The Impact of Drought Stress on the Quality of Spice and Medicinal Plants

Dirk Selmar, Maik Kleinwächter, Sara Abouzeid, Mahdi Yahyazadeh and Melanie Nowak

Abstract This review addresses the well known phenomenon that spice and medicinal plants grown under semi-arid conditions generally reveal significantly higher concentrations of relevant natural products than identical plants, which however are cultivated in moderate climates. Unfortunately, only limited information on this intriguing phenomenon is available. The corresponding data are compiled, the relevant aspects are outlined, and the metabolic background is presented. Based on these reflections, it becomes obvious that drought stress and the related metabolic changes are responsible for the higher natural product accumulation in plants grown in semi-arid regions. In principle, there are three causes: first, the effect might be a consequence of a reduced production of biomass in the stressed plants. Even without an enhancement of biosynthesis of natural products, their concentration on dry or fresh weight basis simply will be elevated. Secondly, the drought stress enhances the actual rate of biosynthesis of natural products due to a passive shift or thirdly, due to an active up-regulation of the enzymes involved in natural product biosynthesis. The latter both options are related to the strongly enhanced reduction status of the leaves exposed to drought stress. The over-reduction, which goes along with a strongly enhanced concentration of $NADPH+H^+$, directly results in a passive increase of all processes consuming $NADPH+H^+$, including the biosyntheses of highly reduced secondary plant products. Alternatively, the enzymes responsible for the biosynthesis of natural products could be actively up-regulated. The corresponding increment in $NADPH+H^+$ consumption significantly contributes to the dissipation of the stress related surplus of energy and thus, is part of the machinery that prevents the generation of toxic oxygen radicals.

Keywords Drought stress · Secondary metabolites · Over-reduced state · Energy surplus · Medicinal plants

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M. Ghorbanpour and A. Varma (eds.), *Medicinal Plants and Environmental Challenges*, https://doi.org/10.1007/978-3-319-68717-9_9

Introduction

One of the most stated assertions with respect to the main issue of this book undoubtedly is: "*Aromatic and spice plants grown in semi-arid areas such as the Mediterranean regions generally are much more aromatic than identical plants of the same species, which however have been cultivated in moderate climates*". Frequently, this well known phenomenon is explained by the trivial statement that plants grown in Southern Europe "*…are exposed to much more sunlight, resulting in enhanced rates of biosynthesis*". Indeed—at least on the first sight—such assertion appears to be consistent. However, sunlight is not at all a limiting factor for plant growth; even in Central Europe—especially, when the plants grow in open areas without any shade. Accordingly, they absorb much more light energy in the leaves than is required and utilized for photosynthetic CO_2-fixation (Wilhelm and Selmar 2011). Consequently, there must be another explanation for this phenomenon, which generally is stated to be a matter of common knowledge (Selmar and Kleinwächter 2013a). This chapter is aimed to illustrate this syndrome and to elucidate the corresponding scientific background. As a matter of fact, in this context we have to consider various levels of contemplation, which are treated consecutively.

We all are aware that—at least in the semi-arid and arid subtropics—high irradiation often is co-occurring with water deficiencies. In consequence, under these conditions, plants frequently suffer drought stress. Since stress related reactions extensively impact the entire metabolism, the synthesis and accumulation of secondary metabolites also should be affected. Whereas in the past these coherences have not been considered adequately, meanwhile this topic is well established (Kleinwächter and Selmar 2014, 2015).

The Concentration of Natural Products Frequently Is Enhanced in Drought Stressed Plants

It is well known that various environmental conditions, such as the temperature, the light regime, the nutrient supply, etc., strongly influence the synthesis and accumulation of secondary plant products (for review see, e.g., Gershenzon 1984; Falk et al. 2007; Das and Bhattacharya 2016). Consequently, much more severe environmental influences, such as typical stress situations, which are known to strongly impact on the entire general metabolism (Sampaio et al. 2016; Bohnert et al. 1995), also must alter the secondary metabolism. By now, a tremendous lot of information on the impact of various biological stresses, e.g., pathogen or herbivore attack, on elicitation of the synthesis of natural products is available (for review see, e.g., Harborne 1988; Hahlbrock et al. 2003; Hartmann 2007; Namdeo 2007; Wink 2010). Further on, many papers deal with the impact of abiotic stresses on the secondary metabolism; nonetheless the knowledge about the related biological background is still limited (for review see, e.g., Ramakrishna and Ravishankar 2011; Selmar and Kleinwächter 2013a, b; Kleinwächter and Selmar 2014).

