

New insights explain that drought stress enhances the quality of spice and medicinal plants: potential applications

Maik Kleinwächter · Dirk Selmar

Accepted: 9 October 2014 / Published online: 21 November 2014
© INRA and Springer-Verlag France 2014

Abstract Drought stress is generally considered as a negative factor in agriculture, being responsible for severe yield losses. However, medicinal plants grown under semi-arid conditions usually produce higher concentrations of active substances than same species grown under moderate climates. Currently, only limited information is available on the physiological background of this well-known phenomenon. To elucidate this issue, we review here the existing findings to unveil the underlying metabolic mechanisms. Indeed, we found that the drought stress-related metabolic changes are responsible for the accumulation of active substances in semi-arid regions. In particular, the biochemical coherences are as follows: due to limited water supply and much higher light intensities, the plants suffer from drought stress. Then, due to water shortage, stomata are closed and the uptake of CO₂ decreases markedly. As a result, CO₂ fixation via Calvin cycle decreases. This decline of CO₂ fixation leads to a massive decrease in the consumption of reduction equivalents (NADPH+H⁺), generating in turn a massive oversupply of NADPH+H⁺. As a consequence, metabolic processes are pushed towards the synthesis of highly reduced compounds, such as isoprenoids, phenols, or alkaloids. Our findings open the path to design practical approaches for enhancing the product quality of spice and medicinal plants. Indeed, by deliberately applying moderate drought stress during their cultivation, the quality of spice and medicinal plants can be enhanced significantly.

Keywords Drought stress · Secondary metabolites · Over-reduced state · Surplus of energy · Medicinal plants

M. Kleinwächter · D. Selmar (✉)
Institute for Plant Biology, Technische Universität Braunschweig,
Mendelssohnstraße 4, 38106 Braunschweig, Germany
e-mail: d.selmar@tu-bs.de

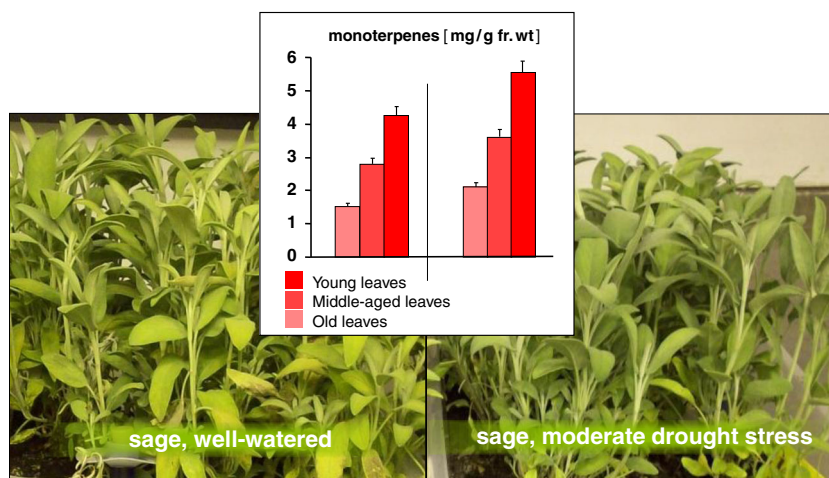
Contents

1. Introduction.....
2. Synthesis and accumulation of natural products is enhanced in drought-stressed plants.....
3. Metabolic background: higher reduction capacity in drought-stressed plants.....
4. Interaction with other factors.....
5. Feasible practical applications.....
6. Conclusion and future prospectus.....

1 Introduction

It is a matter of common knowledge that 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. Apparently, the concentrations of aroma relevant natural products are enhanced when plants are grown in semi-arid regions, i.e. under drought conditions (Fig. 1). Corresponding differences in quality are also observed with regard to medicinal plants: the content of the relevant natural products generally is less in plants cultivated in a moderate Atlantic climate than in those grown in semi-arid regions. Frequently, this 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”. Albeit—on the first sight—such assertion appears to be consistent, plant biology taught us that sunlight is not at all a limiting factor for plant growth. Even in Central Europe, plants grown in open areas without any shade absorb much more light energy in the leaves than the plants require and utilize for photosynthetic CO₂ fixation (Wilhelm and Selmar 2011). Yet, we have to consider that—at least in the subtropics—high irradiation often is co-occurring with water deficiencies. As consequence, under semi-arid conditions, plants

Fig. 1 Sage plants had been grown under well-watered and drought stress conditions for about 6 weeks. As the content of essential oils strongly depends on the developmental stage, monoterpene concentrations were quantified separately for young, middle-aged, and old leaves; data from Nowak et al. (2010)



frequently suffer drought stress. Since stress-related reactions extensively impact the entire metabolism, the synthesis and accumulation of secondary metabolites also should be affected. Unfortunately, in the past, these coherences have not been considered adequately (Selmar 2008). Just recently, Kleinwächter and Selmar (2014) compiled the relevant literature in order to get a clearer picture of this issue. These authors, for the first time, outlined the metabolic background for the stress-related enhancement of natural product synthesis (Fig. 2): Due to water shortage, in combination with high light intensities, stomata are closed. As a result, the uptake of CO_2 is markedly decreased. In consequence, the consumption of reduction equivalents ($\text{NADPH} + \text{H}^+$) for CO_2 fixation via Calvin cycle declines considerably, generating a massive oversupply of $\text{NADPH} + \text{H}^+$. Accordingly, all metabolic processes are pushed towards the synthesis of highly reduced compounds, such as isoprenoids, phenols, or alkaloids (Selmar and Kleinwächter 2013a, b).

Indeed, drought stress is generally considered as negative factor being responsible for severe yield losses in agriculture; however, with respect to spice and medicinal plants, the situation is different. Based on these novel insights, stimuli for practical approaches for enhancing the product quality of spice and medicinal plants are provided. By deliberately applying moderate drought stress during their cultivation, the quality of the related commodities can be enhanced significantly. Yet, as drought stress also reduces the biomass production of spice and medicinal plants, special emphasis is put on the interference of these two stress-related effects.

2 Synthesis and accumulation of natural products is enhanced in drought-stressed plants

The growing conditions, e.g. the temperature, the light regime, the nutrient supply, strongly influence synthesis and accumulation of secondary plant products (for review, see, e.g.

Gershenzon 1984; Falk et al. 2007). Consequently, much more severe environmental influences, such as various stress situations, which strongly impact on general metabolism (Bohnert et al. 1995), also will influence the metabolic pathways responsible for the accumulation of secondary plant products. Whereas a tremendous lot of information dealing with the impact of biological stress (e.g. pathogen or herbivore attack) on the synthesis of secondary plant products is available (for review, see, e.g. Harborne 1988; Hartmann 2007; Wink 2010)—corresponding information, how secondary metabolism is changed in response to abiotic stress—is rare. Mainly, the knowledge on the related biological background is limited (for review, see, e.g. Ramakrishna and Ravishankar 2011; Selmar and Kleinwächter 2013a, b; Kleinwächter and Selmar 2014). In contrast to biotic interactions, where generally only few factors, e.g. a certain pathogen or a certain herbivore is involved, the situation related to abiotic stress frequently seems to be more complex, since various interferences between numerous factors might co-occur: temperatures below freezing are accompanied with water shortage, the increase in light intensity mostly is associated with elevated temperatures, and lower water availability, inducing drought stress, often also entail higher salt concentrations in the soil. Accordingly, numerous studies which had been aimed to investigate the impact of one certain abiotic stress on secondary metabolism lack the distinction to other putative stress factors. Nevertheless, thorough reviewing and evaluating the literature adequately allows sound deductions on the impact of one single factor on the accumulation of natural products. This review focuses on drought stress.

