concentration-dependent responses of melatonin towards Cd contents and/or accumulation (as shown in Tables 1 and 2) in different tissues (roots, stems, leaves) of plant species, suggesting melatonin could improve plant tolerance as well as provide basis for simultaneous biofuel production. In order to prove a reference point for improving growth and Cd remediation potential of hyperaccumulator plants, appropriate screening methods should be adopted to determine optimum melatonin concentration. In view of the above information, it is suggested that optimal concentration of melatonin should not only be applied exogenously to improve plant growth, but also enhance Cd accumulation and phytoremediation capacity of oilseed crops.

Oilseed crops have great economic as well as agronomic value and are grown mainly for its high proteinaceous seeds (Diepenbrock 2000; Sami et al. 2020). Among oilseed crops, *Brassicaceae* spp. have unique stress adaptive mechanisms with exceptionally high Cd accumulating capabilities, apart from the diverse agri-horticultural importance; for example, high (35%) nutritional value in addition to biofuel production (Belimov et al. 2005; Gall and Rajakaruna 2013; Sami et al. 2020). According to the FAOSTAT (2013), *Brassica* oilseeds annually occupies more than 34 million hectares of land worldwide. Within genus Brassica, six economically important species: *Brassica campestris, Brassica carinata*, *Brassica juncea*, *Brassica oleracea, Brassica rapa*, and *Brassica napus* are altogether termed as “Rapeseed-mustard group” (Roy and Mondal 2020) while displaying “U’s relationship triangle” between the species (Nagaharu 1935). Furthermore, *B. napus* (rapeseed) and *B. juncea* (Indian mustard) are listed as the second and third most vital source of oil around the globe, containing about 14% of edible vegetable oil and 40–42% of biofuel oil, in addition to high biomass productivity, enhanced Cd accumulation and Cd tolerance capacity (Salt et al. 1995; Fusco et al. 2005; Farinati et al. 2010; Arnao and Hernández-Ruiz 2019d), highlighting its pivotal role in food security and phytoremediation of Cd-contaminated areas. Addae et al. (2010) demonstrated that *B. oleracea* species can phytoextract elevated levels of Cd and Pb. Nonetheless, Cd stress causes phytotoxic effects in *B. napus* when grown under 500 μM $L^{-1}$ Cd concentration

**Table 1** Impact of melatonin application on Cd accumulation in plants

| S. no. | Plant | Biostimulator | Pollutant | Optimal MEL concentration (μM) | Cd accumulation capacity enhancement (%) | References |
|---|---|---|---|---|---|---|
| 1. | *Solanum melongena* | Melatonin | Cd | 150 | – | Tang et al. (2015) |
| 2. | *Solanum lycopersicum* | Melatonin | Cd | 100 | – | Hasan et al. (2015) |
| 3. | *Cyphomandra betacea* | Melatonin | Cd | 50 | 29 | Lin et al. (2018) |
| 4. | *Galinsoga parviflora* | Melatonin | Cd | 100 | 68 | Tang et al. (2018) |
| 5. | *Malachium aquaticum* | Melatonin | Cd | 200 | 16 | Tang et al. (2018) |
| 6. | *Alfalfa* | Melatonin | Cd | 10–200 | – | Gu et al. (2017) |
| 7. | *Solanum lycopersicum* | Melatonin | Cd | 25–500 | – | Cai et al. (2017), Hasan et al. (2015, 2019), Umapathi et al. (2018a, b) |
| 8. | *Triticum aestivum* | Melatonin | Cd | 50–100 | – | Kaya et al. (2019), Ni et al. (2018) |
| 9. | *Perilla frutescens* | Melatonin | Cd | 150 | 227 | Xiang et al. (2019) |
| 10. | *Cucumis sativus* | 2-Hydroxymelatonin | Cd | 100 | – | Shah et al. (2020) |

**Table 2** Effect of exogenous melatonin on physiological, biochemical, molecular anomalies, Cd tolerance and phytoremediation efficiency of plants (Color table online)

