



Phenolics Biosynthesis, Targets, and Signaling Pathways in Ameliorating Oxidative Stress in Plants

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Abstract

In plant cells, acquaintance to drought, salinity, temperature excesses, air pollutants, heavy metals, ultraviolet radiations, and pathogens outcomes in the reactive oxygen species (ROS) formation due to which intracellular redox milieu modifies ultimately effecting signaling pathways and cell fate. In the context of their response, plants exhibit increased phenolic compounds biosynthesis to cope up with the environmental constraints. Since phenolics are specialized metabolites concerned with essential cell functions like development, cell division, photosynthetic activity, hormonal regulation, and scavenging of damaging ROS and molecular active oxygen species. The signaling pathways influenced involve various targets namely NADPH oxidases, phosphatidylinositol-3-kinases (PI3K), protein kinase targets of rapamycin (TOR) auxin transport, and phenylpropanoid pathway. On the other hand, phenolics as antioxidant act in phenolic/ascorbate/oxidase system that eliminates harmful peroxides. Here, we explore the functions/biosynthesis, targets, and signaling pathways of phenolics not only relative to unfavorable conditions or stress, but also in the wider perspectives of environmental responses and plant development.

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8.1 Introduction

Plants productivity is severely affected by constantly changing environments due to several biotic and abiotic stresses which include drought, salinity, temperature extremes, i.e., chilling and heat, flood, heavy metals, ultraviolet radiations, and pathogens (Choudhary 2012; Ramegowda et al. 2020). Owing to these, an imbalance between amid antioxidants and pro-oxidants occurs, in due course causing oxidative stress in plants. Biochemically in favor of the former, plant cell is considered by an improved metabolism favoring reactive oxygen species (ROS) formation (Van Breusegem and Dat 2006). Environmental stresses inhibit Calvin or C3 cycle which alters ATP and NADPH consumption and carbon dioxide (CO₂) fixation eventually exacerbating the situation in mitochondria and chloroplast where imbalance between reductant consumption and electron acceptor regeneration leads to electron transfer to alternative acceptors, mainly molecular oxygen (Walker et al. 2016) such as, chilling, drought stress, and chemical agents limit CO₂ fixation despite the fact that light-driven transport of electrons proceeds at higher rates. The surplus excitation energy transfer to O₂ or its univalent reduction led to ROS formation which is an inescapable feature of life and plants evolved an antioxidative defense system to keep its level under control (Bhattacharjee 2019). Plants being sessile need to acclimatize with the varying environments caused by several stress conditions and accumulation of phenolics is reflected as an adaptive response to it (Hasanuzzaman et al. 2013).

Polyphenols or plant phenolic compounds are the furthestmost occurring and predominated secondary metabolites in plant kingdom having considerable morphological, biochemical, and physiological (Aviles-Gaxiola et al. 2020; Marchiosi et al. 2020). These are described by a minimum one aromatic ring (C₆) having one or more OH groups and monomeric and polymeric phenols are produced from cinnamic acid; emerge from shikimate or malonate pathway. Plant phenolics act as a key defense compound against unfavorable conditions, moreover they also exhibit vital activities like antioxidant, anti-inflammatory, and antimicrobial activity (Moura et al. 2010). Many phenolic compounds produced in plants are known, identified, and their characterization is ongoing and increasing continuously (Rohela et al. 2020). Plant phenolics constitute flavonoids and their derivatives, hydroxycinnamic acids (HCAs), their glycosides and amides, suberin, lignin, sporopollenin, etc. (Bärlocher and Graça 2020). Polyphenols such as flavonoids and HCAs act as electron donors for guaiacol peroxidases and scavenge hydrogen peroxide (H₂O₂) proficiently (Tsao 2010). In chloroplast under several stress conditions, ascorbate pools get oxidized might exceed their scavenging capacity. Polyphenols as antioxidant play a vital *via* supporting the chief ascorbate-dependent detoxification mechanism by means of standby defense pathway and help to deal with the severe stress

environments (Naikoo et al. 2019). Therefore, this chapter emphasizes targets, signaling, and the roles of phenolics in plant metabolism of ameliorating oxidative stress and tolerance.

