

Scientists' Warning on Climate Change and Medicinal Plants



Authors

Wendy L. Applequist¹, Josef A. Brinckmann², Anthony B. Cunningham³, Robbie E. Hart¹, Michael Heinrich⁴, David R. Katerere⁵, Tinde van Andel⁶

Affiliations

- 1 William L. Brown Center, Missouri Botanical Garden, St. Louis, MO, U.S.A.
- 2 Traditional Medicinals, Sebastopol, CA, U.S.A.
- 3 School of Veterinary and Life Sciences, Murdoch University, Murdoch WA, Australia
- 4 Pharmacognosy and Phytotherapy, UCL School of Pharmacy, University of London, London, U.K.
- 5 Department of Pharmaceutical Science, Tshwane University of Technology, Pretoria, R. S. A.
- 6 Naturalis Biodiversity Center, Leiden, The Netherlands; Biosystematics Group, Wageningen University, The Netherlands

Key words

climate change, ethnobotany, medicinal plants, sustainability, traditional knowledge, traditional medicine

received September 18, 2019

revised October 28, 2019

accepted October 30, 2019

Bibliography

DOI <https://doi.org/10.1055/a-1041-3406>

Published online | *Planta Med* © Georg Thieme Verlag KG
Stuttgart · New York | ISSN 0032-0943

Correspondence

Dr. Wendy Applequist

William L. Brown Center, Missouri Botanical Garden
4344 Shaw Blvd., St. Louis, MO 63110, U.S.A.
Phone: + 1 31 45 77 0267, Fax: + 1 31 45 77 0800
wendy.applequist@mobot.org

Endorsements

This article is endorsed by a number of the world's leading scientists, as detailed in the "Endorsement" section at the end.

ABSTRACT

The recent publication of a World Scientists' Warning to Humanity highlighted the fact that climate change, absent strenuous mitigation or adaptation efforts, will have profound negative effects for humanity and other species, affecting numerous aspects of life. In this paper, we call attention to one of these aspects, the effects of climate change on medicinal plants. These plants provide many benefits for human health, particularly in communities where Western medicine is unavailable. As for other species, their populations may be threatened by changing temperature and precipitation regimes, disruption of commensal relationships, and increases in pests and pathogens, combined with anthropogenic habitat fragmentation that impedes migration. Additionally, medicinal species are often harvested unsustainably, and this combination of pressures may push many populations to extinction. A second issue is that some species may respond to increased environmental stresses not only with declines in biomass production but with changes in chemical content, potentially affecting quality or even safety of medicinal products. We therefore recommend actions including conservation and local cultivation of valued plants, sustainability training for harvesters and certification of commercial material, preservation of traditional knowledge, and programs to monitor raw material quality in addition to, of course, efforts to mitigate climate change.

Introduction

In 1992, the first "World Scientists' Warning to Humanity" [1] highlighted the dangerously unsustainable rates of anthropogenic damage to the atmosphere, topsoil, forests, freshwater and ocean resources, and biodiversity overall. The 1575 signatories, including 99 Nobel laureates, called for stabilization of the human population and reduced consumption to avoid environmental catastrophes. In a recent publication entitled "World Scientists' Warn-

ing to Humanity: a Second Notice" [2], a group including 15364 scientist signatories from 184 countries expressed alarm that in the years following that publication, few of the ominous trends highlighted have been adequately addressed, and most have continued to worsen. Furthermore, the first Warning to Humanity did not enumerate climate change among the major imminent threats, only noting that it was unclear whether the effects of global warming would be tolerable. It is now generally accepted that climate change is likely to cause substantial disruption to

both natural and agricultural ecosystems, making our situation even worse than originally estimated. The Second Warning to Humanity presented up-to-date evidence for the continuing unsustainable loss of major environmental resources on which humanity depends and made broad-scale proposals for steps humanity could take to avoid environmental collapse.

In the wake of this important publication, the Alliance of World Scientists encouraged the scientific community to continue the Scientists' Warning campaign by preparing discipline-specific "Warning" papers highlighting the potential detrimental effects of climate change on specific aspects of environmental or human well-being. For example, the first Scientists' Warning discipline-specific papers included warnings regarding the risk of significant impacts on wetlands [3], microbial communities [4], and wildfire regimes [5]. In this Warning paper, we seek to call attention to the fact that around the world, human populations' access to medicinal plants is likely to be threatened by climate change in addition to the perennial threats of direct anthropogenic habitat loss and overharvesting.