Meanwhile, a large number of studies manifested that plants exposed to drought stress indeed accumulate higher concentrations of secondary metabolites than those cultivated under well watered conditions (Table 1). Obviously, the drought stress related enhancement in the concentration is a common feature, which concerns all different classes of natural products. Corresponding increases are reported for simple as well as for complex phenols, and also for the various classes of terpenes (Table1). In the same manner, the concentrations of nitrogen containing substances, such as alkaloids, cyanogenic glucosides, and glucosinolates, are also positively impacted by drought stress (Table 1). There is no doubt that drought stress consistently enhances the concentration of secondary plant products. However, in this context, we have to consider that the drought stressed plants generally are reduced in their growth. Accordingly, the stressed plants reveal a far lesser biomass than the well watered controls.Drought stress increases the concentration of natural products

Due to this reduced production of biomass—even without any enhancement in the rate of biosynthesis of natural products—their concentration on dry or fresh weight basis simply will be elevated. Corresponding explanations frequently are reported in the literature for review see Kleinwächter and Selmar (2014). As most of the related studies focus on the concentration of active compounds and do not consider the overall plant production, very often data on the overall biomass per plant are lacking. A further reason for this deficit of information might be due to the fact that mostly only one certain plant part or plant organ was studied, e.g., roots, leaves, or seeds. Nonetheless, in few papers the total contents of secondary plant products per entire plants are given or could be calculated from the data published.

The Overall Amount of Natural Products Is Increased by Drought Stressed

In sage (*Salvia officinalis*) drought stress results in a massive increase in the concentration of monoterpenes (Nowak et al. 2010). As this enhancement is far higher than the corresponding reduction in biomass, the entire amount of monoterpenes present in the sage plants suffering drought stress is significantly higher than in the well watered controls. In consequence, in this particular case, the actual biosynthesis of monoterpenes is increased in response to drought stress. Corresponding experiments with parsley (*Petroselinum crispum*) revealed that the drought stress related concentration enhancement of monoterpenes in the leaves is more or less completely compensated by the accompanied loss in biomass. Thus, the overall contents of essential oils are quite similar in drought stressed and in well watered plants (Petropoulos et al. 2008). Corresponding results for Greek oregano (*Origanum vulgare*) have been elaborated by Ninou et al. 2017, which showed that the overall content of essential oils per plant remained constant although the

Table 1 Drought stress increases the concentration of natural products

Simple Phenols			
Helianthus annuus	chlorogenic acid	massive increase (tenfold)	del Moral 1972
Prunus persica	total phenols	higher contents	Kubota et al. 1988
Thymus capitatus	phenolics	higher contents	Delitala et al. 1986
Echinacea purpurea	total phenols	strong increase (67 %)	Gray et al. 2003
Crataegus spp.	chlorogenic acid	massive increase (2 - 6fold)	Kirakosyan et al. 2004
Hypericum brasiliense	total phenols	strong increase (over 80 %)	de Abreu & Mazzafera 2005
Trachyspermum ammi	total phenols	strong increase (100 %)	Azhar et al. 2011
Labisia pumila	total phenols	significant increase (50 %)	Jaafar et al. 2012
Complex Phenols			
Pisum sativum	flavonoids	strong increase (45%)	Nogués et al. 1998
Pisum sativum	anthocyanins	strong increase (over 80 %)	Nogués et al. 1998
Crataegus spp.	catechins / epicatechins	massive increase (2 - 12fold)	Kirakosyan et al. 2004
Hypericum brasiliense	rutine / quercetin	massive increase (fourfold)	de Abreu & Mazzafera 2005
Hypericum brasiliense	xanthones	strong increase (over 80%)	de Abreu & Mazzafera 2005
Camellia sinensis	epicathecins	higher contents	Hernández et al. 2006
Salvia miltiorrhiza	furoquinones	significant increase	Liu et al. 2011
Prunella vulgaris	rosmarinic acid	slight increase	Chen et al. 2011
Labisia pumila	anthocyane / flavonoids	significant increase	Jaafar et al. 2012
Monoterpenes / Essential Oils			
Mentha x piperita ssp.	essential oils	significant increase	Charles et al. 1990
Cymbopogon pendulus	geraniol & citral	strong increase	Singh-Sangwan et al. 1994
Pinus halepensis	α-pinen, carene	strong increase	Llusià & Penuelas, 1998
Cistus monospeliensis	caryophyllene	enormous increase	Llusià & Penuelas, 1998
Satureja hortensis	essential oils	increase	Baher et al. 2002
Picea abies	monoterpenes	strong increase	Turtola et al. 2003
Pinus silvestris	monoterpenes	strong increase	Turtola et al. 2003
Petroselinum crispum	essential oils	strong increase (double)	Petropoulos et al. 2008