A large numbers of studies manifested that plants exposed to drought stress accumulate higher concentrations of secondary metabolites than those cultivated under well-watered conditions (Table 1). There is evidence to suggest that the drought stress-related concentration enhancement is a common feature of all different classes of natural products. Corresponding increases are reported for simple as well as for complex

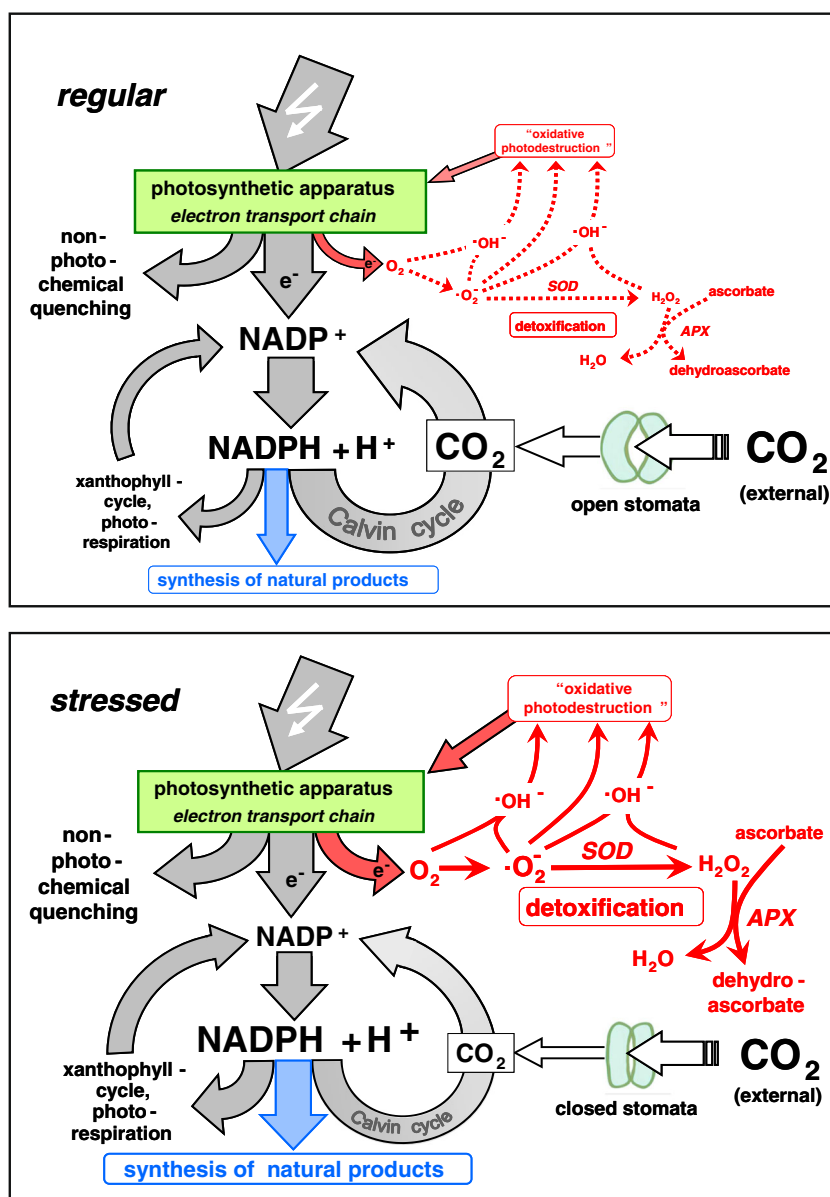


Fig. 2 Model scheme for the drought stress-related increase of natural product biosynthesis according to Selmar and Kleinwächter (2013a) and Kleinwächter and Selmar (2014). The light energy absorbed by the photosynthetic apparatus is much higher than the energy required for the CO_2 fixation. Consequently, large amounts of energy have to be dissipated via non-photochemical quenching and effective re-oxidation of $\text{NADPH} + \text{H}^+$, e.g. via xanthophyll cycle and photorespiration. Under well-watered conditions, the surplus of reduction power does not result in significant amounts of radicals. In contrast, in drought-stressed plants, energy fluxes are markedly shifted. Due to the elevated diffusion resistance caused by stomata closure, the internal concentration of CO_2 is much lower. In consequence, much less $\text{NADPH} + \text{H}^+$ is consumed within the Calvin cycle for the fixation and reduction of CO_2 . Accordingly, a

much higher share of energy has to be dissipated. Although the corresponding protective processes (non-photochemical quenching, photorespiration, xanthophyll cycle) are enhanced by feedback mechanisms, numerous electrons are transferred to molecular oxygen (Mehler reaction). The superoxide radicals generated subsequently produce a wide range of further reactive oxygen species (ROS). Due to the stress-related induction of superoxide dismutase (SOD) and ascorbate peroxidase (APX), the superoxide radicals are detoxified, and thus, the production of large amounts of ROS is prevented. According to the law of mass action, the strong increase in the reduction potential (ratio of $\text{NADPH} + \text{H}^+$ to NADP^+) enhances the synthesis of highly reduced natural products, i.e. compounds revealing a higher degree of reduction than carbohydrates

phenols, and also for the various classes of terpenes (Table 1). In equal measure, the concentrations of nitrogen-containing substances, such as alkaloids, cyanogenic glucosides, and glucosinolates, are positively impacted by drought stress, too (Table 1). There is no doubt that drought stress consistently

enhances the concentration of secondary plant products. In this context, however, we have to consider that the drought-stressed plants generally are reduced in their growth. Thus, due to the reduction in biomass—even without any enhancement of the overall amount of natural products—their