8.2 Molecular Structure, Classification, and Biosynthesis of Phenolics

Phenolics are very large group of chemical compounds having great structural diversity extending from simple molecules to polymers known as polyphenols and can also exist as esters and methyl esters functional derivatives (Vuolo et al. 2019). They contain a minimum one aromatic benzene ring (C₆) with one or more OH groups attached. Phenolics are classified in various means such as carbon atoms number present in the molecule, i.e., simple phenolics, benzoquinones containing 6 carbon atoms, acetophenones, and phenylacetic acids containing 8 carbon atoms, phenylpropanoids (coumarins, isocoumarins, chromones, chromenes) containing 9 carbons, rare hydroxycinnamic acids, rare to common naphthoquinones containing 10 carbons, xanthenes containing 13 carbons, rare stilbenes and anthraquinones containing 14 carbons, rare flavonoids and isoflavonoids containing 15 carbons, common betacyanins containing 18 carbons, rare lignans and neolignans containing 18 carbons (C₆–C₃)₂, biflavonoids, exceptional lignin (C₆–C₃)_n, melanins containing *N* carbons (C₆)_n, condensed tannins (proanthocyanidins flavolans) (C₆–C₃–C₆)_n (Naikoo et al. 2019). The distinctive biological, physical, and biochemical activities of each compound depend in the number of carbon atoms present and their characteristics. In plants, glycolysis and hexose monophosphate pathway (HMP) intermediate, i.e., phosphoenolpyruvate and erythrose-4-phosphate act as precursors for phenolics biosynthesis through phenylpropanoid or shikimic acid pathway or specific flavonoid pathway (Lavhale et al. 2018). Firstly, ribulose-5-phosphate is formed from glucose-6-phosphate with the help of glucose-6-phosphate dehydrogenase enzyme through which HMP converts into erythrose-4-phosphate which reacts with phosphoenolpyruvate generated through glycolysis, to form phenylalanine through shikimic acid pathway. Then phenylalanine converts into trans-cinnamic acid with the help of phenylalanine ammonia lyase (PAL) enzyme. Some other phenolic compounds for example flavonoids, lignins, tannins, coumarins, lignans, and monolignols are synthesized by phenylpropanoid pathway (Lavhale et al. 2018).

8.3 ROS Generation, Oxidative Stress, and Phenolics

Plants being sessile are vulnerable to formation of ROS because of their exposure to various unfavorable environmental conditions (Dvorak et al. 2020). Normally under the nonstressed conditions, these toxic reduced oxygen species are produced in fewer amounts through redox reactions occurring in some specialized organelles such as mitochondria, chloroplast, nucleus, and cytoplasm as well (Zechmann 2014). But when plant is under the stress conditions either abiotic such as temperature

extremes, drought, salinity, UV-light exposure, heavy metals or biotic stress such as pathogen or herbivore attack, their production enhanced to a large extent which has the devastating impact on plants; survival as these reduced oxygen species are exceptionally reactive and can oxidize a large number of biological molecules (Vinod 2012).

The ROS formation results from reduction of oxygen molecule by adding one, two, or three e^- (s) to form oxygen free radical ($O_2^{\cdot-}$), hydrogen peroxide (H_2O_2), or hydroxyl radical ($\cdot OH$) (Mehler reaction), respectively or by transfer of excess excitation energy to O_2 resulting in singlet oxygen formation (1O_2). Firstly during O_2 reduction, oxygen-free radical ($O_2^{\cdot-}$) is produced by Mehler reaction, secondly reduction of O_2 produces H_2O_2 , which is a relatively long-lived molecule and can oxidize SH groups (Singh et al. 2019) and thirdly formation of hydroxyl radical ($\cdot OH$) which is utmost reactive amongst ROS thereby causing oxidative stress. It has been reported that H_2O_2 in the presence of $\cdot O_2^-$ can generate highly reactive hydroxyl radicals ($\cdot OH$) by Haber Weiss reaction which is a metal-catalyzed process; therefore H_2O_2 scavenging is vital to circumvent oxidative impairment in plant cells (Kehrer 2000). In the occurrence of heavy metals like Cu^+ and Fe^{2+} , H_2O_2 converts into $\cdot OH$ via metal-catalyzed Fenton reaction. In chloroplast, ROS restricts CO_2 fixation as it rejoins with chlorophyll and forms triplet state which produces 1O_2 rapidly which damages photosynthetic complex particularly PSII, as a result of disturbing photosynthetic reactions (Foyer 2018). Approximately 1–5% of oxygen utilized in mitochondria leads to the formation of H_2O_2 , successively producing $\cdot OH$ which results in protein oxidation. Apart from this, peroxisomes are likewise leading sites for generation of ROS, chiefly H_2O_2 which is in comparatively much higher concentration.

The presence of excess ROS in the cellular environment is threatened to structure of various sub-cellular organelles, biochemical processes, micromolecules, macromolecules, and eventually it devastates the plants' defense system, producing oxidative stress, cellular damage, and cell disease (Kohli et al. 2019). Contrary to excess generation of ROS, redox state obstructs cellular processes and disturbs plant growth and development, signifying that an optimum ROS level is required for usual plant functioning. The excess ROS production in rejoinder to various unfavorable stresses has been anticipated to coordinate various defense mechanisms in plants cells to defend them from oxidative impairment and has been a chief reason for the advent of some specified natural products (Lattanzio 2013). In response to the former, biosynthesis and accumulation of secondary metabolites comprising phenolics get boosted in plant tissues reflecting as an adaptive phenomenon. Various studies showed the augmentation of phenolics in various plant tissues in stress or unfavorable conditions (Naikoo et al. 2019). Plant phenolics perform several physiological functions which are necessary for plants' adaptation and existence in response to different disturbances and act as antioxidants thereby scavenge excess ROS eventually defending the plant from harsh impacts of oxidative stress (Lattanzio et al. 2012).