(continued)

Table 1 (continued)

Salvia officinalis	essential oils	massive increase (2 - 4fold)	Beattaieb et al. 2009
Salvia officinalis	monoterpenes	strong increase	Nowak et al. 2010
Scrophularia ningpoen.	iridoid glycosides	increase	Wang et al. 2010
Nepeta cataria	essential oils	significant increase	Manukyan, 2011
Ocimum basilicum	essential oils	significant increase	Forouzandeh et al. 2012
Thymus vulgaris	monoterpenes	increase	Kleinwächter et al. 2015
Petrosilinum crispum	essential oils	massive increase	Kleinwächter et al. 2015
Origanum vulgare	essential oils	increase	Ninou et al. 2017
Origanum vulgare			
subsp. gracile	essential oils	significant increase	Morshedloo et al. 2017
subsp. virens	essential oils	no significant increase	Morshedloo et al. 2017
Di- and Triterpenes			
Solanum tuberosum	steroid alkaloids	strong increase	Bejarano et al. 2000
Hypericum brasiliense	betulinic acid	strong increase	de Abreu et al. 2005
Bupleurum chinense	saikosaponin	significant increase	Zhu et al. 2009
Prunella vulgaris	triterpenes	slight increase	Chen et al. 2011
Glycyrrhiza glabra	glycyrrhizinc	massive increase	Nasrollahi et al. 2014
Alkaloids			
Senecio longilobus	pyrrolizidine alkaloids	strong increase	Briske & Camp, 1982
Lupinus angustifolius	quinolizidin alkaloids	strong increase	Christiansen et al. 1997
Solanum tuberosum	steroid alkaloids	strong increase	Bejarano et al. 2000
Glycine max	trigonelline	higher contents	Cho et al. 2003
Papaver somniferum	morphine alkaloids	strong increase	Szabó et al. 2003
Catharanthus roseus	indole alkaloids	strong increase	Jaleel et al. 2007
Phellodendron amurense	benzylisoquinolines	strong increase	Xia et al. 2007
Senecio jacobaea	pyrrolizidine alkaloids	massive increase	Kirk et al. 2010
Nicotiana tabacum	Nicotiana-alkaloids	strong increase	Çakir & Çebi, 2010
Chelidonium majus	benzylisoquinolines	increase	Kleinwächter et al. 2015
Various Classes			
Manihot esculenta	cyanogenic glucosides	strong increase	de Bruijn, 1973
Triglochin maritima	cyanogenic glucosides	strong increase	Majak et al. 1980

(continued)

Table 1 (continued)

Brassica napus	glucosinolates	massive increase	Jensen et al. 1996
Coffea arabica	γ-aminobutyric acid	massive increase (tenfold)	Bytof et al. 2005
Brassica oleracea	glucosinolates	significant increase	Radovich et al. 2005
Brassica carinata	glucosinolates	significant increase	Schreiner et al. 2009
Phaseolus lunatus	cyanogenic glucosides	higher content in stressed plants	Ballhorn et al. 2011
Tropaeolum majus	glucotropaeolin	higher content in stressed plants	Bloem et al. 2014