Medicinal plants are an important component of health care for most of the world's population: they constitute the primary materia medica for 70 to 95% of citizens of most developing countries and are increasingly utilized by large numbers of people residing in wealthier countries [6, 7]. The contribution of medicinal plants to modern human medicine and their crucial role in traditional medicine have been documented by many authors. This is not the place to attempt to review the voluminous literature that has confirmed useful biological activities to be present in thousands of medicinal plant species, or demonstrated health benefits in human clinical trials of (minimally) hundreds of species. Suffice it to say that most of the world's people derive benefit from the use of medicinal plants (e.g., [8]), either because they are preferred to or complementary to Western (conventional) medical alternative(s) or because conventional treatments are unaffordable or inaccessible, and that those people would suffer harm from reduced or lost access to effective and affordable medicinal plants. Additionally, medicinal plants are widely used in traditional veterinary medicine (e.g., [9]), in which the improvement of livestock health has obvious benefits for their owners' economic security. Moreover, millions of people earn a living as traditional healers or collectors or vendors of medicinal plants. The harvest of and trade in medicinal plants provide an important source of income to both rural and urban people, as the global export trade value for herbal ingredients was recently estimated at over US\$32.6 billion per year [10].

Detrimental effects of climate change on medicinal plants and their users may obviously include decreases in availability, most dramatically in the extinction of species. Though the concern that access to plants will be lost through the diminution or loss of plant populations is emphasized here, it should be noted that some human populations will also be deprived of access to medicinal plants through displacement from their traditional homelands as climate refugees. A second major issue is that climate change may affect not only the accessibility and productivity of medicinal plants but the phytochemical content of surviving populations, especially of alpine plants (e.g., [11]), potentially affecting their pharmaceutical properties.

Decreased Availability and Extinction of Populations

It is well known that many plant species are or soon will be threatened with local or global extinction. A recent study reported that nearly 600 plant species have gone extinct in the past 250 years [12]. Even without climate change, wild plant populations are endangered around the world by human activities, especially habitat destruction and fragmentation (e.g., [13–16]), which create small, isolated populations that are at higher risk of local extinction (e.g., [17]). Additional threats include the introduction and spread of invasive species and exotic pathogens (e.g., [18–20]) and increased herbivory resulting from the extirpation of large predators (e.g., [21]).

High-value medicinal plants face an additional threat of unsustainable harvesting pressures. For example, the important tonic herb American ginseng (*Panax quinquefolius* L.), which is used for conditions including fatigue, hypertension, and upper respiratory infections [22–25], is sold in large quantities to the Chinese market. Demand is so great that illegal harvesting is a serious problem, and the species has declined over time in both abundance and average stature [26–28]. Other slow-growing medicinal plants, such as snow lotus (*Saussurea laniceps* Hand.-Mazz.) and goldenseal (*Hydrastis canadensis* L.), show similar declines in size or abundance [29–31]. At worst, commercial harvest and habitat destruction can result in the complete extinction of a valued species, as shown by the case of the North African herb *silphium* (probably *Ferula* sp.), extirpated in classical times [32, 33].

Climate change will alter environmental conditions in many localities such that they are no longer ideal – or survivable – for some species that now inhabit them. The predicted suitable range for many species, including medicinal plants, will narrow or move substantially following expected climate changes [34–39], though other species will enjoy expansions of potential range. Distributions of many organisms are already shifting rapidly towards higher latitudes or elevations [40–42], which increases competitive pressure on existing species in these ranges. Habitat fragmentation increases the risk that a species will be unable to migrate and will be driven to extinction. For some species, relationships with pollinators and other commensal organisms may be disrupted by phenological change (e.g., [43–45]). Insect populations have already been greatly reduced by human activities [46], especially habitat destruction and pollution from pesticides and other chemicals, and worsening climate change will exacerbate this problem.

Conversely, in North America, increased populations of damaging insects (particularly bark beetles) due to warmer winters, combined with the spread of fungal pathogens such as blister rust, have decimated millions of hectares of coniferous forests [47, 48]. With continued warming, both plant diseases and exotic insect pests may increase in range (e.g., [49–51]), with newly exposed populations perhaps being particularly vulnerable (e.g., [52]). In Central Canadian black spruce [*Picea mariana* (Mill.) Britton, Stearns & Pogenb.] forests, for example, the combined effects of logging, insect attacks, and fire have changed net primary productivity, carbon stocks, and soil nitrogen levels [53]. Yet in-

teractions between insect population dynamics, climate, and wildfires due to insect-induced tree die-offs are complex, as are long-term effects of successional dynamics, highlighting the need for long-term monitoring of selected slow-growing, habitat-specific medicinal plants within these coniferous forests. It should further be kept in mind that, not only may climate change increase the damage caused by such factors as drought, fire, pests, and pathogens, but those influences may in turn increase climate change, leading to, as yet, inadequately understood but perhaps catastrophic positive feedback loops. For example, die-off or greatly reduced productivity of forest trees due to the effects of climate change could convert forests from carbon sinks into carbon sources (e.g., [54–57]), worsening climate change, which in turn would further exacerbate the factors responsible for forest die-off.