8.4 Phenolics Targets and Modulation of Various Signaling Pathways

In this, we focus on the targets of plant-derived phenolics and signaling pathways of various biochemical processes which are essential for survival and adaptation in response to environmental disturbances. The association between targets and signaling pathways may play an imperative role in providing the information regarding the importance of phenolics in ameliorating oxidative stress and acting as a defense molecule as elucidated in Fig. 8.1.

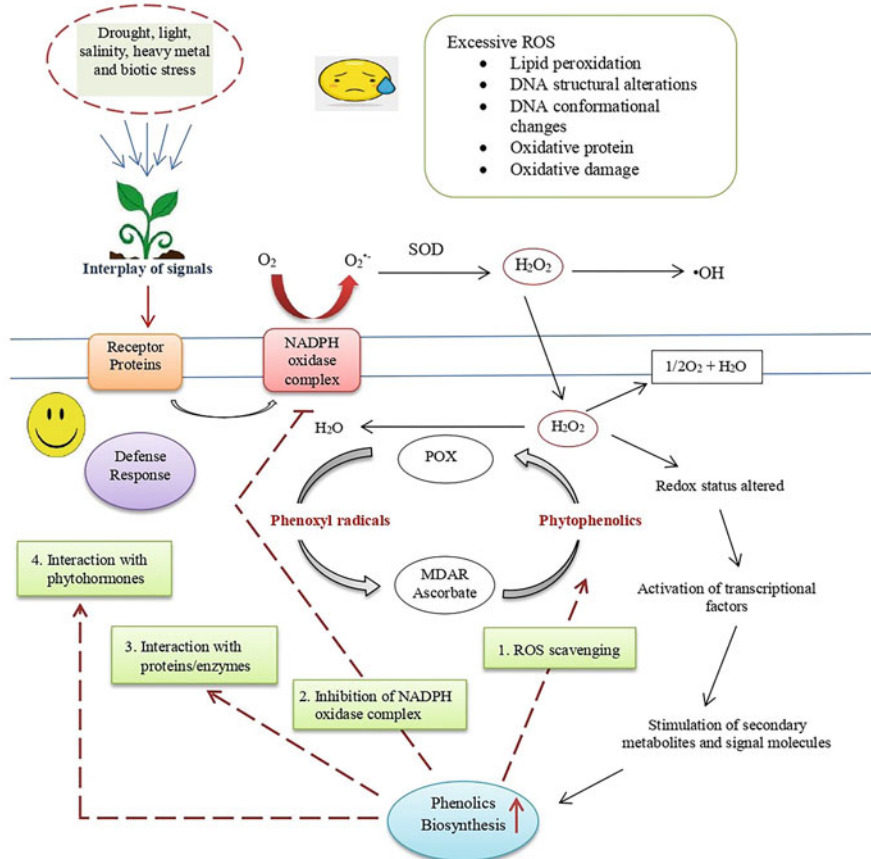


Fig. 8.1 Role of phenolics and signaling pathways involved in ameliorating the oxidative stress in plants. *Abbreviations:* MDAR monodehydroascorbate reductase, POX peroxidase, ROS reactive oxygen species, SOD superoxide dismutase

8.4.1 Antioxidant Defense System: Phenolics as Antioxidants

ROS in plants is primarily formed by the photosynthetic ETC (electron transport chain) under the unfavorable conditions (Dumanović et al. 2020). Amongst all, H_2O_2 is of great stability and is permeable across the plasma membrane and can generate OH^- which is highly reactive (Sharma et al. 2012); therefore, to avoid its deleterious effect in plants, it is very crucial to scavenge H_2O_2 . Usually, ascorbate-glutathione pathway is the most vital mechanism to detoxify H_2O_2 into water. But later on, it has been demonstrated that polyphenols are also efficient in H_2O_2 scavenging by serving as e^- donor for guaiacol peroxidases. During extreme stress conditions when chloroplast ascorbate pools turn out to be oxidized, polyphenolics serve as the standby antioxidant defense system thereby supporting chief ascorbate-dependent scavenging system (Świątek et al. 2019). Additionally, *in vitro* studies revealed that phenolics can directly scavenge ROS ($^{\bullet}O_2^-$, H_2O_2 , $^{\bullet}OH$, and 1O_2) because of their antioxidant action to give e^- (s) or hydrogen atoms (Moukette et al. 2015). On the other hand, there is one other mechanism elucidating antioxidant role of phenolics that they inhibit peroxidation of lipids through deceptive alkoxy radical which cringe free radical chain oxidation under oxidative stress (Félix et al. 2020). However, this activity varies depending upon phenolic structure, presence, and position of hydroxyl groups. Later on, it has been revealed that phenolics alter lipid peroxidation kinetics by changing their packaging in such a way that they can bind phospholipids polar head resulting in stabilization of membranes and integrity maintenance by this means limits diffusion of free radicals, access of damaging molecules toward phospholipids bilayer hydrophobic part and peroxidative reactions.