concentrations significantly increased. On the first sight, it seems that in these cases no change in the rate of monoterpene biosynthesis occurs. However, if we consider that the equal amount of monoterpenes is produced by a far lower biomass, it becomes obvious that the biosynthetic activity per dry weight must strongly be elevated. This problem to use an appropriate reference value was exemplarily outlined for the stress related increase of monoterpenes in thyme (Paulsen and Selmar 2016). As already mentioned for parsley, also in drought stressed thyme plants a lower gain of biomass seemed to be responsible for the increase in monoterpene concentration. Accordingly, no change in the total content of monoterpenes and thus in their overall biosynthesis could be pointed out. However, a detailed and thorough consideration revealed that the rate of biosynthesis on dry weight basis was indeed different in stressed and well watered plants. Whereas the biosynthetic activity (on dry weight basis) in the first phase of the experiment was much higher in the stressed plants in comparison to the well watered controls, the situation was reverse, when the stress situation was prolonged (Paulsen and Selmar 2016). For clarification, this complex situation—with special emphasis on the importance of the employment of appropriate reference values—is displayed in Fig. 1. These intricate coherences suggest that—over the course of time—an adaption to the drought stress occurred, which finally leads to a reduction of the formerly enhanced rate of biosynthesis. Unfortunately, due to the large efforts required, these multifactorial coherences cannot be studied and considered adequately in routinely investigations. Consequently, the interest and aim of a certain study determine the focus on appropriate reference values, such as concentration, total amount, overall production, or composition.

Similar situations have been observed with respect to phenolic compounds. In *Hypericum brasiliense* plants, both, concentration and the total amount of the phenolic compounds, are drastically enhanced under drought stress (de Abreu and Mazzafera 2005). Although the stressed *H. brasiliense* plants were quite smaller than the well watered controls, due to their tremendous increase in the concentration of phenolic compounds, their overall content (product of biomass and concentration) was significantly higher in the stressed plants (de Abreu and Mazzafera 2005). In the same manner, the overall amount of anthocyanins was about 25% higher in stressed peas (*Pisum sativum*) than in plants cultivated under standard conditions

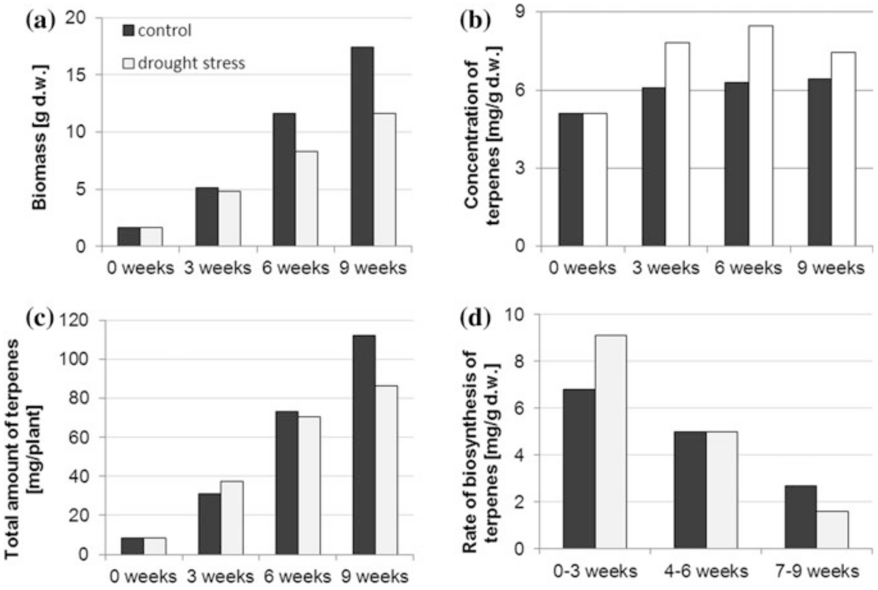

Fig. 1 Juxtaposition of the relevant parameters in well-watered and drought stressed thyme plants. The comparison of biomass (**a**), concentration of terpenes (**b**), total amounts of terpenes (**c**) and rates of bio-synthesis of terpenes (**d**) in drought stress thyme (Paulsen and Selmar 2016) illustrates the complex problematic of choosing the correct reference value as well the multilayered metabolic processes that change in the course of the prolongation of the stress situation

(Nogués et al. 1998). Jaafar et al. (2012) reported that in *Labisia pumila* plants not only the concentration, but also the overall production of total phenolics and flavonoids per plant was increased in plants suffering drought stress.

Unfortunately, nearly all of the studies dealing with the impact of drought stress on nitrogen containing natural products focus just on the concentrations of these compounds in certain organs. In most of the cases no data on the biomass and thus on the total amount of natural products per entire plant are available. Kleinwächter et al. (2015) demonstrated that the stress related increase in the concentration of coptisine is overcompensated by the strongly reduced gain in biomass of the stressed plants, resulting in significant lower overall alkaloid content in the stress plants. Up to now, no conclusion about the impact of drought stress on the biosynthesis of these natural products could be drawn.