Medicinal plants will not be exempt from these effects. Examples where highly suitable habitat for a given species will clearly decrease receive the most attention (e.g., [36,39]), but sometimes the situation is more complex. For example, ecological niche modeling (ENM) by You et al. [37] predicted that the geographic range of *Rhodiola quadrifida* will contract, but the potential ranges of other *Rhodiola* species will expand. In contrast, Zhang et al. [58], who also used ENM, projected shrinkage of *Rhodiola crenulata* populations. Likewise, MaxEnt modeling of three medicinal asclepiads in Pakistan predicts that each species would both lose some of its current habitat and gain some new potential habitat [59]. Though such species may survive by spreading into newly appropriate habitats, human populations would still suffer harm if medicinally or economically important plants are lost from locally accessible lands. For example, “complete loss of habitat” was predicted for *Tylophora hirsuta* (Wall.) Wight, used to treat asthma and urinary retention, in parts of northern Punjab, Khyber Pakhtun Khuwa, and Baluchistan [59]. Valued medicinal plants are, likewise, among the species experiencing dramatic phenological change [60]. In addition to threatening declines in populations, phenological changes may also reduce the predictable or consistent availability of medicines to the peoples who depend upon them [61,62].

Species in montane ecosystems, and especially nival or subnival species, are at greatest risk of habitat loss (e.g., [40,63]), and future climate changes are predicted to be most severe in northern latitude mountains (e.g., [64]). Alpine meadows, among the most at-risk plant communities, can encompass both high biodiversity and a high percentage of useful plants [65,66], and they are shrinking, with the warming-influenced upslope encroachment of shrubs [67]. Species growing at the highest altitudes are believed to be at greatest risk of extinction, because if they are outcompeted by the lower elevation species now extending their ranges to higher elevations, they will have “nowhere to go” [66]. As intuitive as the “nowhere to go” hypothesis may be for alpine and nival medicinal plant species, it may not be universally applicable. Loarie et al. [68] projected that (for those species that do have somewhere to go) migration may be more successful in montane areas than in flat lands due to the steeper spatial gradient of temperature change and concomitantly much lesser required migration velocity; for some species, simply moving from south-facing to north-facing slopes could permit survival.

Arid zone medicinal plants may also be at special risk. Deserts and arid shrublands are predicted to be among the biomes with the highest velocities of climate change, making compensatory migration difficult [68]. As an example, the desert steppe habitat of one of the most widely used wild medicinal plants in Chinese medicine, *Glycyrrhiza uralensis* Fisch., has degraded significantly in recent decades, attributed to intensifying climate change and anthropogenic disturbance [69]. The species is traditionally wild collected in China’s northern autonomous regions (Inner Mongolia, Ningxia Hui, and Xinjiang Uyghur) but is now classified as an endangered and nationally protected medicinal plant species, with harvesting subject to national controls [70,71]. While cultivating this plant for its use in Chinese medicine had been viewed as a possible solution to declining wild populations and shortages, the content of active ingredients (e.g., glycyrrhizic acid and liquiritin) of cultivated *G. uralensis* root is considerably lower than that of mature (5-year-old) wild roots. Thus, China, a former major exporter of this species, has become a major importer in recent years to satisfy quality and quantity requirements for medicinal use [72], potentially threatening the sustainability of wild populations in arid zones of other countries now supplying China (e.g., Uzbekistan, Kazakhstan, Pakistan, Afghanistan).