8.4.2 NADPH Oxidase, a Key Source of ROS: Phenolics as Inhibitors

NADPH oxidase, a multisubunit complex enzyme, is the utmost significant source of ROS generation. Excessive increase in ROS under stress conditions is very deleterious as it leads to the damage to lipid membranes, cellular organelles, and disruption of cellular homeostasis. It has been reported that expression of NADPH oxidase is augmented under the excessive ROS condition (Huang et al. 2019). Both *in vitro* and *in vivo* conditions, phenolics especially flavonoids inhibit NADPH oxidase activity ultimately devastating excess ROS generation. This activity of phenolics is due to their high antioxidant strength and ability to disrupt the assembly of NADPH subunits (Yousefian et al. 2019). In this way, phenolics can decline oxidative stress through inhibiting ROS producing enzymes, i.e., NADPH oxidase, direct free radicals scavenging or metal interaction. As phenolics are classified to several groups according to their structure, this activity varies amongst different classes of phenolics and highest being possessed by flavonoids due to the occurrence of two OH groups in the ortho position of ring B of their base skeleton which generates a steady radical with ROS indirectly scavenges excess ROS (Baskar et al. 2018). Moreover, occurrence of other OH groups in the ring B increases their activity due to

formation of stable half quinone radical (Trembl and Šmejkal 2016). Likewise, 2,3-double bond and 4-keto in ring C basic structure of flavonoids enhances this activity. Thus, quercetin possesses developed bioactivity than catechin due to better delocalization of the formed radical electron (Salehi et al. 2020). However, the model structure for NADPH oxidase inhibition is the presence of benzene ring with OH group and a methoxy group at the ortho position and a saturated bond and a keto group at position 2–3 and 4 respectively, in ring C. Hence, phenolics possessing such type of structure are further influential in contrast to those which have two OH groups in benzene ring.

8.4.3 Targets of Rapamycin (TOR) and Phosphotidyl Inositol-3-Kinases (PI3K): Potential Targets of Phenolics

TOR kinase recognized as a chief regulator of development in plants and incorporates nutrient and environmental signals in eukaryotes (McCready et al. 2020). This is predominantly imperative in plants, as due to their sessile nature, they requisite to sense and retort to outward signals to appropriately synchronize multicellular progression. However, TOR activity must be in control as its over expression can lead to the cellular over-proliferation ultimately leading to tumor formation in plants. Thus, TOR is crucial for proper development of plants in milieu of available resources for their growth.

Unregulated and uncontrolled cellular proliferation is the core hallmark of developmental deformities. Cells proliferation is under the control of sequences of various cyclin-dependent kinases which are basically serine tyrosine kinases and act as a checkpoint to decide whether the cell has to go through division or arrest at that point (Atkins and Cross 2018). Various phenolic compounds act as cell cycle regulatory agents. Epigallocatechin-3-gallate as an enriched polyphenol extracted from green tea has shown various antiproliferative properties via targeting PI3K and Akt ultimately decreasing its phosphorylation level (Mirza-Aghazadeh-Attari et al. 2020). Pomegranate being enriched with polyphenols showed antitumor properties on various types of cancerous. Likewise, Banerjee et al. reported in Sprague-Dawley rats that decline in cellular proliferation was found when it was supplied with pomegranate juice (Banerjee et al. 2013). A flavonoid called myricetin present in grapes and berries possesses antiproliferative properties on glioblastoma multiform cells because of its binding to PI3K and JNK ultimately declining PI3K/Akt and JNK signaling pathway expressions (Vidak et al. 2015). Both in vivo and in vitro studies demonstrated that a flavonoid called fisetin showed satisfactory decline in proliferation of cancer-causing cells by inhibiting PI3K/Akt/mTOR signaling pathways.

8.4.4 Auxin Transport and Phenylpropanoid Pathway: Role in Photoprotection

Plant's shape is controlled by the irradiance of sunlight, such as shady plants or sciophytes with large and thin leaves and extended internodes and sunstroke plants or heliophytes with small internodes and short, thick leaves. Phenolics are optimally located either in vacuoles, trichomes, epidermal cell walls, and chloroplast or in nucleus reduce oxidative damage induced by sunlight irradiance or UV-B stress in the sites of ROS production eventually protects DNA damage (Agati et al. 2020). The interactions between the phenolics and auxins which are synthesized through shikimate pathway from different precursors have biochemical, morphological, and physiological alteration in the metabolism of plants likewise phenolics affect the auxin transport and act as defense signaling molecules (Ahmed et al. 2020). Phenolic compounds especially flavonoids modify auxin movement and actively inhibiting basipetal transportation for being capable of binding to the ATP sites of auxin efflux facilitator proteins called PIN proteins, hence capable of regulating plant development under varying sunlight irradiance intensity (Peer and Murphy 2007). This property is dependent on structure of flavonoids, B-ring orthodihydroxy substitution, and degree of C2–C3 bonds unsaturation. As morphological traits in sunlight irradiance like plant's shape, internodes length, leaf size, and thickness are under control of hormones especially auxins and flavonoids-controlled auxin movement plays a role in regulating architecture of individual-organ and whole-plant and increases self-shading (Buer and Djordjevic 2009). Some phenolics such as flavonoids with substituted orthodihydroxy B-ring inhibit free radicals' formation either via metal ions chelation or decreasing xanthine oxidase activity (Eghbaliferiz and Iranshahi 2016). This property may provide a good explanation of sudden rise in dihydroxy to monohydroxy B-ring substituted flavonoids ratio under UV radiation or high sunlight stress. Hence, modifications in phenylpropanoid metabolism in stress conditions primarily reduced the oxidative damage.