| S.No | Plant | Study scale | Experiment duration (days) | Medium | Cadmium (Cd) source | Cd conc. | Optimal Cd conc. | Melatonin (MEL) application | Doses | MEL conc. | Optimal MEL conc | Observations | References |
|---|---|---|---|---|---|---|---|---|---|---|---|---|---|
| 1. | Tomato (*Solanum lycopersicum* L. cv.AilsaCraig) | Pot/ Greenhouse | 14 | Soil-less culture (vermiculite and perlite) and hydroponics | $CdCl_2$ | 25 and 100 µM | 100 µM | Exogenous/ Foliar | split | 0, 25, 50, 100, 250, and 500 µM | 100 µM. | ↑Cd and melatonin contents<br>↓Cd-induced phytotoxicity | (Hasan et al. 2015) |
| 2. | Tamarillo (*Cyphomandra betacea*) | Pot | 40 | Combined soil-less (vermiculite and pearlite medium) and soil | $CdCl_2·2.5H_2O$ | 10 mg L$^{-1}$; 10 mg kg$^{-1}$ | - | Exogenous | split | 0, 50, 100, 150, and 200 µM | 50 µM | ↑low MEL level: antioxidant enzyme activities, plant growth<br>↑50 µM MEL: Cd contents in stems, leaves, and shoots<br>↓high MEL: seedling biomass, photosynthetic pigment contents, antioxidant enzyme | (Lin et al. 2018) |
| 3. | Stone Bamboo (*Malachium Aquaticum*) and Gallant Soldier (*Galinsoga parviflora*) | Pot/ Greenhouse | 70 | Soil | $CdCl_2·2.5H_2O$ | 10 mg kg$^{-1}$ | 10 | Exogenous/ Foliar | split | 50, 100, 150 and 200 µM L$^{-1}$ | 100 (*G. parviflora*), 200 (*M. Aquaticum)* µM L$^{-1}$ | ↑shoot biomass, photosynthetic pigment content and antioxidant enzyme activity<br>↑Cd content in shoots of *G. parviflora*<br>↑high MEL (200 µM L$^{-1}$): Cd accumulation in *M. aquaticum*<br>↑low MEL (100 µM L$^{-1}$): Cd accumulation in in *G. parviflora*<br>↓Cd content in shoots of *M. aquaticum* | (Tang et al. 2018) |
| 4. | Wheat (*Triticum aestivum* cv. Lianmai) | Petri plates/laboratory | 5 | - | $CdCl_2$ | 200 mM | - | Exogenous | single | 50 mM | - | ↑plant height, biomass accumulation, and root growth<br>↑GSH (reduced glutathione) content and the GSH/GSSG (oxidized glutathione) ratio, ascorbate peroxidase (APX) and superoxide dismutase (SOD)<br>↑expression of melatonin biosynthesis-related genes<br>↑endogenous melatonin level, the hydrogen peroxide homeostasis via regulation of the antioxidant systems<br>↓cadmium toxicity, level of hydrogen peroxide, catalase (CAT) and peroxidase (POD) | Ni et al. 2018 |
| 5. | Periwinkle (*Catharanthus roseus* L. G. Don) | Petri plates/ laboratory | 10 | - | $CdSO_4.8H_2O$ | 0, 50, 100, 200, 400, 800 µM | 50 µM | Exogenous | single | 0, 50, 100, 200, and 400 µM | 100 µM | ↑seed germination, germination rate, seedling length, and vigor index<br>↑NO content in seeds | (Nabaei and Amooaghaie 2019a) |
| 6. | Periwinkle (*Catharanthus roseus* L. G. Don) | Pot/greenhouse | 120 | Soil | $CdSO_4$ | 50, 100, 200 mg kg$^{-1}$ | 50 | Exogenous/ Foliar | split | 100 µM | 100 µM | ↑shoot biomass, chlorophyll *a* and *b* content, POD and CAT activities, ↑leaf essential cationic homeostasis, tolerance capability,<br>↑Cd accumulation and phytoremediation efficiency<br>↑Cd uptake and translocation from root to shoot<br>↑root and shoot bioconcentration factor (BCF) and translocation factors (TF).<br>↓electrolyte leakage | (Nabaei and Amooaghaie 2019b) |
| 7. | Radish (*Raphanus sativus*) | Growth chamber/ laboratory | 30 | Hoagland nutrient solution | $CdCl_2$ | 50 µM L$^{-1}$ | 50 µM L$^{-1}$ | Exogenous/ Foliar | single | 10, 25, 50, 100, and 200 µM L$^{-1}$ | 50 µM L$^{-1}$ | ↓root and shoot Cd contents | (Xu et al. 2020) |
| 8. | *Rapeseed (Brassica napus)* | Petri plates/ laboratory | 16 | Hoagland nutrient solution | $CdCl_2$ | 25 µM | 25 µM | Exogenous | single | 50 and 100 µM | 100 µM | ↑germination rate, shoot length, root length, fresh and dry weight; antioxidant enzymes; proline, chlorophyll, anthocyanin contents and photosynthetic rate.<br>↑expression of melatonin biosynthesis-related *Brassica napus* genes *Caffeic acid, O-methyl transferase* (*BnCOMT*)<br>↑BnCOMT-1, BnCOMT-5 and BnCOMT-8 upregulated<br>↓BnCOMT-4 and BnCOMT-6 downregulated | (Sami et al. 2020) |

**Table 2** (continued)

The significance of coloured (*green*) up arrow means "increased", the (*red*) down arrow means "decreased"