Table 1 Drought stress-related concentration increase of natural products

Simple phenols			
<i>Helianthus annuus</i>	Chlorogenic acid	Massive increase (tenfold)	del Moral 1972
<i>Prunus persica</i>	Total phenols	Higher contents	Kubota et al. 1988
<i>Thymus capitatus</i>	Phenolics	Higher contents	Delitala et al. 1986
<i>Echinacea purpurea</i>	Total phenols	Strong increase (67 %)	Gray et al. 2003
<i>Crataegus</i> spp.	Chlorogenic acid	massive increase (two-to sixfold)	Kirakosyan et al. 2004
<i>Hypericum brasiliense</i>	Total phenols	Strong increase (over 80 %)	de Abreu and Mazzafera 2005
<i>Trachyspermum ammi</i>	Total phenols	Strong increase (100 %)	Azhar et al. 2011
<i>Labisia pumila</i>	Total phenols	Significant increase (50 %)	Jaafar et al. 2012
Complex phenols			
<i>Pisum sativum</i>	Flavonoids	Strong increase (45 %)	Nogués et al. 1998
<i>Pisum sativum</i>	Anthocyanins	Strong increase (over 80 %)	Nogués et al. 1998
<i>Crataegus</i> spp.	Catechins/epicatechins	Massive increase (two- to 12-fold)	Kirakosyan et al. 2004
<i>Hypericum brasiliense</i>	Rutin/quercetin	Massive increase (fourfold)	de Abreu and Mazzafera 2005
<i>Hypericum brasiliense</i>	Xanthones	Strong increase (over 80 %)	de Abreu and Mazzafera 2005
<i>Camellia sinensis</i>	Epicatechins	Higher contents	Hernández et al. 2006
<i>Salvia miltiorrhiza</i>	Furoquinones	Significant increase	Liu et al. 2011
<i>Prunella vulgaris</i>	Rosmarinic acid	Slight increase	Chen et al. 2011
<i>Labisia pumila</i>	Anthocyanes/flavonoids	Significant increase	Jaafar et al. 2012
Monoterpenes/essential oils			
<i>Mentha × piperita</i> ssp.	Essential oils	Significant increase	Charles et al. 1990
<i>Cymbopogon pendulus</i>	Geraniol and citral	Strong increase	Singh-Sangwan et al. 1994
<i>Pinus halepensis</i>	α-Pinene, carene	Strong increase	Llusià and Peñuelas 1998
<i>Cistus monspeliensis</i>	Caryophyllene	Enormous increase	Llusià and Peñuelas 1998
<i>Satureja hortensis</i>	Essential oils	Increase	Baher et al. 2002
<i>Picea abies</i>	Monoterpenes	Strong increase	Turtola et al. 2003
<i>Pinus sylvestris</i>	Monoterpenes	Strong increase	Turtola et al. 2003
<i>Petroselinum crispum</i>	Essential oils	Strong increase (double)	Petropoulos et al. 2008
<i>Salvia officinalis</i>	Essential oils	Massive increase (two-to fourfold)	Bettaieb et al. 2009
<i>Salvia officinalis</i>	Monoterpenes	Strong increase	Nowak et al. 2010
<i>Scrophularia ningpoensis</i>	Iridoid glycosides	Increase	Wang et al. 2010
<i>Nepeta cataria</i>	Essential oils	Significant increase	Manukyan 2011
<i>Ocimum basilicum</i>	Essential oils	Significant increase	Forouzandeh et al. 2012
Di- and triterpenes			
<i>Solanum tuberosum</i>	Steroid alkaloids	Strong increase	Bejarano et al. 2000
<i>Hypericum brasiliense</i>	Betulinic acid	Strong increase	de Abreu and Mazzafera 2005
<i>Bupleurum chinense</i>	Saikosaponin	Significant increase	Zhu et al. 2009
<i>Prunella vulgaris</i>	Triterpenes	Slight increase	Chen et al. 2011
Alkaloids			
<i>Senecio longilobus</i>	Pyrrrolizidine alkaloids	Strong increase	Briske and Camp 1982
<i>Lupinus angustifolius</i>	Quinolizidin alkaloids	Strong increase	Christiansen et al. 1997
<i>Solanum tuberosum</i>	Steroid alkaloids	Strong increase	Bejarano et al. 2000
<i>Glycine max</i>	Trigonelline	Higher contents	Cho et al. 2003
<i>Papaver somniferum</i>	Morphine alkaloids	Strong increase	Szabó et al. 2003
<i>Catharanthus roseus</i>	Indole alkaloids	Strong increase (with Ca ²⁺)	Jaleel et al. 2007
<i>Phellodendron amurense</i>	Benzylisoquinolines	Strong increase	Xia et al. 2007
<i>Senecio jacobaea</i>	Pyrrrolizidine alkaloids	Massive increase	Kirk et al. 2010
<i>Nicotiana tabacum</i>	Nicotiana alkaloids	Strong increase	Çakir and Çebi 2010

Table 1 (continued)

Various classes			
<i>Manihot esculenta</i>	Cyanogenic glucosides	Strong increase	de Bruijn 1973
<i>Triglochin maritima</i>	Cyanogenic glucosides	Strong increase	Majak et al. 1980
<i>Brassica napus</i>	Glucosinolates	Massive increase	Jensen et al. 1996
<i>Coffea arabica</i>	γ -Aminobutyric acid	Massive increase (tenfold)	Bytof et al. 2005
<i>Brassica oleracea</i>	Glucosinolates	Significant increase	Radovich et al. 2005
<i>Brassica carinata</i>	Glucosinolates	Significant increase	Schreiner et al. 2009
<i>Phaseolus lunatus</i>	Cyanogenic glucosides	Higher content in stressed plants	Ballhorn et al. 2011

concentration on dry or fresh weight basis simply could be enhanced. Accordingly, corresponding explanations frequently are reported in the literature. Unfortunately, in most of the studies dealing with the impact of drought on natural product, biosynthesis data on the overall biomass per plant are lacking. One obvious reason for this deficit of information is due the fact that mostly only some certain plant parts or organs, i.e. roots, leaves, or seeds, had been in the centre of focus, whilst the overall content of the natural products on a whole plant basis was not of interest. However, in some papers, the total content of secondary plant products per entire plant is given or could be calculated from the data presented.

In *Hypericum brasiliense* plants grown under drought stress both concentration and the total amount of the phenolic compounds is drastically enhanced in comparison to the control plants (de Abreu and Mazzafera 2005). Despite the fact that the stressed *H. brasiliense* plants were quite smaller, the product of biomass and concentration of the related phenolics yield in 10 % increase of the total amount of these natural products. In the same manner, in stressed peas (*Pisum sativum*), the overall amount of anthocyanins (product of biomass and anthocyanin concentration) is about 25 % higher as in plants cultivated under standard conditions (Nogués et al. 1998): although the biomass of the stressed pea plants is only about one third of the control plants, the massive increase in the concentration of phenolic compounds still resulted in a real increase of anthocyanins in the stressed plants. In the same manner, Jaafar et al. (2012) reported that not only the concentration but also the overall production of total phenolics and flavonoids per plant is enhanced in plants suffering drought stress, although the explicit data on biomass per plant are not displayed by the authors. In contrast, the overall yield of flavonoids was nearly the same, when the plants were either grown under drought stress or under well-watered, non-stress conditions. In stressed red sage plants (*Salvia miltiorrhiza*), the overall content of furoquinones is slightly lower in plants grown under water deficiency than that of the well-watered controls, although drought stress caused a significant increase of their concentration (Liu et al. 2011).

Focussing on terpenoids, there are only few reports available which soundly document a drought stress-related increase in the total amount of terpenoids per plant. In sage

(*Salvia officinalis*), drought stress results in a massive increase in the concentration of monoterpenes, which easily overcompensate the reduction in biomass (Nowak et al. 2010). As a result, the entire amount of monoterpenes synthesized in sage plants suffering moderate drought stress is significantly higher than that of the well-watered controls. Yet, in parsley (*Petroselinum crispum*), the drought stress-related concentration enhancement of essential oils in leaves is more or less completely counterweighed by the related loss in biomass, resulting in nearly the same overall contents of essential oils in drought-stressed and well-watered plants (Petropoulos et al. 2008). In contrast, in drought-stressed catmint and lemon balm plants, the slight increase in the concentrations of monoterpenes could not compensate the stress-related detriment of growth and biomass. Accordingly, the overall content of terpenoids in the drought-stressed plants of *Melissa officinalis* and *Nepeta cataria* is lower than that in the corresponding well-watered controls (Manukyan 2011).

Unfortunately, most of the reports dealing with the impact of drought stress on nitrogen-containing natural products focus on the concentrations of these compounds in certain organs and no data on the biomass of the entire plants are available. Accordingly, no deductions on the impact of drought on the overall content of natural products could be drawn. The only exception is the work of Xia et al. (2007), who analyzed the stress-related influence on accumulation of benzylisoquinoline alkaloids in cork tree seedlings (*Phellodendron amurense*) on concentration as well as on total content basis, whereas the concentration of berberine, jatrorrhizine, and palmatine is strongly enhanced by drought stress. Due to the growth reduction of drought-stressed plants, the overall content of alkaloids is considerably reduced and accounted only for about one fourth of the control.

In conclusion, in nearly all plants analyzed, the concentrations of secondary plant products are significantly enhanced under drought stress conditions. However, 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.