Furthermore, climate change will interact additively, sometimes synergistically, and perhaps catastrophically, with other threats to medicinal plants. For example, *Boswellia* species, which produce the culturally and economically important resin frankincense, have already declined substantially due to factors including farmland expansion, fire, overexploitation for resin and/or wood, wood-boring beetle infestation, and intensive grazing of seedlings and young plants, resulting in adult mortality and failure of sapling recruitment [73–75]. A detailed study of 12 northern Ethiopian populations of *Boswellia papyrifera* Hochst. [76] concluded that if current practices continue, there will be a 50% decline in frankincense yield within 15 years and a 90% decline in both tapped and untapped populations within 50 years. If “business as usual” continues, by 2040 the stem densities of populations in the Metema and Abergelle districts are predicted to be reduced to as little as 3 and 11%, respectively, of their current values [77]. Climate change could compound these predicted declines through the effects of higher fire intensities on the recruitment from seeds after periods of higher rainfall. Greater grass biomass and high fire intensity after 2 preceding years of high rainfall is well known in southern African savanna [78], but still needs to be built into predictive models for medicinal plant species in seasonally dry savannas.

Overharvesting for global consumer markets is a particular threat when combined with climate change. In North America, the extinction risk for a population of American ginseng of median size over 70 years was estimated to be 8% over 70 years with harvesting alone, 6% with climate change alone, but 65% with the two combined [28]. Inhabitants of the Colombian Andes reported that the herb *Draba litamo* L. Uribe, endemic to the high-altitude páramo vegetation and a revitalizing tonic traditionally claimed to convey eternal youth, was increasingly scarce due to the combination of climate change and commercial harvesting [79]. In Africa, *Pterocarpus angolensis* DC. is harvested not only for medicine, with the bark and roots used to treat a variety of conditions, but for do-

mestic wood use and timber exports (particularly to South Africa and Asia [80]); other factors responsible for past population declines include habitat loss due to clearing for agriculture, and poor fire management. Climate change predictions show that *Pterocarpus angolensis* populations will be seriously affected in drier parts of its range (such as Namibia and Botswana [81]), while in higher rainfall portions of its range, fungal wilt disease is also affecting populations [82]. Thus, climate change, habitat loss, logging and other forms of harvest, grazing, and fire can all interact in seasonally dry African woodlands to have crushing impacts on vulnerable species.

Climate change is predicted to have negative impacts on human health, particularly by the obvious effects of increasing exposure to temperature extremes and contributing to food insecurity and poorer nutritional status (e.g., [83]). Additional indirect effects will include extending the range of vector-borne diseases such as malaria (e.g., [84, 85]) and the range and sometimes potency of some toxic or allergenic plants, such as ragweed (*Artemisia ambrosiifolia* L. [86, 87]); pollen counts of other species that contribute to hay fever appear already to be increasing in response to increased carbon dioxide (e.g., [88–90]). These impacts, combined with human population growth, will further increase harvesting pressure on plants used to treat the health conditions that will be exacerbated by climate change. It should be emphasized that many of the proposed means of preventing the global extinction of species in general, such as *ex situ* conservation and assisted migration to counter the deadly combination of rapid climate change and habitat fragmentation [91, 92], though certainly of great importance, will do nothing to reduce the harm that local human populations, especially Indigenous Peoples, will suffer from decreased availability of or loss of access to economically and culturally important plants, including medicinal plants.

Changes in Plant Quality or Productivity

Even if a changing climate does not affect a given species' range, it may affect its productivity or its quality – in the case of a medicinal plant, primarily its potency or chemical composition – either positively or negatively. While variation in chemical content in food plants may also be more relevant to human health than is commonly acknowledged (e.g., [93–96]), the entire purpose for consumption or other use of medicinal plants is to derive health benefits from their bioactivities. Those bioactivities arise mainly from the plant's content of secondary metabolites, whether autogenous or produced by endophytic symbionts. Therefore, people who are deriving benefits from the use of a plant would suffer if its composition changed in a detrimental or unpredictable way. This is particularly true for consumers from traditional societies and less wealthy populations, who lack the resources to perform elaborate chemical testing to identify such changes and adjust doses to compensate. Decreased potency of a plant medicine might well go unnoticed or might be misinterpreted by a new generation of consumers as inherent lack of efficacy, leading to abandonment of useful plants.

As noted previously, both climate change and its ecological effects are predicted to be greatest in montane habitats (e.g., [11, 65, 97]), and plants living at the highest altitudes are feared to be

at particular risk of extinction (e.g., [66]). Many high-altitude regions are occupied by populations with limited access to Western medicine, for whom botanicals are particularly important. Many medicinal species are traditionally believed to be more potent when collected from higher altitudes (e.g., [98]), and this has been confirmed for some important plants, e.g., bush tea (*Athrixia phylicoides* DC. [99]), chamomile (*Matricaria chamomilla* L. [100]), and arnica (*Arnica montana* L. [101]). The responsible factors are usually unknown. An experimental study of arnica found that temperature had a strong influence on chemical content [102]; contrarily, for bush tea, the correlation between altitude and chemical content does not appear to be related to temperature [99]. If montane species whose chemical content is affected by temperature migrate to higher altitudes and thereby remain in the same temperature regime, their medicinal quality will not necessarily improve, but populations that persist at their original altitudes might decline in quality. Obviously, more information is needed to understand the relationships between medicinal potency and elevation in individual species.