In summary: in nearly all plants analyzed, the concentrations of secondary plant products are significantly elevated under drought stress conditions. Unfortunately, only in few cases, also a corresponding increase of the total content of the natural compounds per plant is reported. This could be either due to the lack of data on the biomass of the corresponding plants, or to the fact that the stress related decrease in biomass frequently overcompensates the increase in the concentration of relevant natural products.

Metabolic Background

Due to our recurring experience in daily life, we all have internalized that energy saving represents one of the most important issues in our subsistence. Indeed—on the first sight—it seems reasonable to transfer such statements and considerations also into plant biology. However, when beholding more closely, it becomes obvious that—in contrast to heterotrophic organisms—plants have no problem to cover their energy requirements. By contrast, in general, they absorb much more energy than being required for photosynthetic CO_2-fixation (Wilhelm and Selmar 2011). This basic statement easily can be deduced from a fact we all are familiar with: elevation of ambient CO_2 concentration results in a massive enhancement of photosynthesis—the corresponding rate of photosynthesis easily could be doubled or even tripled (Wilhelm and Selmar 2011). This however means that the tremendous oversupply of energy has to be dissipated in order to avoid massive damages by oxygen radicals, which otherwise would be generated by an overflow of the electron transport chain (Reddy et al. 2004; Szabó et al. 2005). During evolution, plants have developed various mechanisms for effective energy dissipation, i.e., non-photochemical quenching, photorespiration, or xanthophyll cycle (Fig. 2). Indeed, this protecting system operates properly under regular environmental conditions, however, any stress situation induces massive imbalances. This especially accounts for the drought stress. Water shortage induces stomata closure, which massively diminishes the CO_2-influx into the leaves. In consequence, far less reduction equivalents ($NADPH+H^+$) are consumed and re-oxidized, respectively via the Calvin cycle. Although the various energy dissipating mechanisms are up-regulated, the reduction status of the chloroplasts increases massively (Selmar and Kleinwächter 2013a, b; Kleinwächter and Selmar 2015). As result, electrons from the photosynthetic electron transport chain will directly be conveyed to oxygen, generating superoxide radicals, which subsequently have to be detoxified by superoxide dismutase (SOD) and ascorbate peroxidase (APX). As a further consequence of this over-reduction, the ratio of $NADPH+H^+$ to $NADP^+$ is strongly enhanced. According to the law of mass action, all processes consuming $NADPH+H^+$, e.g. for the biosyntheses of highly reduced secondary plant products, such as isoprenoids, phenols or alkaloids (Selmar and Kleinwächter 2013b; Kleinwächter and Selmar 2015) will be favoured even without changing any enzyme activity (Fig. 2). These straightforward coherences easily but conclusively explain why the rate of biosynthesis of certain natural products might be enhanced under stress conditions although the corresponding enzyme activities had not been changed at all.

Alternatively, to the increase in natural product biosynthesis due to the passive shift mentioned above, the biosynthesis might also be elevated by a stress related up-regulation of the corresponding enzymes. Unfortunately, up to now, only limited data are available on this very interesting issue. In contrast to the tremendous lot of information dealing with the impact of biological stress (e.g., pathogen or herbivore attack) on the expression of enzymes involved in natural product biosynthesis, only