3 Metabolic background: higher reduction capacity in drought-stressed plants

Based on our recurring experience in daily life, we all have internalized that energy saving represents one of the most important issues in our subsistence, and, on the first sight, it seems reasonable to transfer such statements and considerations also into plant biology. In this manner, even in reputable textbooks and in scientific publications, corresponding claims and statements can frequently be found. Despite the fact that we all know that light energy in general is not the limiting factor of photosynthesis in plants (for review, see Wilhelm and Selmar 2011), it is frequently stated: “In order to save energy, plants have evolved a certain mechanism...” or “Due to cost-benefit equations, the energy costs for a certain metabolic process must be minimized”. However, when looking at more closely, it becomes obvious that—in contrast to heterotrophic organisms—quite other cardinal coherences are crucial for the autotrophic plants. Usually, plants absorb much more energy than being required for photosynthetic CO₂ fixation. This basic statement easily can be deduced from evidence we all are aware of: elevation of ambient CO₂ concentration results in a massive enhancement of photosynthesis, quite often the rate is doubled or even tripled. In order to avoid massive damages, the tremendous surplus of the energy absorbed is dissipated by various mechanisms, i.e. non-photochemical quenching, photorespiration, or xanthophyll cycle (Fig. 2). Whereas, this protecting machinery operates flawless under regular environmental conditions, any stress induces massive imbalances. This especially accounts for the drought stress-induced stomata closure, which massively diminishes the CO₂ influx into the leaves. In consequence, far less reduction equivalents (NADPH+H⁺) are consumed and re-oxidized, respectively. Although the various energy dissipating mechanisms are raised, the chloroplastic reduction status increases. In consequence, electrons from the photosynthetic electron transport chain directly are conveyed to oxygen, generating superoxide radicals, which subsequently have to be detoxified by superoxide dismutase (SOD) and ascorbate peroxidase (APX). As result of this over-reduction, the ratio of NADPH+H⁺ to NADP⁺ is enhanced and according to the law of mass action, all processes consuming NADPH+H⁺, such as the biosyntheses of highly reduced secondary plant products, will be favoured even without changing any enzyme activity (Fig. 2).

Apart from the various well-established ecological functions, the stress-related increase in the rate of biosynthesis of highly reduced natural products seems to have also relevance as additional mechanism for energy dissipation, since large amounts of NADPH+H⁺ are consumed and the over-reduced state is lowered significantly. Such alternative significance of natural products could also be deduced from the strong isoprene emission of numerous plants (e.g. Fall 1999; Sharkey

and Yeh 2001). Whereas, under standard conditions, the energy consumption for this isoprene biosynthesis accounts for less than 1 %, it increases under stress conditions tremendously. Magel et al. (2006) calculated that at elevated temperatures, the amount of energy dissipated by the strongly enhanced isoprene emission might rise up to 25 % of the energy supply for net photosynthesis. Accordingly, it could be postulated that the energy and reduction equivalents required for the biosynthesis of the isoprene emitted by leaves indeed contribute significantly to the dissipation of the excess of photosynthetic energy.

These considerations expound that the biosynthesis of natural products indeed may represent a relevant system to dissipate the surplus of energy. Accordingly, secondary metabolites—apart from their ecological significance—also could be crucial as part of a supplemental energy dissipation machinery (Grace and Logan 2000; Wilhelm and Selmar 2011). Yet, these coherences suggest that the corresponding processes might not only be enhanced passively by shifts in the concentration of reduction equivalents, but might also be accelerated actively by increasing the corresponding catalytic abilities, i.e. the activities of the enzymes involved in the biosynthesis of the natural products. For further elucidation of this auspicious issue, much more research focussing on the impact of various abiotic stressors on the biosynthesis and accumulation of secondary metabolites is required.

4 Interaction with other factors

As outlined in detail, the concentrations of natural products are generally enhanced in plants suffering drought stress. There are two putative explanations for this phenomenon: either a real increase in biosynthesis or a stress-related change in the benchmark, i.e. alterations in the biomass used as reference value. In the latter case, the drought stress-related decrement in biomass production might be associated with a more or less unchanged rate of biosynthesis of natural products. Accordingly, this increase in the concentration—either on dry or on fresh weight base—just corresponds to purely arithmetic terms. In contrast, an authentic increase of the total content of secondary plant products due to an enhanced biosynthesis indeed is based on massive metabolic changes, putatively on the over-reduction in drought-stressed plants. However, when looking more closely, these simplified causal coherences are getting much more untransparent, since the both issues mentioned, frequently are overlaid and interfere with numerous further factors and side effects.

It is well established that secondary plant products reveal a high significance for the plants by accomplishing various ecological functions within the complex interactions of plants with their environment, e.g. to repel herbivores, to protect against pathogens, or to attract pollinators (e.g. Harborne

1988; Wink 2010; Hartmann 2007). Moreover, also with respect to abiotic stress, various putative functions for secondary plant products are known, e.g. protection against UV light or too high light intensities, action as compatible solutes, radical scavenging, or reduction of the transpiration (e.g. Edreva et al. 2008; Wink 2010). Initiated by the tremendous progress in molecular biology, we are aware that the synthesis of the relevant secondary metabolites frequently is induced, modulated, and regulated by numerous environmental impacts and abiotic factors, respectively. Yet, the situation becomes even more complex, if we consider that the biosynthesis of phytoalexins is elicited by pathogen attack (e.g. Hahlbrock et al. 2003; Saunders and O'Neill 2004) and various defence compounds effective against herbivores are synthesized as result of very complex induction mechanisms (e.g. Ferry et al. 2004). In consequence, the actual synthesis and accumulation of a certain natural product frequently is influenced and determined by numerous factors. Moreover, we have to take into account that a particular stress situation in general influences several factors, e.g. a high irradiation is frequently accompanied with elevated temperatures, elevated temperatures co-occur with higher evaporation rates, or high irradiation often parallels with UV radiation. Yet, corresponding interferences between biotic and abiotic factors are not yet understood or even considered. In this manner, we do not know if drought may impact on the entire ecosystem in a manner that it might be associated with a higher herbivore pressure, or a lesser number of pathogens. Consequently, we have to be aware that in plants exposed to drought stress complex interferences of numerous factors occur, which in concert impact on the entire metabolism and thereby on the synthesis and accumulation of natural products. For further and sound elucidation of this complex metabolic syndrome, appropriate and reliable markers are required.

When scientifically dealing with the consequences of drought stress, we thoroughly have to differentiate between the related effect on the osmotic potential and the water availability within the cell on the one hand, and the increase in redox potential due to the decline of the CO₂ influx caused by stomata closure on the other hand. With respect to the decrease in water availability, on the first sight, water potential seems to be a reliable parameter. Yet, if we consider that in response to drought, many plants produce and accumulate osmotic active substances—denoted as compatible solutes—which significantly reduce the water potential without changing the amount of water, the actual water content, seems to be a better option. In addition to the classical gravimetric methods to determine the water content, a new alternative methodology based on terahertz technology was recently presented (Breitenstein et al. 2011). However, a sound and conclusive outline of the difficult and complex contraposition of water potential and water content has to be given in a separate treatise.