(Ali et al. 2013a). Likewise, it was also reported that the percentage of seed oil in *B. juncea* decreased as a result of Cd accumulation (Ahmad et al. 2015; Mourato et al. 2015). It is noteworthy that melatonin not only alleviated Cd phytoxicity in *B. napus* (Table 2), but also improved Cd phytoremediation capacity through modulation of antioxidant hyperactivities and Cd sequestration in subcellular compartments (Sami et al. 2020), thus enhanced tissue tolerance capability of rapeseed plant. Considering the ubiquity of melatonin in all life forms including plants, animals and microorganism, the very first study till date on Cd-induced melatonin response in oilseed plant (i.e., *B. napus* L.) was performed by Sami et al. (2020). This study elaborated the phenomenon of melatonin-induced improvement in plant biomass, chlorophyll contents, antioxidant potential and Cd sequestration in subcellular compartments (cell wall, soluble fractions). Moreover, the study provided physiological, biochemical and molecular basis for further exploration of the associated mechanisms involved in melatonin-mediated Cd tolerance in oilseed crops. Interestingly, Park et al. (2012) reported that more than half of Cd remained in the residues during oil production extracted from *B. napus* seeds grown in heavy metal-contaminated soil, suggesting that melatonin may also play a vital role in food security beside providing a valuable bioenergy source for future generations. Here, we suggest that researchers should find indicator oilseed crops having active Cd homeostasis and Cd detoxification mechanisms.

## Conclusions and Future Proposals

This review paper evaluates different aspects of stress-induced melatonin responses including Cd tolerance and Cd detoxification mechanisms in plants, including oilseed crops. Likewise, the present review shows that melatonin application is a novel, environment friendly, and sustainable approach to alleviate Cd phytotoxicity and enhance Cd tolerance of oilseed crops for phytoremediation and simultaneous biofuel production while considering the fact that melatonin benefits plant growth, development, and confers Cd tolerance in plants by modulating chlorophyll contents, antioxidant enzymes, PCs biosynthesis, and subsequent Cd sequestration in vacuole. Moreover, melatonin-mediated biosynthetic genes (TDC, T5H, SNAT, ASMT, and COMT) play positive role in plant metabolic activities which consequently increased plant growth rate and enhanced phytoremediation capacity during Cd stress. When the concentration of Cd found in soil exceeds the threshold limit and there is a high risk of trophic chain contamination, a sustainable and human friendly Cd detoxification approach must be ensured. Physicochemical remediation techniques are expensive, inconsistent, laborious, and cause secondary pollution. Alternatively, there are several bioremediation techniques for Cd detoxification and/or removal from contaminated soil, such as microbial remediation and phytoremediation.

Phytoremediation, a viable green technology, not only improves crop productivity, but also enhances metal accumulation capacity under Cd stress. Nevertheless, phytoremediation processes are limited due to low bioavailability of Cd in contaminated soil, slow growth, and low biomass hyperaccumulator plants. Therefore, it is necessary to find high biomass and fast-growing metal-accumulator plants having exceptionally high bioenergy value for the effective remediation of Cd-contaminated soil and simultaneous biofuel production. Moreover, the exploration of natural plant growth promoter and/or biostimulator for improving phytoremediation processes is still underway. In addition to genetically modified plants that over-accumulate melatonin, the use of exogenous melatonin or induced biosynthesis through environmental elicitors can be exceptional strategies for Cd decontamination and phytoremediation purposes. Novel technologies and scientific enhancements have revealed that melatonin has emerged as a research highlight regarding its impeccable role as an effective natural plant growth promoter, broad spectrum antioxidant, and more specifically an efficient biostimulator to improve Cd-induced tolerance and phytoremediation processes of crops in changing environment. In addition, modes of melatonin application have a great impact on plant growth, Cd accumulation, and tolerance capabilities in a variety of plants. Besides the involvement of the mitogen-activated protein kinase (MAPK) pathway, the upstream regulation of stress-induced melatonin biosynthesis and/or synthetic gene expression in higher plant remains obscure. Moreover, stress-induced melatonin biosynthesis genes i.e., AANAT and TPH have not yet been characterized in plants.

Although there are a number of publications on multifunctionality of melatonin, little is understood about the mechanistic basis of melatonin in plant growth improvement and Cd resistance due to the lack of genetic evidences. Similarly, Cd-induced melatonin biosynthesis pathway is still unclear in plants including edible and oilseed crops, which thus provided a gap for future investigation. Furthermore, there is a lack of data on the cellular location, transport of melatonin in plant tissues, and its subcellular compartmentalization. Future studies will provide more genetic evidences about melatonin-mediated heavy metal stress responses along with detoxification mechanisms in higher plants. Moreover, additional research may explore the viability of exogenous melatonin application on potential microbial community dynamics and plant–microbe interactions (beneficial as well as pathogenic) in agriculture soil.

The discovery of Cd-induced melatonin biosynthetic gene COMT in oilseed crop may help to better understand the basic mechanisms of Cd-induced melatonin production. Moreover, there are ample data on the potential of melatonin to improve phytoremediation, but the final crucial step needs to be taken: testing at field level. We herein provide future research direction for the utilization of melatonin in alleviating Cd toxicity and producing sustainable Cd-resistant oilseed crops. Conclusively, this study may, thus, provide basis for further exploration in the regulatory mechanism of melatonin-mediated tolerance and Cd detoxification against Cd stress in other oilseed crops.

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## Declarations

**Conflict of interest** The authors declare that they have no competing interests.

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