Expected consequences of climate change in many parts of the world include harsher weather extremes, such as more intense droughts, heavy rainfalls, heat waves, and cold snaps [84]. All of these extremes can impair growth and reproductive success of plants that are not adapted to such conditions, reducing sustainable harvest levels. However, these factors do not have consistent effects on concentrations of active metabolites. Drought stress that is not so severe as to kill plants often increases the concentration of bioactive secondary metabolites, either by decreasing biomass or by increasing actual production of the metabolites. Two recent literature reviews [103, 104] summarize evidence that drought stress increases the concentration of bioactive compounds in a variety of species; compound classes affected can include simple and complex phenolic compounds, essential oils and terpenes, alkaloids, and glucosinolates. In some wild plant products, such as shea butter (from *Vitellaria paradoxa* Gaertn.), active metabolites occur at higher levels in drier areas [105].

It is therefore possible that increased drought stress in some regions would increase the potency of some medicinal plants from those regions. However, a decrease in biomass with uncontrolled natural drought would frequently be so great as to outweigh any gains in concentration of active metabolites, even if those gains were known to consumers and the dosage was decreased to compensate. Second, sometimes chemical content is higher under water stress but lower at high temperature, e.g., in *di huang* (*Rehmannia glutinosa* (Gaertn.) Steud. [106]). If drought is accompanied by increased temperature, any beneficial effect of the former on chemical content in such species could be counteracted by the latter. High temperatures, like drought stress, may also lead to an increased concentration of secondary metabolites as a consequence of a significantly reduced biomass, as has been shown for American ginseng [107]. If people are accustomed to harvesting a certain quantity of material, either for personal use or for sale for economic subsistence, a large decline in biomass production due to drought and high temperature would result in severe economic harm and increased unsustainability of harvest levels.

Third, increased CO₂ levels may at least partially counteract the metabolic effect of drought. According to a theoretical framework outlined by Selmar and Kleinwächter [103], drought stress causes stomatal closure and reduces CO₂ available to the plant, which in turn reduces the amount of NADPH + H⁺ consumed by the Calvin cycle and requires that it be consumed instead by increased production of secondary metabolites. At high atmospheric CO₂ levels, the amount of CO₂ available to the plant despite stomatal closure is greater, so less NADPH + H⁺ is redirected towards producing secondary metabolites. In an experimental model using sage (*Salvia officinalis* L.), the monoterpene concentration increased with drought stress but decreased with elevated CO₂, so that when CO₂ was elevated, the imposition of drought stress was necessary merely to equal the concentrations in well-watered plants at ambient CO₂ [108]. It should be noted that that model is not true for all species. Most studies that have reported an increased concentration of desirable metabolites with elevated CO₂ have not held other growing conditions constant. However, in controlled conditions, increasing CO₂ levels led to an increased concentration of several flavonoids and phenolic compounds in ginger (*Zingiber officinale* Roscoe) rhizome [109] and of artemisinin in sweet Annie or *qing hao* (*Artemisia annua* L. [110]).

Finally, if in some species the concentration of plant metabolites did increase sufficiently to compensate for the reduction in harvestable biomass, this is not always a desirable effect. While the botanicals tolerated for over-the-counter sale in the West are generally safe plants, some species used in local and traditional medical systems around the world, as well as many used by formally trained practitioners, contain levels of toxic compounds that pose a real risk of harm with excessive use or use by susceptible individuals. Secondary metabolites reported to increase in concentration as a result of drought stress include toxic metabolites, e.g., pyrrolizidine alkaloids in *Senecio* species [111, 112]. If these plants were to become unexpectedly more toxic due to increased environmental stress, increased harm could result. As for the changes in geographic range and phenology noted above, unpredictable shifts in a species' qualities could threaten its usability as medicine.