When focussing on the stress-induced enhancement of redox potential, the most appropriate and reliable markers should either be the increased ratio of NADPH+H⁺ to NADP⁺, or the amount of oxygen radicals generated. Unfortunately, the real in situ concentration of both components could not be quantified without inappropriate efforts and expenditures. As alternative, frequently, the enzymes responsible for the detoxification of the reactive oxygen species (ROS) generated are estimated, i.e. the superoxide dismutases (SOD) and the ascorbate peroxidases (APX). Sad to say, these enzymes occur in various isoforms and are also part of various signal transduction chains. Accordingly, they do not indicate reliably a specific stress situation and their significance as stress markers is limited. Another candidate as general stress marker is glutathione, which also is part of the antioxidative defence against ROS. Yet, the ratio of oxidized to reduced glutathione is not always reflecting the actual redox state (for review, see Tausz et al. 2004). Moreover, the stress-induced responses of the glutathione system are multilayered and biphasic: an initial response phase is followed by an acclimation phase. Thus, the use of the glutathione system as general stress marker for routine analysis is limited (Tausz et al. 2004). As alternative, the occurrence of characteristic stress metabolites, which are synthesized and accumulated pretty much specifically in response to a particular stress situation, could be estimated to determine and quantify its metabolic impact. In this context, proline is in the centre of focus, since this amino acid is accumulated as compatible solute in plants suffering drought stress (for review, see Rhodes et al. 1999). However, the drought stress-induced proline accumulation does not occur in all plant species. A further option might be the quantification of γ -amino butyric acid (GABA), a stress metabolite produced by decarboxylation of glutamic acid (for review, see Kinnersley and Turano 2000). Indeed, GABA is produced to a high extent in response to drought stress, but it also is accumulated under various other stress conditions (Satya Narayan and Nair 1990; Bown and Shelp 1997). Thus, alternative markers are required. One of the most promising options is the abundance of dehydrins. It is well established that dehydrins are frequently synthesized in plant cells suffering drought stress (for review, see Close 1997; Allagulova et al. 2003; Bouché and Fromm 2004). It is assumed that these small hydrophilic proteins reveal various protective functions in desiccating cells (for review, see Hara 2010). Indeed, these small protective proteins had been first discovered in maturing seeds in the course of late embryogenesis. Yet, meanwhile, we have realized that the occurrence of dehydrins during seed development is related to the appearance of maturation drying (Radwan et al. 2014), and also in seed dehydrins are synthesized in response to water deficiency. Accordingly, the expression of dehydrins seems to be the best option to monitor the impact of drought stress. However, we have to consider that any stress situation is really complex and eclectic. This

vividly was demonstrated by Kramer et al. (2010), who found that in coffee seeds whilst drying the expression of dehydrins and the accumulation of the stress metabolite GABA follow different time patterns. Obviously, in the course of stress responses, several metabolic responses occur in parallel and/or subsequently. As outlined above, we have to consider that in leaves exposed to drought stress, apart from the impact of the decrease in water availability, also the over-reduction due to stomata closure, entail numerous metabolic responses. Consequently, any comprehensive elucidation of the entire metabolic stress syndrome in medicinal plants requires a combination of several markers. In this context, apart from the accumulation of GABA and the expression of dehydrins, especially markers, which reflect the status of the various energy dissipation systems (e.g. the non-photochemical quenching, the xanthophyll cycle, or the photorespiration), have to be determined.

5 Feasible practical applications

As outlined in detail, the stress-related responses are complex and the impacts on secondary metabolism are multifarious: various elicitation and induction mechanisms are overlaid, and numerous reactions and processes are counteracting. Apart from the basic influence on secondary metabolism, above all, the consequences and aftereffects of drought stress on the general metabolism are most prominent and cause severe repercussions. In this context, losses in biomass, retards in development, or changes in growth behaviour are of special interest. Moreover, the general metabolic status is frequently altered and the ratio between generative and vegetative characteristics is shifted (e.g. Houter and Nederhoff 2007). Furthermore, drought stress could change the *source-sink* properties of the entire plant. Thus, in addition to the inducing factors already mentioned, drought stress impacts on the overall performance of the biosynthesis and the allocation and accumulation of natural products by altering the overall physiological nature of a certain organ or tissue.

In conclusion, the effects of drought stress on secondary metabolism, and thus on the quality of medicinal plants are multilayered and very complex. Due to the coherences mentioned, a deliberate application of drought stress during the cultivation of medicinal plants should principally result in an increase of biosynthesis of secondary metabolites. But, due to the other, co-occurring impacts and effects, this enhancement frequently might be compensated or even overcompensated. Accordingly, a general recommendation for the deliberate application of drought stress to increase the quality of medicinal plants cannot be given. Nevertheless, in many cases, such approach undoubtedly will be successful. However, we always have to sound out the advantages and the drawbacks of corresponding approaches. To facilitate

corresponding assessments, Selmar and Kleinwächter (2013a) have proposed to answer some simple questions:

- What kind and which level of stress enhance the accumulation of the desired compounds without causing too high losses in biomass?
- What is required, a high concentration or a large bulk (total amount of natural products versus high concentrations in the drug)?
- Are the substances synthesized and accumulated in *source* or in *sink* tissues?
- Are the substances synthesized and accumulated in generative or vegetative organs?
- Could the accumulation also be increased by phytohormone treatments (e.g. methyl jasmonate, salicylic acid)?
- Should the stress be applied only within a certain phase of cultivation or whilst a special developmental phase in order to obtain maximal quality?

It is arguable whether these considerations could be transferred into appropriate agricultural applications. One of the simplest approaches is to alter the irrigation regime (e.g. Radovich et al. 2005). This, however, is restricted to semi-arid regions, where supplemental watering is required, which could be reduced. In contrast, in moderate climates, the water supply by rainfall cannot be influenced directly. Nonetheless, also in these areas, the moisture content of the soil could be altered, e.g. by the choice of the cultivation area or by some simple measures. In this context, the design and shaping of the acreage directly impacts on the drainage properties, e.g. fields with slope will retain the water markedly less than flat plains consisting of soils with the same water holding capacity. In fact, even in plains, the drainage capability could be modulated artificially by certain cultivation measures. The establishment of a furrow and ridge system, which frequently is used for surface irrigation in arid regions, seems to be appropriate also for generating drought stress situations by increasing the gradients of soil moisture contents. When irrigation is omitted, the soil water content in the furrows will nearly be the same as in untreated fields, but the moisture content in the ridges strongly decreases due to an enhanced drainage effect. Indeed, drainage alternatively could be also achieved by increasing the proportion of sand in the soil. However, such measure would irreversibly change the character of the soil and should only be applied in exceptional cases.

An auxiliary strategy to influence the product quality via a stress-related enhancement of secondary metabolite synthesis is based on the application of phytohormones or growth regulators, being part of the signal transduction chain of stress responses. In this context, the application of methyl jasmonate is the most promising approach. Methyl jasmonate is a volatile ester of jasmonic acid, which first was successfully employed in numerous tissue and cell culture systems to enhance the concentration of secondary metabolites (for review, see

Namdeo 2007). After the uptake into the cells, the ester is hydrolysed to yield the active growth regulator. Meanwhile, methyl jasmonate was also employed for the effective elicitation of natural products in intact plants. In this manner, the synthesis of indole alkaloids was increased in seedlings of *Catharanthus roseus* and *Cinchona ledgeriana* (Aerts et al. 1994), the content of phenols and monoterpenes had been enhanced in *Ocimum basilicum* (Kim et al. 2006), and the concentration of glucosinolates was increased in *Brassica rapa* (Loivamäki et al. 2004). Based on such promising approaches, the usage of methyl jasmonate for quality improvement of medicinal and spice plants seems to be an encouraging alternative for a direct drought treatment. In the same manner, salicylic acid, an endogenous key signal substance, responsible for systemic resistance (for review, see Durrant and Dong 2004), was also used for influencing the synthesis and accumulation of secondary metabolites: the content of phenolics could strongly be increased by the application of salicylic acid to *Echinacea purpurea* plants (Kuzel et al. 2009), as well as the accumulation of glucosinolates in oilseed rape (Kiddle et al. 1994). Unfortunately, apart from their effects on secondary metabolism, salicylic acid and methyl jasmonate also impact on primary metabolism and developmental processes. In this context, the induction of senescence and retardation of growth are of special interest, when the application of growth regulators and phytohormones are considered to increase product quality. Thus, in the same manner, as in the case of deliberately applying drought stress directly, also in the case of utilizing salicylic acid and methyl jasmonate, a thorough balancing of pros and cons is required. This however necessitates a sound and comprehensive knowledge of the related scientific background.