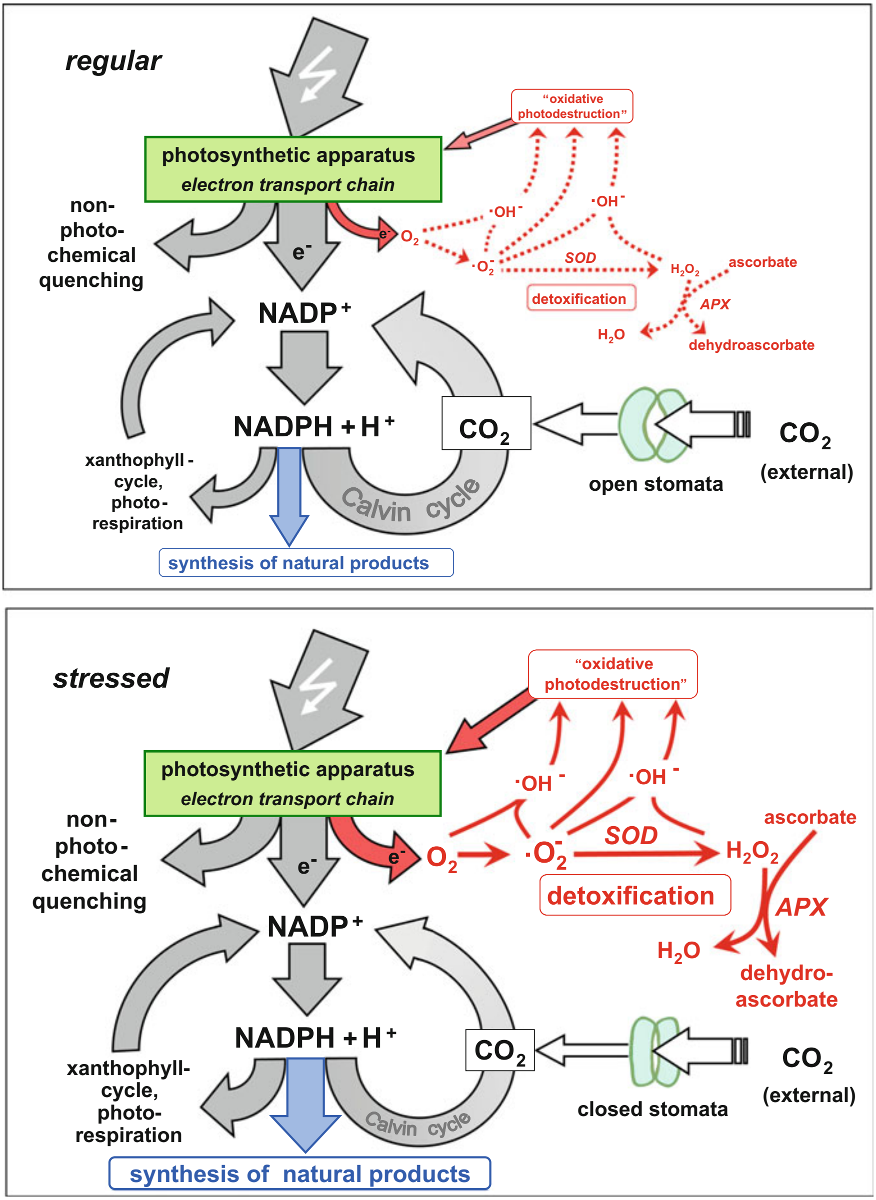

Fig. 2 Drought stress induced metabolic changes. The model scheme according to Kleinwächter and Selmar (2014) outlines the coherences between drought the stress induced increase in reduction status and the enhancement of natural product biosynthesis

very few analogous investigations with respect to drought stress have been performed. Moreover, we have to consider that plants with different genotypes might behave differentially under drought stress. In this context two native subspecies of *Origanum vulgare* (*subsp. virens and subsp. gracile*) were studied under drought stress. It turned out that the subspecies exhibited significant differences in essential oil content, compositions, and patterns of gene expression under drought stress conditions (Morshedloo et al. 2017).

Just recently, expression studies on monoterpene synthases (Radwan et al. 2017) demonstrated that the stress related enhancement of monoterpenes in sage is not only due to a passive shift as outlined above, but might also be caused—at least in part—by an elevated expression of the enzymes responsible for the biosynthesis of the essential oils. In the same manner, the stress induced increase in the glycyrrhizin concentration in *Glycyrrhiza glabra* is accompanied by an up-regulation of genes encoding the major enzymes responsible for the triterpenoid biosynthesis (Nasrollahi et al. 2014). Using semi-quantitative RT-PCR assays the authors showed that the expression of the genes encoding a squalene synthase and a ß-amyrin synthase is enhanced under drought stress. There is a massive need for further research in order to elucidate, whether or not these findings represent a quite general issue. If however, forthcoming studies will confirm that such stress related up-regulation of genes responsible for natural product biosynthesis will occur frequently, the question on the biological significance of this effect will arise. In general, the interaction with pathogens or herbivores should not be affected by drought. Accordingly, apart from this coherency, there has to be a different and additional relevance for the observed up-regulation of terpene biosynthesis. In this context, the strong isoprene emission of numerous plants (e.g., Fall 1999; Sharkey and Yeh 2001) attracts special attention: under standard conditions the isoprene emission is neglectable and the energy consumption for its biosynthesis accounts for less than 1% of the entire photosynthetic energy. However, isoprene synthesis and emission increases drastically, when the plants suffer stress. Magel et al. (2006) outlined that at elevated temperatures, the amount of energy dissipated by the strongly enhanced isoprene emission might rise up to 25% of the energy used for net photosynthesis. From these coherences it could be deduced that the energy demand and the re-oxidation of reduction of $NADPH+H^+$ for the biosynthesis of the isoprene contribute significantly to the dissipation of the excess of photosynthetic energy. Moreover the emission of isoprene will cool down the stressed leaves as well (Behnke et al. 2007). Hence an increase in the biosynthesis of highly reduced natural products seems to be necessary to enhance the amount of energy dissipation, which strongly has to be elevated under stress conditions.