8.5 Role of Phenolics in Stress Tolerance

Phenolics in plants are mostly deliberated as key defense compounds contrary to oxidative stress produced by the ROS accumulated under environmental stresses, such as salinity, temperature extremes, UV light, heavy metals, nutrient deficiency, and heavy metals (Kumar et al. 2020b; Naikoo et al. 2019). Then increased phenolics content deliberates an array of physiological roles which help the plants to acclimatize and endure in such environmental disturbances (Table 8.1).

8.5.1 Light Stress

Oxidative stress induced by high sunlight exposure or UV-B radiation in plants modifies metabolism and badly affects membranes, DNA, and proteins. In response

Table 8.1 Role of phenolics in ameliorating diverse stresses (UV light, salinity, drought, heavy metal, and temperature stress)

S. no.	Stress	Plant species	Status of phenolic compound	Reference
1.	UV light	<i>Ribes nigrum</i>	Escalation in phenolics content especially anthocyanins, hydroxycinnamic acids, flavonols, and hydroxybenzoic acids	Huyskens-Keil et al. (2012)
		<i>Kalanchoe pinnata</i>	Rise in total flavonoids and quercitrin content	Nascimento et al. (2015)
		<i>Arbutus unedo</i>	Increase in phenolics such as theogallin, avicularin, and juglanin	Nenadis et al. (2015)
		<i>Vitis vinifera</i>	Proliferation in phenolics such as astilbin, quercetin, malvidin, myricetin, gallic acid, vanillic acid, protocatechuic acid, and kaempferol	Berli et al. (2011), Alonso et al. (2016)
		<i>Brassica oleracea</i>	Increase gallic acid and sinapic acid content	Moreira-Rodriguez et al. (2017)
		<i>Solanum lycopersicum</i>	Rise in total phenolics	Mariz-Ponte et al. (2018)
		<i>Lactuca sativa</i>	Rise in total phenolics contents, flavonoids and anthocyanins, phenolic acids	Sytar et al. (2018)
		<i>Caryopteris mongolica</i>	Upregulation of phenylpropanoid pathway enzymes resulting in increased phenolics content	Liu et al. (2012)
		<i>Vigna radiate</i>		Goyal et al. (2014)
		<i>Fragaria</i> × <i>ananassa</i>		Xu et al. (2017)
		<i>Triticum aestivum</i>		Chen et al. (2019a, b)
		<i>Cuminum cyminum</i>		Ghasemi et al. (2019)
		<i>Daucus carota</i>		Increase in phenolics biosynthesis
		<i>Cichorium intybus</i>	Phenolics content enhanced	Sytar et al. (2020)
2.	Salinity	<i>Cynara cardunculus</i>	Rise in phenolics including luteolin-O-glucoside, gallic acid, leucocyanidin, and quercetin	Lucini et al. (2016)
		<i>Olea europaea</i>	Enhanced expression of phenylpropanoid pathways resulted in the increased amount of total phenolics, kaempferol, and quercetin	Rossi et al. (2016)
		<i>Solanum lycopersicon</i>	Rise in total caffeoylquinic acid	Martinez et al. (2016)
		<i>Thymus spp.</i>	Rise in phenolics including caffeic acid, luteolin, gallic acid, cinnamic acid, trans-2-hydroxycinnamic acid,	Bistgani et al. (2019)

(continued)

Table 8.1 (continued)