When reflecting our experiences from daily life, we will be aware that—in addition to the well-known quality enhancement of medicinal plants grown under semi-arid conditions—there are various further examples that illustrate the relevance of stress induction. Sometimes the opposite, i.e. the omission of stress, could also be used for an enhancement of the quality of plant derived commodities: To achieve the highest quality of Japanese green teas exhibiting lowest concentrations of undesired compounds, the *Camellia sinensis* plants frequently are grown under artificial shading. As result, these plants suffer less photo-oxidative stress in comparison to plants, which are exposed to full sunlight. As outlined above, in these tea plants—as result of a significantly decreased over-reduced status—the synthesis of secondary plant products should be declined—and, indeed, corresponding analysis revealed that the content of monoterpenes as well as that of coumarin is significantly lower in the shaded, non-stressed plants (Shimoda et al. 1995). Another vivid example for stress reduction by shading which results in a corresponding decrease of secondary plant products is the production of certain cured tobacco leaves. When *Nicotiana tabacum* plants are generally grown

in Southern and Middle-America in full sunlight, they reveal the typical dark colours of the so-called Brazilian quality. The shading of the tobacco plants, even when grown in Brazil, yields in much brighter hues, comparable to those of tobacco leaves grown in Sumatra, where the solar irradiance is much lower due to the foggy climate. Phytochemical analysis revealed that the concentrations of total phenols and alkaloids indeed are lower in tobacco leaves grown in shade (Andersen et al. 1985), and thus, confirming once again, the interrelation between oxidative stress and synthesis of secondary plants products.

6 Conclusion and future prospectus

Indeed, drought stress is always considered as negative factor being responsible for severe yield losses in agriculture; however, with respect to spice and medicinal plants, the situation is different. From the novel insights and cognitions mentioned, it could be deduced that the generation of drought stress situations, either directly induced by water shortage, or indirectly elicited via the application of growth regulators, frequently leads to an enhancement of the contents of secondary plant products and thereby increasing the quality of plant-derived commodities. However, due to numerous interactions, the related increase could be compensated by other metabolic responses, especially by growth reduction, by a decrease in biomass production, or an onset of senescence. Thus, for each particular plant-derived commodity, a thorough balancing of pros and cons is necessary. This however, requires much more research on this complex issue.

References

- Aerts RJ, Gisi D, de Carolis E, de Luca V, Baumann TW (1994) Methyl jasmonate vapor increases the developmentally controlled synthesis of alkaloids in *Catharanthus* and *Cinchona* seedlings. *Plant J* 5:635–643. doi:10.1111/j.1365-313X.1994.00635.x
- Allagulova CR, Gimalov FR, Shakirova FM, Vakhitov VA (2003) The plant dehydrins: structure and putative functions. *Biochem-US* 68: 945–951. doi:10.1023/A:1026077825584
- Andersen RA, Kasperbauer MJ, Burton HR (1985) Shade during growth—effects on chemical composition and leaf color of air-cured burley tobacco. *Agron J* 77:543–546. doi:10.2134/agronj1985.00021962007700040009x
- Azhar N, Hussain B, Ashraf YM, Abbasi KY (2011) Water stress mediated changes in growth, physiology and secondary metabolites of Desi Ajwain (*Trachyspermum ammi* L.). *Pak J Bot* 43(SI):15–19
- Baher ZF, Mirza M, Ghorbanli M, Rezaei MB (2002) The influence of water stress on plant height, herbal and essential oil yield and composition in *Satureja hortensis* L. *Flavour Frag J* 17:275–277. doi:10.1002/ffj.1097