Effects of climate change on plants with dual use as food and medicine, which contribute to people's health through use as a staple food, are particularly important to determine. Soybean has been reported to suffer a 90% reduction in isoflavone content when grown at elevated temperatures, although the effect can be partially reversed by the addition of drought stress and elevated CO₂ levels [113]. Several major oilseed crops have lower oil content when grown at higher temperatures, and the relative proportion of highly unsaturated fatty acids often decreases [114, 115]. At least according to current nutritional dogma, the latter effect could worsen the nutritional quality of the extracted oils (e.g., [116–118]), potentially reducing individuals' ability to ameliorate or avoid chronic diseases, especially cardiovascular disease, by consuming healthful traditional foods. Additionally, crops in many areas affected by climate change are expected to be more vulnerable to pathogens, including mycotoxin-producing fungi (e.g., [119–122]), threatening both food security and the quality and short- and long-term safety of staple foods.

There can be no doubt that medicinal plants – like all species – are affected by the multiple changes inflicted by humans on the environment, especially in highly vulnerable regions such as high mountain ecosystems. However, experimental or observational data on changes to medicinal plant populations or their phytochemical constituents and the impact of specific factors (such as the rise in CO₂ or temperature and rainfall changes) on individual species remain rare. Such studies are urgently needed in order to come to a better understanding of the true impacts of climate change on medicinal and other high-value useful plants.

Conclusion and Recommendations

Increased environmental extremes and economic losses due to climate change are expected to be harmful to public health in many parts of the world, and, simultaneously, the resilience provided by access to beneficial medicinal plants is expected to decline. This may be foreseen to contribute to increased human suffering and preventable deaths if steps are not taken quickly. Ideal would be a reversal of the current trends, and, of course, we advocate strenuous efforts to mitigate climate change in order to reduce its negative effects on the biosphere and human communities worldwide. However, since it appears that mitigation, aggressive and rapid enough to entirely prevent disruptive climate change, will be politically impossible, efforts focused on adaptation to reduce the harm that will be suffered are also essential, and often can be undertaken locally. We strongly urge local and national governments, nongovernmental organizations, and the public health and ethnobotanical communities to take actions to help all communities, particularly those who depend upon medicinal plants for their health care or income, retain access to high-quality traditional medicines.

Actions that may help to support medicinal plant populations include promoting the cultivation of medicinal plants in community gardens to maintain local access, preserving and respecting the value of traditional knowledge about plants and their sustainable use, training harvesters in sustainable practices, encouraging or requiring the use of certification programs for wild-collected material, especially in international commerce, and implementing urgent, large-scale conservation programs, including habitat protection. Regional phytochemical research or quality control programs that monitor biomarker content in economically important medicinal plants, especially alpine species, could identify alterations in their content and quality due to climate change, providing an opportunity to inform consumers and product manufacturers should there be a need to adjust use patterns. As last resorts, assisted migration and *ex situ* seedbanking may be essential to prevent permanent global extinction of useful species, but we emphasize that those measures will not reduce the harm to present-day human communities.

Acknowledgements

We thank Peter Raven, Nancy Turner, Vera De Cauwer, and William Ripple for helpful discussions, the reviewers of this manuscript for helpful suggestions, and *Planta Medica* for supporting its publication via open access.

Endorsements

This paper has been endorsed by the following additional scientists and scholars: Anna Rita Bilia (University of Florence, Florence, Italy), Frans Bongers (Wageningen University, Wageningen, The Netherlands), Vera De Cauwer (Namibia University of Science and Technology, Windhoek, Namibia), Javier Echeverría (Universidad de Santiago de Chile, Santiago, Chile), Fang Zhendong (Shangri-La Alpine Botanical Garden, Shangri-La, China), Stefan Gafner (American Botanical Council, Austin, TX, U.S.A.), Suresh Ghimire (Tribhuvan University, Kirtipur, Nepal), De-An Guo (Shanghai Institute of Materia Medica, Shanghai, China), Ameenah Gurib-Fakim (CIDP Research and Innovation, Phoenix, Mauritius), Linfang Huang (Institute of Medicinal Plant Development, Chinese Academy of Medical Sciences and Peking Union Medical College, Beijing, China), Holly Johnson (American Herbal Products Association, Silver Spring, MD, U.S.A.), Rizwana Khan (Pakistan Museum of Natural History, Islamabad, Pakistan), Aiping Lyu (School of Chinese Medicine, Hong Kong Baptist University, Hong Kong, China), Lyndy McGaw (University of Pretoria, Pretoria, South Africa), Pulok Kumar Mukherjee (Jadavpur University, Kolkata, India), Cassandra Quave (Emory University, Atlanta, GA, U.S.A.), Peter Raven (Missouri Botanical Garden, St. Louis, MO, U.S.A.), Mireia Alcántara Rodríguez (Leiden University, Leiden, The Netherlands), Judith Rollingher (University of Vienna, Vienna, Austria), Satya Sarker (Liverpool John Moores University, Liverpool, U.K.), Nancy Turner (University of Victoria, Victoria, B.C., Canada), Alvaro Viljoen (Tshwane University of Technology, Pretoria, South Africa).