S. no.	Stress	Plant species	Status of phenolic compound	Reference
			syringic acid, rosmarinic acid, rutin, naringenin, quercitrin, vanillic acid, and apigenin	
		<i>Ocimum basilicum</i>	Enhanced content of phenolics especially caffeic acid, rosmarinic acid, caftaric acid, quercetin-rutinoside, and cinnamyl malic acid	Scagel et al. (2019)
		<i>Lonicera japonica</i> Thunb.	Elicited phenolics biosynthesis	Yan et al. (2020)
3.	Drought	<i>Vitis vinifera</i>	Rise in the phenolics like caffeic acid, ferulic acid, trans-resveratrol-3- <i>O</i> -glucoside, cis-resveratrol-3- <i>O</i> -glucoside, kaempferol-3- <i>O</i> -glucoside, cyanidin-3- <i>O</i> -glucoside, quercetin-3- <i>O</i> -glucoside, and catechin, epicatechin, caftaric acid, epicatechin gallate, and enhanced expression of phenylpropanoid pathway	Castellarin et al. (2007), Griesser et al. (2015)
		<i>Olea europaea</i>	Phenolics accumulation increased	Mechri et al. (2020)
		<i>Salix daphnoides</i> and <i>Salix purpurea</i>	Increase in phenolics biosynthesis	Köhler et al. (2020)
		<i>Olea europaea</i>	Rise in content of phenolics such as kaempferol derivatives, oleuropein, and lucidumoside C	Dias et al. (2021)
4.	Heavy metal	<i>Erica andevalensis</i>	Phenolics biosynthesis enhanced under Cd stress	Márquez-García et al. (2012)
		<i>Fagopyrum esculentum</i>	Rise in total phenolics, flavonoids, anthocyanin content, and phenylpropanoid pathway enzymes	Smirnov et al. (2015)
		<i>Ocimum basilicum</i>	Phenolics biosynthesis enhanced under Al and Cd stress	Đogić et al. (2017)
		<i>Vaccinium corymbosum</i> L.	Increase in content of phenolic compounds under Al and Cd stress	Manquían-Cerda et al. (2018)
		<i>Solanum lycopersicum</i>	Increase in phenolics biosynthesis under heavy metal stress	Dursun et al. (2019)
		<i>Cicer arietinum</i>	Phenolics enhanced under heavy metal stress	Bhagyawant et al. (2019)
		<i>Kandelia obovata</i>	Increased biosynthesis of phenolics under Cd and Zn stress	Chen et al. (2020)
		<i>Hordeum vulgare</i>	Phenolics accumulation increased under combined Cd and Cu stress	Lwalaba et al. (2020)

(continued)

Table 8.1 (continued)

S. no.	Stress	Plant species	Status of phenolic compound	Reference
		<i>Malva parviflora</i>	Enhanced phenolics accumulation under Cd stress	Zoufan et al. (2020)
5.	Heat and cold	<i>Juglans regia</i> L.	Increased expression of phenylpropanoid pathway enzymes leading to accumulation of phenolics under cold stress	Christopoulos and Tsantili (2015)
		<i>Nicotiana langsdorffii</i>	Total phenolics content including <i>p</i> -coumaric acid, chlorogenic acid, cryptochlorogenic acid, and ferulic acid increased under heat stress	Ancillotti et al. (2015)
		<i>Lens culinaris</i>	Rise in total phenolics and flavonoids including gallic acid, chlorogenic acid, ferulic acid, salicylic acid, and naringenin under heat stress	Swieca (2015)
		<i>Nicotiana tabacum</i>	Modifications in the several metabolites of phenylalanine metabolic pathway resulting in increased accumulation of phenolics under heat stress	Zhou et al. (2018)
		<i>Festuca trachyphylla</i>	Rise in phenolic compounds content such as salicylic acid and vanillic acid under heat stress	Wang et al. (2019a)
		<i>Prunus persica</i>	Enhanced phenolic compounds content such as catechin, chlorogenic acid, neo-chlorogenic acid, rutinoid under cold stress	Wang et al. (2019b)
		<i>Solanum lycopersicum</i> L.	Increase in phenolics biosynthesis under heat stress	Alsamir et al. (2021)

to it, phenolics synthesized in plants protect them from these harmful radiations by acting as UV direct shields and amending antioxidant defense system at cellular and molecular levels. It has been demonstrated in literature in various plant species that synthesis of phenolics especially flavonoids, isoflavonoids, psoralens, and phenolic acid esters enhanced under light stress (Michalak 2006; Falcone Ferreyra et al. 2012; Winkel-Shirley 2002; Liang et al. 2006) and prevent from deleterious effects of harmful radiations. With light manipulation using different colors and intensities, many phenols, flavones, and flavonols elicited and reported to have many health beneficial bioactivities like antioxidant, cardioprotective, and anti-inflammatory (Gutiérrez-Grijalva et al. 2020). A study on the mutants of *Arabidopsis* that has the blocked biosynthesis of flavonoids showed the functions of phenolics in stress tolerance which coincides with the increase content of ROS. This higher ROS accumulation preceded the rise in membrane injury, lipid peroxidation, and decrease in chlorophyll content, CO₂ assimilation, and biochemical pathways alterations (Wani et al. 2018). Applying UV radiations in whole cucumber and barley seedlings enhanced the phenolics biosynthesis. Various reports in literature showed that

exogenous supply of phenolics augments plant growth and productivity under light stress conditions. Likewise, phenolic compounds especially flavonoids production increased in the roots of pea plants, *Picea abies* and *Catharanthus roseus* during exposure to UV (300–400 nm) light. Moreover, Perez-Lopez et al. (2018) phenolics content augmented in lettuce when developed in high light and elevated CO₂. It has been verified in numerous plant species that the chalcone synthase expression is enhanced transcriptionally under UV light, providing a good explanation of increase in flavonoids under such type of stress (Kreuzaler et al. 1983; Jenkins et al. 2001; Qian et al. 2019; Park et al. 2020). In general, effects of phenolics in mitigating the adverse effects of light stress have been ascribed to some enzymatic reactions' activation, stabilization, and protection of membranes and the photosynthetic apparatus from oxidative damage