- Ballhorn DJ, Kautz S, Jensen M, Schmitt S, Heil M, Hegeman AD (2011) Genetic and environmental interactions determine plant defences against herbivores. *J Ecol* 99:313–326. doi:10.1111/j.1365-2745.2010.01747.x
- Bejarano L, Mignolet E, Devaux A, Espinola N, Carrasco E, Larondelle Y (2000) Glycoalkaloids in potato tubers: the effect of variety and drought stress on the α -solanine and α -chaconine contents of potatoes. *J Sci Food Agric* 80:2096–2100. doi:10.1002/1097-0010(200011)80:14<2096::AID-JSFA757>3.0.CO;2-6
- Bettaieb I, Zakhama N, Aidi Wannas W, Kchouk ME, Marzouk B (2009) Water deficit effects on *Salvia officinalis* fatty acids and essential oils composition. *Sci Hortic-Amsterdam* 120(2):271–275. doi:10.1016/j.scienta.2008.10.016
- Bohnert HJ, Nelson DE, Jensen RG (1995) Adaptations to environmental stresses. *Plant Cell* 7:1099–1111. doi:10.1105/tpc.7.7.1099
- Bouché N, Fromm H (2004) GABA in plants: just a metabolite. *Trends Plant Sci* 9:100–115. doi:10.1016/j.tplants.2004.01.006
- Bown AW, Shelp BJ (1997) The metabolism and functions of γ -aminobutyric acid. *Plant Physiol* 115:1–5
- Breitenstein B, Scheller M, Shakfa MK, Kinder T, Müller-Wirts T, Koch M, Selmar D (2011) Introducing terahertz technology into plant biology: a novel method to monitor changes in leaf water status. *J Appl Bot Food Qual* 82(2):158–161
- Briske DD, Camp BJ (1982) Water stress increases alkaloid concentrations in threadleaf groundsel (*Senecio longilobus*). *Weed Sci* 30(1):106–108
- Bytof G, Knopp S-E, Schieberle P, Teutsch I, Selmar D (2005) Influence of processing on the generation of γ -aminobutyric acid in green coffee beans. *Eur Food Res Technol* 220:245–250. doi:10.1007/s00217-004-1033-z
- Çakir R, Çebi U (2010) The effect of irrigation scheduling and water stress on the maturity and chemical composition of Virginia tobacco leaf. *Field Crop Res* 119:269–276. doi:10.1016/j.fcr.2010.07.017
- Charles DJ, Joly RJ, Simon JE (1990) Effects of osmotic stress on the essential oil content and composition of peppermint. *Phytochemistry* 29:2837–2840. doi:10.1016/0031-9422(90)87087-B
- Chen Y, Guo Q, Liu L, Liao L, Zaibiao Z (2011) Influence of fertilization and drought stress on the growth and production of secondary metabolites in *Prunella vulgaris* L. *J Med Plants Res* 5(9):1749–1755
- Cho Y, Njitiv N, Chen X, Lightfoot DA, Wood AJ (2003) Trigonelline concentration in field-grown soybean in response to irrigation. *Biol Plant* 46(3):405–410. doi:10.1023/A:1024390522259
- Christiansen JL, Jørnsgard B, Buskov S, Olsen CE (1997) Effect of drought stress on content and composition of seed alkaloids in narrow-leaved lupin, *Lupinus angustifolius* L. *Eur J Agron* 7:307–314. doi:10.1016/S1161-0301(97)00017-8
- Close TJ (1997) Dehydrins: a commonality in the response of plants to dehydration and low temperature. *Physiol Plant* 100:291–296. doi:10.1111/j.1399-3054.1997.tb04785.x
- de Abreu IN, Mazzafera P (2005) Effect of water and temperature stress on the content of active constituents of *Hypericum brasiliense* Choisy. *Plant Physiol Biochem* 43:241–248. doi:10.1016/j.plaphy.2005.01.020
- de Bruijn GH (1973) The cyanogenic character of cassava (*Manihot esculenta*). In: Nestel B, MacIntyre R (eds) Chronic cassava toxicity. International Development Research Centre, Ottawa, pp 43–48
- del Moral R (1972) On the variability of chlorogenic acid concentration. *Oecologia* 9:289–300. doi:10.1007/BF00345238
- Delitala I-F, Gessa C, Solinas V (1986) Water stress and flexibility of phenolic metabolism in *Thymus capitatus*. *Fitoterapia* 57(6):401–408
- Durrant WE, Dong X (2004) Systemic acquired resistance. *Annu Rev Phytopathol* 42:185–209. doi:10.1146/annurev.phyto.42.040803.140421
- Edreva A, Velikova V, Tsonev T, Dagnon S, Gürel A, Aktaş L, Gesheva E (2008) Stress-protective role of secondary metabolites: diversity of functions and mechanisms. *Gen Appl Plant Physiol* 34(1–2):67–78
- Falk KL, Tokuhisa JG, Gershenzon J (2007) The effect of sulfur nutrition on plant glucosinolate content: physiology and molecular mechanisms. *Plant Biol* 9:573–581. doi:10.1055/s-2007-965431
- Fall R (1999) Biogenic emissions of volatile organic compounds from higher plants. In: Hewitt CN (ed) Reactive hydrocarbons in the atmosphere. Academic Press, pp 41–95
- Ferry N, Edwards MG, Gatehouse JA, Gatehouse AMR (2004) Plant–insect interactions: molecular approaches to insect resistance. *Curr Opin Biotechnol* 15:155–161. doi:10.1016/j.copbio.2004.01.008
- Forouzandeh M, Fanoudi M, Arzanjou E, Tabiei H (2012) Effect of drought stress and types of fertilizers on the quantity and quality of medicinal plant basil (*Ocimum basilicum* L.). *Ind J Innov Dev* 1(10):734–737
- Gershenzon J (1984) Changes in the levels of plant secondary metabolites under water and nutrient stress. *Recent Adv Phytochem* 18:273–320
- Grace SC, Logan BA (2000) Energy dissipation and radical scavenging by the plant phenylpropanoid pathway. *Philos T Roy Soc B* 355:1499–1510. doi:10.1098/rstb.2000.0710
- Gray DE, Pallardy SG, Garrett HE, Rottinghaus G (2003) Acute drought stress and plant age effects on alkamide and phenolic acid content in purple coneflower roots. *Planta Med* 69(1):50–55. doi:10.1055/s-2003-37026
- Hahlbrock K, Bednarek P, Ciolkowski I, Hamberger B, Heise A, Liedgens H, Logemann E, Nürnberger T, Schmelzer E, Somssich IE (2003) Non-self recognition, transcriptional reprogramming, and secondary metabolite accumulation during plant/pathogen interactions. *Proc Natl Acad Sci U S A* 100(2):14569–14576
- Hara M (2010) The multifunctionality of dehydrins: an overview. *Plant Signal Behav* 5:1–6. doi:10.4161/psb.5.1.10306
- Harborne JB (1988) Introduction to ecological biochemistry, 3rd edn. Academic Press, London
- Hartmann T (2007) From waste products to ecochemicals: fifty years research of plant secondary metabolism. *Phytochemistry* 68:2831–2846. doi:10.1016/j.phytochem.2007.09.017
- Hernández I, Alegre L, Munné-Bosch S (2006) Enhanced oxidation of flavan-3-ols and proanthocyanidin accumulation in water-stressed tea plants. *Phytochemistry* 67:1120–1126. doi:10.1016/j.phytochem.2006.04.002
- Houter B, Nederhoff E (2007) Controlling plant growth, part 3. Plant balance: ‘vegetative’ or ‘generative’. *Grower* 62(2):42–44
- Jaafar HZ, Ibrahim MH, Mohamad Fakri NF (2012) Impact of soil field water capacity on secondary metabolites, phenylalanine ammonia-lyase (PAL), malondialdehyde (MDA) and photosynthetic responses of Malaysian kacip fatimah (*Labisia pumila* Benth). *Molecules* 17(6):7305–7322. doi:10.3390/molecules17067305
- Jaleel CA, Manivannan P, Sankar B, Kishorekumar A, Gopi R, Somasundaram R, Panneerselvam R (2007) Induction of drought stress tolerance by ketoconazole in *Catharanthus roseus* is mediated by enhanced antioxidant potentials and secondary metabolite accumulation. *Colloid Surf B* 60(2):201–206. doi:10.1016/j.colsurfb.2007.06.010
- Jensen CR, Mogensen VO, Mortensen G, Fieldsend JK, Milford GFJ, Andersen MN, Thage JH (1996) Seed glucosinolate, oil and protein contents of field-grown rape (*Brassica napus* L.) affected by soil drying and evaporative demand. *Field Crop Res* 47:93–105. doi:10.1016/0378-4290(96)00026-3
- Kiddle GA, Doughty KJ, Wallsgrave RM (1994) Salicylic acid-induced accumulation of glucosinolates in oilseed rape (*Brassica napus* L.) leaves. *J Exp Bot* 45(278):1343–1346. doi:10.1093/jxb/45.9.1343
- Kim HJ, Chen F, Wang X, Rajapakse NC (2006) Effect of methyl jasmonate on secondary metabolites of sweet basil (*Ocimum basilicum* L.). *J Agric Food Chem* 54(6):2327–2332. doi:10.1021/jf051979g
- Kinnersley AM, Turano FJ (2000) Gamma aminobutyric acid (GABA) and plant responses to stress. *Cr Rev Plant Sci* 19:479–509. doi:10.1080/07352680091139277
- Kirakosyan A, Kaufman P, Warber S, Zick S, Aaronson K, Bolling S, Chul Chang S (2004) Applied environmental stresses to enhance the