Conflict of Interest

The authors declare that they have no conflict of interest.

References

- Union of Concerned Scientists. World Scientists' Warning to Humanity. Cambridge: Union of Concerned Scientists; 1992. Available at <https://www.ucsusa.org/about/1992-world-scientists.html#.XD5D4ml7ncs>. Accessed November 12, 2019
- Ripple WJ, Wolf C, Newsome TM, Galetti M, Alamgir M, Crist E, Mahmoud MI, Laurance WF, and 15, 364 scientist signatories from 184 countries. World Scientists' warning to humanity: a second notice. *Bioscience* 2017; 67: 1026–1028
- Finlayson CM, Davies GT, Moomaw WR, Chmura GL, Natali SM, Perry JE, Roulet N, Sutton-Grier AE. The second warning to humanity – providing a context for wetland management and policy. *Wetlands* 2019; 39: 1–5
- Cavicchioli R, Ripple WJ, Timmis KN, Azam F, Bakken LR, Baylis M, Behrenfeld MJ, Boetius A, Boyd PW, Classen AT, Crowther TW, Danovaro R, Foreman CM, Huisman J, Hutchins DA, Jansson JK, Karl DM, Koskella B, Welch DBM, Martiny JBH, Moran MA, Orphan VJ, Reay DS, Remais JV, Rich VI, Singh BK, Stein LY, Stewart FJ, Sullivan MB, van Oppen MJH, Weaver SC, Webb EA, Webster NS. Scientists' warning to humanity: microorganisms and climate change. *Nat Rev Microbiol* 2019; 17: 569–586
- Coogan SCP, Robinne FN, Jain P, Flannigan MD. Scientists' warning on wildfire – a Canadian perspective. *Can J For Res* 2019; 49: 1015–1023
- World Health Organization. WHO traditional Medicine Strategy 2002–2005. Geneva: World Health Organization; 2002
- Robinson MM, Zhang X. The World Medicines Situation 2011. Traditional Medicines: global Situation, Issues and Challenges. Geneva: World Health Organization; 2011
- Heinrich M, Jaeger AK, eds. *Ethnopharmacology*. Chichester: Wiley; 2015
- Katerere DR, Luseba D. *Ethnoveterinary botanical Medicine. Herbal Medicines for Animal Health*. Boca Raton: CRC Press; 2010
- Brinckmann JA. *Sustainable Sourcing: Markets for certified Chinese medicinal and aromatic Plants*. Geneva: International Trade Centre; 2016: 22
- Gairola S, Shariff NM, Bhatt A, Kala CP. Influence of climate change on production of secondary chemicals in high altitude medicinal plants: issues needs immediate attention. *J Med Plants Res* 2010; 4: 1825–1829
- Humphreys AM, Govaerts R, Ficinski SZ, Lughadh EN, Vorontsova MS. Global dataset shows geography and life form predict modern plant extinction and rediscovery. *Nature Ecol Evol* 2019; 3: 1043–1047
- Skole D, Tucker C. Tropical deforestation and habitat fragmentation in the Amazon: satellite data from 1978 to 1988. *Science* 1993; 260: 1905–1910
- Riitters KH, Wickham JD, O'Neill RV, Jones KB, Smith ER, Coulston JW, Wade TG, Smith JH. Fragmentation of continental United States forests. *Ecosystems* 2002; 5: 815–822
- Harper CJ, Steiner MK, Tucker CJ, Juhn D, Hawkins F. Fifty years of deforestation and forest fragmentation in Madagascar. *Environ Conserv* 2007; 34: 325–333
- Haddad NM, Brudvig LA, Clobert J, Davies KF, Gonzalez A, Holt RD, Lovejoy TE, Sexton JO, Austin MP, Collins CD, Cook WM, Damschen EI, Ewers RM, Foster BL, Jenkins CN, King AJ, Laurance WF, Levey DJ, Margules CR, Melbourne BA, Nicholls AO, Orrock JL, Song DX, Townshend JR. Habitat fragmentation and its lasting impact on Earth's ecosystems. *Sci Adv* 2015; 1: e1500052
- Matthies D, Bräuer I, Maibom W, Tschardtke T. Population size and the risk of local extinction: empirical evidence from rare plants. *Oikos* 2004; 105: 481–488
- Brasier CM. Rapid evolution of introduced plant pathogens via interspecific hybridization: Hybridization is leading to rapid evolution of Dutch elm disease and other fungal plant pathogens. *Bioscience* 2001; 51: 123–133
- Siegert NW, McCullough DG, Liebhold AM, Telewski FW. Dendrochronological reconstruction of the epicentre and early spread of emerald ash borer in North America. *Divers Distrib* 2014; 20: 847–858
- Callen ST, Miller AJ. Signatures of niche conservatism and niche shift in the North American kudzu (*Pueraria montana*) invasion. *Divers Distrib* 2015; 21: 853–863
- McGraw JB, Furedi MA. Deer browsing and population viability of a forest understory plant. *Science* 2005; 307: 920–922
- McElhaney JE, Simor AE, McNeil S, Predy GN. Efficacy and safety of CVT-E002, a proprietary extract of *Panax quinquefolius* in the prevention of respiratory infections in influenza-vaccinated community-dwelling adults: a multicenter, randomized, double-blinded, and placebo-controlled trial. *Influenza Res Treat* 2011; 2011: 759051
- Seida JK, Durec T, Kuhle S. North American (*Panax quinquefolius*) and Asian ginseng (*Panax ginseng*) preparations for prevention of the common cold in healthy adults: A systematic review. *Evid Based Complement Altern Med* 2011; 2011: 282151
- Barton DL, Liu H, Dakhil SR, Linquist B, Sloan JA, Nichols CR, McGinn TW, Stella PJ, Seeger GR, Sood A, Loprinzi CL. Wisconsin Ginseng (*Panax quinquefolius*) to improve cancer-related fatigue: a randomized, double-blind trial. *N07C2. J Natl Cancer Inst* 2013; 105: 1230–1238
- Mucalo I, Jovanovski E, Rahelić D, Božikov V, Romić Z, Vuksan V. Effect of American ginseng (*Panax quinquefolius* L.) on arterial stiffness in subjects with type-2 diabetes and concomitant hypertension. *J Ethnopharmacol* 2013; 150: 148–153
- McGraw JB. Evidence for decline in stature of American ginseng plants from herbarium specimens. *Biol Conserv* 2001; 98: 25–32
- Case MA, Flinn KM, Jancaitis J, Alley A, Paxton A. Declining abundance of American ginseng (*Panax quinquefolius* L.) documented by herbarium specimens. *Biol Conserv* 2007; 134: 22–30
- Souther S, McGraw JB. Synergistic effects of climate change and harvest on extinction risk of American ginseng. *Ecol Appl* 2014; 24: 1463–1477