8.5.2 Salinity

Salinity outcomes excessive ROS production in plants and necessitates the stimulation of well-organized antioxidant defense system to counteract its propagation. Being influential antioxidative agents, phenolics scavenge detrimental ROS under salinity in various plants such as *Salvia mirzayanii* (Valifard et al. 2014), *Triticum aestivum* (Kaur and Zhawar 2015), *Chenopodium quinoa* (Aloisi et al. 2016), *Mentha piperita* (Çoban and Baydar 2016), *Amaranthus tricolor* (Sarker and Oba 2018), *Thymus vulgaris* L. (Bistgani et al. 2019), and *Hordeum vulgare* (Ma et al. 2019). Likewise, increase in total phenols and flavonoids has been showed by Wang et al. 2016 in *Carthamus tinctorius*. Additionally, increase in various phenolic compounds content such as caffeic acid, caftaric acid, cinnamyl malic acid, feruloyl tartaric acid, quercetin-rutinoside, and rosmarinic acid has been reported in *Ocimum basilicum* (Scagel et al. 2019). Al-Ghamdi and Elansary (2018) demonstrated that phenolics such as caffeic acid, robinin, chlorogenic acid, rutin, and apigenin enhanced in *Asparagus aethiopicus* under salinity stress. It has been studied that phenolic content augmentation induced by salinity stress is primarily by the outcome of phenylpropanoid pathway activation which leads to the accretion of several phenolic compounds possessing sturdy antioxidative property. Ben-Abdallah et al. 2019 reported that increase in quercetin 3-β-D-glucoside, caffeic acid, and total phenolic levels in *Solanum villosum* due to enhanced phenylalanine ammonia lyase and flavonol synthase expression. Similarly, in *Fragaria ananassa*, *Salvia mirzayanii*, and *Salvia acrosiphon*, increased transcript levels of phenylalanine ammonia lyase and flavonol synthase were demonstrated in salt stress (Perin et al. 2019; Valifard et al. 2015).

8.5.3 Drought

Drought stress has an adverse impact on agricultural productivity owing to its damaging effects on plant survival and development. Various studies showed that

phenolics level heightened in drought conditions in several plants such as *Triticum aestivum* (Ma et al. 2014), *Lactuca sativa* (Galieni et al. 2015), *Larrea* spp. (Varela et al. 2016), and *Ocimum* spp. (Pirbalouti et al. 2017). It has been revealed by metabolomic and transcriptomic approaches that accumulation of phenolics is imperative to develop drought resistance in wild-type *Arabidopsis thaliana* mutants by Nakabayashi et al. (2014). Drought stress delimited the biosynthetic pathways resulting in enhanced-to-enhanced accumulation of phenolics and flavonoids in plants which efficiently detoxify ROS induced by water scarcity conditions ultimately protecting it from adverse effect and abnormalities caused by stressful conditions (Kumar et al. 2020a) such as quercetin contents improved considerably in white clover (Ballizany et al. 2012), flavonols in *Crataegus laevigata*, *Crataegus monogyna* (Kirakosyan et al. 2003), and *Cistus clusii* (Hernández et al. 2004), flavonoids like kaempferol and quercetin in tomato (Sanchez-Rodriguez et al. 2011), flavonoids in wheat leaves (Ma et al. 2014), total phenolics in *Brassica napus* (Rezayian et al. 2018), phenolic metabolites like vanillic acid and 4-hydroxycinnamic acid in *Cucumis sativus* (Li et al. 2018), and total flavonoids and polyphenols in *Thymus vulgaris* (Khalil et al. 2018) under drought stress. Phenolic compounds accumulation induced by drought stress is basically the outcome of phenylpropanoid biosynthetic pathway alteration as it controls several chief genes encoding main enzymes of this pathway ultimately stimulating phenolics biosynthesis. Similarly, content of phenolics such as luteolin-7-*O*-glycoside, rutin, chlorogenic acid, kaempferol, caffeic acid, apigenin, 1,3-dicaffeoylquinic acid, and luteolin increased under drought stress of 21 days due to enhanced transcript levels of phenylalanine ammonia lyase, chalcone synthase, chalcone isomerase, and flavonol synthase in *Achillea* spp. (Gharibi et al. 2019). Under water scarcity conditions, enhanced expression of various enzymes of phenylpropanoid pathway is reported in *Lotus japonicas* (Garcia-Calderon et al. 2015), *Chrysanthemum morifolium* (Hodaei et al. 2018), *Nicotiana tabacum* (Silva et al. 2018), and *Fragaria ananassa* (Perin et al. 2019).