- levels of polyphenolics in leaves of hawthorn plants. *Physiol Plant* 121(2):182–186. doi:10.1111/j.1399-3054.2004.00332.x
- Kirk H, Vrieling K, van der Meijden E, Klinkhamer PGL (2010) Species by environment interactions affect pyrrolizidine alkaloid expression in *Senecio jacobaea*, *Senecio aquaticus*, and their hybrids. *J Chem Ecol* 36:378–387. doi:10.1007/s10886-010-9772-8
- Kleinwächter M, Selmar D (2014) Influencing the product quality by applying drought stress during the cultivation of medicinal plants. In: Ahmad P, Wani MR (eds) *Physiological mechanisms and adaptation strategies in plants under changing environment -volume 1*. Springer New York, pp 57–73. doi: 10.1007/978-1-4614-8591-9_3
- Kramer D, Breitenstein B, Kleinwächter M, Selmar D (2010) Stress metabolism in green coffee beans (*Coffea arabica* L.): expression of dehydrins and accumulation of GABA during drying. *Plant Cell Physiol* 51(4):546–553. doi:10.1093/pcp/pcq019
- Kubota N, Mimura H, Shimamura K (1988) The effects of drought and flooding on the phenolic compounds in peach fruits. *Scientific Reports of the Faculty of Agriculture, Okayama University* 171:17–21
- Kuzel S, Vydra J, Triska J, Vrchtova N, Hruba M, Cigler P (2009) Elicitation of pharmacologically active substances in an intact medicinal plant. *J Agric Food Chem* 57(17):7907–7911. doi:10.1021/jf9011246
- Liu H, Wang X, Wang D, Zou Z, Liang Z (2011) Effect of drought stress on growth and accumulation of active constituents in *Salvia miltiorrhiza* Bunge. *Ind Crop Prod* 33:84–88. doi:10.1016/j.indcrop.2010.09.006
- Llusià J, Peñuelas J (1998) Changes in terpene content and emission in potted Mediterranean woody plants under severe drought. *Can J Bot* 76:1366–1373. doi:10.1139/b98-141
- Loivamäki M, Holopainen JK, Nerg AM (2004) Chemical changes induced by methyl jasmonate in oilseed rape grown in the laboratory and in the field. *J Agric Food Chem* 52(25):7607–7613. doi:10.1021/jf049027i
- Magel E, Mayrhofer S, Müller A, Zimmer I, Hampp R, Schnitzler JP (2006) Photosynthesis and substrate supply for isoprene biosynthesis in poplar leaves. *Atmos Environ* 40:138–151. doi:10.1016/j.atmosenv.2005.09.091
- Majak W, McDiarmid RE, Hall JW, van Ryswyk AL (1980) Seasonal variation in the cyanide potential of arrowgrass (*Triglochin maritima*). *Can J Plant Sci* 60(4):1235–1241. doi:10.4141/cjps80-176
- Manukyan A (2011) Effect of growing factors on productivity and quality of lemon catmint, lemon balm and sage under soilless greenhouse production: I. Drought stress. *Med Aromat Plant Sci Biotechnol* 5(2):119–125
- Namdeo AG (2007) Plant cell elicitation for production of secondary metabolites: A review. *Pharmacogn Rev* 1(1):69–79
- Nogués S, Allen DJ, Morison JIL, Baker NR (1998) Ultraviolet-B radiation effects on water relations, leaf development, and photosynthesis in droughted pea plants. *Plant Physiol* 117:173–181. doi:10.1104/pp.117.1.173
- Nowak M, Manderscheid R, Weigel H-J, Kleinwächter M, Selmar D (2010) Drought stress increases the accumulation of monoterpenes in sage (*Salvia officinalis*), an effect that is compensated by elevated carbon dioxide concentration. *J Appl Bot Food Qual* 83:133–136
- Petropoulos SA, Daferera D, Polissiou MG, Passam HC (2008) The effect of water deficit stress on the growth, yield and composition of essential oils of parsley. *Sci Hortic-Amsterdam* 115:393–397. doi:10.1016/j.scienta.2007.10.008
- Radovich TJK, Kleinhenz MD, Streeter JG (2005) Irrigation timing relative to head development influences yield components, sugar levels, and glucosinolate concentrations in cabbage. *J Am Soc Hort Sci* 130(6):943–949
- Radwan A, Hara M, Kleinwächter M, Selmar D (2014) Dehydrin expression in seeds and maturation drying: a paradigm change. *Plant Biol* 16:853–855. doi:10.1111/plb.12228
- Ramakrishna A, Ravishankar GA (2011) Influence of abiotic stress signals on secondary metabolites in plants. *Plant Signal Behav* 6(11):1720–1731. doi:10.4161/psb.6.11.17613
- Rhodes D, Verslues PE, Sharp RE (1999) Role of amino acids in abiotic stress resistance. In: Singh BK (ed) *Plant amino acids: biochemistry and biotechnology*. Marcel Dekker Inc, New York, Basel, Hong Kong, pp 319–356
- Satya Narayan V, Nair PM (1990) Metabolism, enzymology and possible roles of 4-aminobutyrate in higher plants. *Phytochemistry* 29:367–375. doi:10.1016/0031-9422(90)85081-P
- Saunders J, O'Neill NR (2004) The characterization of defense responses to fungal infection in alfalfa. *Biocontrol* 49:715–728. doi:10.1007/s10526-004-5281-4
- Schreiner M, Beyene B, Krumbein A, Stützel H (2009) Ontogenetic changes of 2-propenyl and 3-indolylmethyl glucosinolates in *Brassica carinata* leaves as affected by water supply. *J Agric Food Chem* 57(16):7259–7263. doi:10.1021/jf901076h
- Selmar D (2008) Potential of salt and drought stress to increase pharmaceutical significant secondary compounds in plants. *Landbauforsch Völk* 58:139–144
- Selmar D, Kleinwächter M (2013a) Influencing the product quality by deliberately applying drought stress during the cultivation of medicinal plants. *Ind Crop Prod* 42:558–566. doi:10.1016/j.indcrop.2012.06.020
- Selmar D, Kleinwächter M (2013b) Stress enhances the synthesis of secondary plant products: the impact of stress-related over-reduction on the accumulation. *Plant Cell Physiol* 54(6):817–826. doi:10.1093/pcp/pct054
- Sharkey TD, Yeh S (2001) Isoprene emission from plants. *Annu Rev Plant Physiol* 52:407–436. doi:10.1146/annurev.arplant.52.1.407
- Shimoda M, Shigematsu H, Hideki S, Yutaka O (1995) Comparison of volatile compounds among different grades of green tea and their relations to odour attributes. *J Agric Food Chem* 43:1621–1625. doi:10.1021/jf00054a038
- Singh-Sangwan N, Abad Farooqi AH, Sangwan RS (1994) Effect of drought stress on growth and essential oil metabolism in lemon-grasses. *New Phytol* 128(1):173–179. doi:10.1111/j.1469-8137.1994.tb04000.x
- Szabó B, Tyihák E, Szabó LG, Botz L (2003) Mycotoxin and drought stress induced change of alkaloid content of *Papaver somniferum* plantlets. *Acta Bot Hung* 45(3/4):409–417. doi:10.1556/ABot.45.2003.3-4.15
- Tausz M, Šircelj H, Grill D (2004) The glutathione system a stress marker in plant ecophysiology: is a stress-response concept valid? *J Exp Bot* 55(404):1955–1962. doi:10.1093/jxb/erh194
- Turtola S, Manninen A-M, Rikala R, Kainulainen P (2003) Drought stress alters the concentration of wood terpenoids in Scots pine and Norway spruce seedlings. *J Chem Ecol* 29:1981–1995. doi:10.1023/A:1025674116183
- Wang DH, Du F, Liu HY, Liang ZS (2010) Drought stress increases iridoid glycosides biosynthesis in the roots of *Scrophularia ningpoensis* seedlings. *J Med Plants Res* 4(24):2691–2699. doi:10.5897/JMPR09.338
- Wilhelm C, Selmar D (2011) Energy dissipation is an essential mechanism to sustain the viability of plants: the physiological limits of improved photosynthesis. *J Plant Physiol* 168(2):79–87. doi:10.1016/j.jplph.2010.07.012
- Wink M (2010) Introduction: biochemistry, physiology and ecological functions of secondary metabolites. In: Wink M (ed) *Biochemistry of plant secondary metabolism*. Wiley-Blackwell, pp 1–19
- Xia L, Yang W, Xiufeng Y (2007) Effects of water stress on berberine, jatrorrhizine and palmatine contents in amur corktree seedlings. *Acta Ecol Sin* 27(1):58–64. doi:10.1016/S1872-2032(07)60011-0
- Zhu Z, Liang Z, Han R, Wang X (2009) Impact of fertilization on drought response in the medicinal herb *Bupleurum chinense* DC.: growth and saikosaponin production. *Ind Crop Prod* 29(2–3):629–63. doi:10.1016/j.indcrop.2008.08.002