We have to realize that—apart from all the well established ecological functions—the drought stress related increase in the biosynthesis of highly reduced natural products might also have a relevance as an additional mechanism for energy dissipation (Grace and Logan 2000; Wilhelm and Selmar 2011).

It is a matter of fact that drought stress generally has to be filed as negative factor, being responsible for severe yield losses in agriculture. With respect to spice and medicinal plants, however, the situation seems to be different. Since the content of active natural products determines the quality of the plant derived commodities, any approaches to increase this quality could be favourable. Based on the novel insights displayed in this review, we have to recognize that the concentration of natural products and thus the product quality of spice and medicinal plants could be enhanced by deliberately applying moderate drought stress during their cultivation. However, as drought stress also reduces the biomass production, special emphasis has to be put on the interference of these two stress related effects and the decision what is required, a high quality, i.e. high concentrations of relevant compounds or a high yield, i.e. a large amount of these compounds.

Case Study: Change in the Composition of Indole Alkaloids by Stress

Apart from the desired high concentrations of active compounds also their chemical composition influences the quality of spices and medicinal plants. Up to now—with special emphasis on the impact of drought stress—only limited data on this issue are available. To display the tremendous possibilities in modulating the composition of active compounds of certain medicinal plants, a model experiment with lesser periwinkle (*Vinca minor*) was performed. In order to preferably perceive the most distinctive effects, not a real drought situation was applied, but the stress situation was mimicked by spraying of methyl jasmonic acid (MeJA). MeJA and jasmonic acid, respectively are potent regulators of genes involved in cell growth and in most biotic and abiotic stress responses, including drought stress (Turner et al. 2002; Kazan and Manners 2008) and, moreover these growth regulators promote senescence (Cree and Mullet 1997). Accordingly, a treatment with MeJA should promote most severe and comprising stress situations that also impact secondary metabolism (Kim et al. 2006; Bloem et al. 2014; Kleinwächter et al. 2015). A corresponding approach using *Catharanthus roseus* revealed that the content and the composition of indole alkaloids strongly were affected by MeJA application (Aerts et al. 1994).

The indole alkaloids extracted from the leaves of *V. minor* were analyzed by HPLC-DAD. Although a certain difference in the alkaloid pattern of well watered control and stressed plants had been predicted, the outcome of this experiment was surprising and unexpected (Abouzeid et al. 2017). Whereas the alkaloid spectrum of the control plants was in accordance with the literature (Proksa and Grossmann, 1991; D´Amelio et al. 2012), and vincamine (B) and vincadifformine (D) had been identified as major components, the alkaloid composition of the MeJA treated plants was drastically different (Fig. 3). As response to the MeJA treatment, the concentration of vincamine and vincadifformine was strongly decreased whereas two other alkaloids (A and C) massively increased in their concentration. It can be assumed that vincamine and vincadifformine are converted to the two other, so far unidentified alkaloids. To verify this assumption, the structures as well as the