8.5.4 Heavy Metals

Amongst abiotic stresses, toxicity caused by heavy metals is very prevalent harmfully affecting the plants by modifying various metabolic and physiological mechanisms. It has been reported in literature that phenolics content enhanced under high ions concentration and protects the plant by chelating transition metal ions ultimately inhibiting ROS production (Mira et al. 2002; Williams et al. 2004; Kaur et al. 2017a; Kohli et al. 2018; Handa et al. 2019). These metal ions chelation under their high concentration is an active form of defense in plants as reported by Kidd et al. (2001). Betalains production was enhanced in hairy roots under high metal stress to improve their tolerance (Thimmaraju and Ravishankar 2004). Increase in phenolics like anthocyanin, kaempferol, caffeic acid, catechin, and coumaric acid under heavy metal Cu stress (Poonam et al. 2015), flavonoids, polyphenols, and anthocyanin under Cd stress (Kaur et al. 2017b, 2018) and Pb

stress (Kohli et al. 2018) were reported. Likewise increase in total phenolics and polyphenols such as chlorogenic and vanillic acid in *Zea mays* under Cu, Pb, and Cd stress (Kisa et al. 2016) and increase in total flavonoids and phenolics content were studied in *Withania somnifera* in cadmium stress (Mishra and Sangwan 2019). Level of phenolics like kaempferol, diosmin, ferulic acid, daidzein, luteolin, cinnamic acid, resveratrol, caffeic acid, naringenin, vitexin, quercetin, and myricetin got enhanced under Pb stress in *Prosopis farcta* (Zafari et al. 2016) and significant rise in total phenolics, flavonoid, and anthocyanin content were reported in *Fagopyrum esculentum* under Al stress (Smirnov et al. 2015). Augmentation of phenolics in the presence of heavy metals is primarily due to the transcriptional activation of various enzymes of phenylpropanoid pathway and its precursors (Michalak 2006; Kovacik et al. 2009; Keilig and Ludwig-Mueller 2009; Mishra et al. 2014; Leng et al. 2015; Handa et al. 2019; Chen et al. 2019a; Mishra and Sangwan 2019). Enhanced expression of phenylpropanoid pathway enzymes was reported in *Brassica juncea* under Cr (Handa et al. 2018, 2019), Cd (Kaur et al. 2017b), and Pb (Kohli et al. 2017) stresses; in *Kandelia obovata* in Cd and Zn stress (Chen et al. 2019b); in *Vitis vinifera* under Cu stress (Leng et al. 2015); and in *Prosopis farcta* under Pb stress (Zafari et al. 2016).

8.5.5 Heat and Cold Stress

The temperature stress enhances the biosynthesis of phenolics in plants (Isah 2019; Naikoo et al. 2019). *Brassica oleracea* when exposed to extreme temperatures (heat and cold) leads to the high phenolic compounds' accumulation due to enhancement of antioxidative defenses in response to high concentration of ROS produced under these conditions (Soengas et al. 2018). Higher phenolic content helps the plant to combat the unfavorable circumstances. Likewise, Rivero et al. (2001) demonstrated that high amount of phenolics in tomato and watermelon provide resistance to heat and cold stress. Short-term temperature stress when applied to kale enhanced the phenolic antioxidants level (Lee and Oh 2015). Król et al. (2015) studied that when two varieties of grapevine were exposed to constant low temperature stress, more resistant variety is considered by high phenolics accumulation. The temperature stress outcomes the stimulation of enzymes convoluted in the biosynthetic processes of phenolics ultimately enhancing its production (Lattanzio et al. 2001; Sharma et al. 2019). It has been revealed that temperature treatments resulted in elicitation of phenylpropanoid pathway and phenolic accumulations in *Phaseolus vulgaris* (Ampofo et al. 2020). The transcriptome analysis of *Saccharum spontaneum* roots envisaged that phenylpropanoid pathway responds to the cold stress and arouse the phenolics biosynthesis (Dharshini et al. 2020).

8.6 Conclusion and Future Prospects

Phenolic compounds are the utmost vital and widespread secondary metabolites, consisting of a wide array of natural diverse compounds. In response to the hostile environmental stress conditions like salinity, heavy metal, drought, temperature stress, and pathogen attack, phenolic compounds' biosynthesis enhanced in order to combat with such conditions. Phenolics alter antioxidant defense system, biochemical pathways, and the emerging status of the plant self-reliantly by acting as antioxidant or intermingling with other signaling molecules subsequently upregulating the phenylpropanoid pathway transcriptionally. Upsurged plant's resistance is interrelated by way of the manifold roles of phenolics essentially comprising their ROS scavenging capability and the ability to defend the plant from extreme stress conditions such as light, temperature, drought, etc. By understanding the targets and signaling pathways of phenolics under stress conditions, the corresponding mechanism responsible for their resistance can be easily elucidated which can be further besieged to enhance their resistance through novel approaches by modifying the signaling pathways and associated targets. Apart from the vast matter available on this context, advance research is looked-for on the way to excavate, for instance, the title role of focused and specific phenolic compound as an adaptive comeback to explicit intensive stress mechanism involved in response to the particular unfavorable condition to define the resistance providing contrivances including the up-regulation of phenylpropanoid and other biochemical pathways involved, which is one of the chief targets to combat with numerous stressors.

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