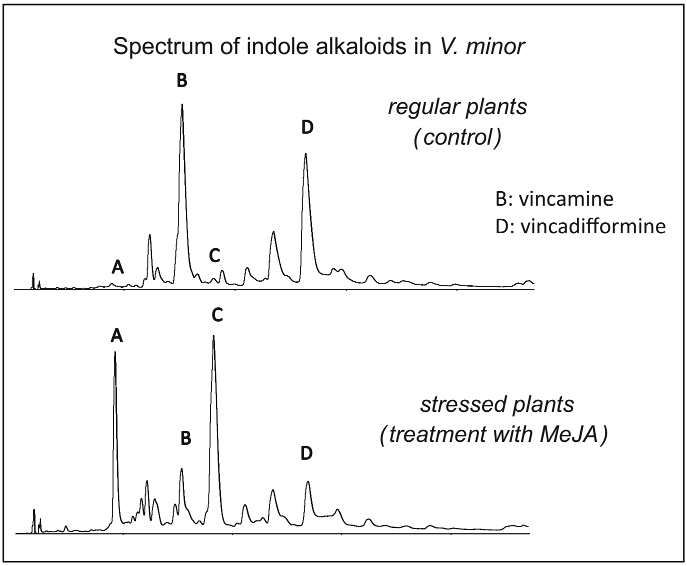

Fig. 3 Drought stress induced changes in the indole alkaloid spectrum of *V. minor*. HPLC chromatograms of the alkaloids extracted from leaves of *V. minor* according to Abouzeid et al. (2017). The upper graph shows the pattern of indole alkaloids extracted from the well watered controls, the lower one corresponds to those from *V. minor* plants which have been treated with MeJA fraction. Details of the treatment are outlined by Abouzeid et al. (2017). The identification and structure elucidation, respectively, of the A and C, whose concentrations are tremendously enhanced in the plants treated with MeJA, is under way

enzymes putatively responsible for such conversion must be identified. Right now, these compounds were highly purified to ensure the required NMR studies for their characterization and structure elucidation.

This example vividly displays that stress not only induces quantitative changes in natural product biosynthesis but also may alter the composition of the relevant substances. Much more research is required to elucidate the molecular coherences of this fascinating issue.

Conclusion

Apart from the tremendous negative effects of drought situations on growth and development, the corresponding stress situations frequently lead to an increase in the concentration of natural products. In principle, there are three possibilities to explain this enhancement (Fig. 4). First, it could be the consequence of a reduced production of biomass in the stressed plants: when the rate of biosynthesis of natural products is not changed or only slightly reduced, their concentration on dry

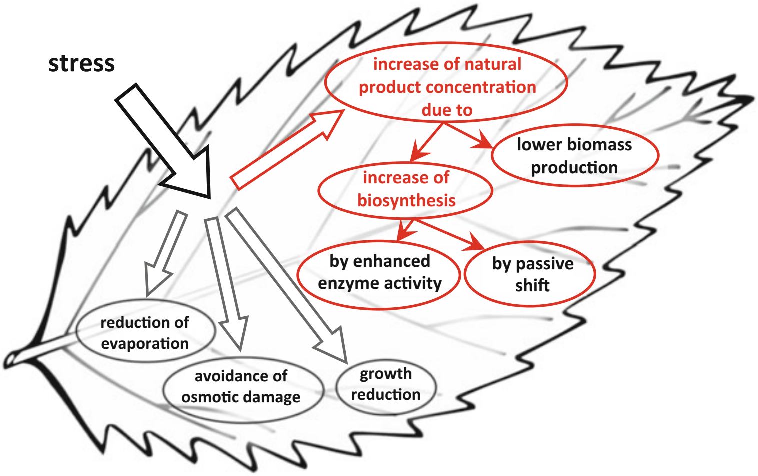

Fig. 4 The impact of drought stress on natural product concentration. The scheme displays the three different causes, why the natural product concentration is enhanced in plants suffering drought stress

or fresh weight basis simply will be elevated. Alternatively, the drought stress enhances the actual rate of biosynthesis. This could be due either to a passive shift or an active up-regulation of the enzymes involved in natural product biosynthesis. Both options are related to the strongly enhanced reduction status of the leaves exposed to drought stress. In the first case (Fig. 4), the over-reduction, which goes along with a huge increase in concentration of NADPH+H^+ and results - according to the law of mass action—in an acceleration of all processes consuming NADPH +H^+, including the biosyntheses of highly reduced secondary plant products, such as isoprenoids, phenols or alkaloids. In the second case, the enzymes responsible for the biosynthesis of natural products are actively up-regulated. The corresponding increment in NADPH+H^+ consumption significantly contributes to the dissipation of the stress related surplus of energy contributes to prevent the generation of toxic oxygen radicals (Fig. 2).

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