- [29] Mulligan MR, Gorchov DL. Population loss of goldenseal, *Hydrastis canadensis* L. (Ranunculaceae), in Ohio. *J Torrey Bot Soc* 2004; 131: 305–310
- [30] Law W, Salick J. Human-induced dwarfing of Himalayan snow lotus, *Saussurea laniceps* (Asteraceae). *Proc Natl Acad Sci U S A* 2005; 102: 10218–10220
- [31] Oliver L. *Hydrastis canadensis*. The IUCN Red List of Threatened Species 2017: e.T44340011A44340071. Available at <http://dx.doi.org/10.2305/IUCN.UK.2017-2.RLTS.T44340011A44340071.en>. Accessed November 12, 2019
- [32] Parejko K. Pliny the Elder's silphium: first recorded species extinction. *Conserv Biol* 2003; 17: 925–927
- [33] Kiehn M. Silphion revisited. *Med Plant Conserv* 2007; 13: 4–8
- [34] Shafer SL, Bartlein PJ, Thompson RS. Potential changes in the distributions of western North American tree and shrub taxa under future climate scenarios. *Ecosystems* 2001; 4: 200–215
- [35] Pompe S, Hanspach J, Badeck F, Klotz S, Thuiller W, Kühn I. Climate and land use change impacts on plant distributions in Germany. *Biol Lett* 2008; 4: 564–567
- [36] Guo Y, Wei H, Lu C, Gao B, Gu W. Predictions of potential geographical distribution and quality of *Schisandra sphenanthera* under climate change. *PeerJ* 2016; 4: e2554
- [37] You J, Qin X, Ranjitkar S, Lougheed SC, Wang M, Zhou W, Ouyang D, Zhou Y, Xu J, Zhang W, Wang Y, Yang J, Song Z. Response to climate change of montane herbaceous plants in the genus *Rhodiola* predicted by ecological niche modelling. *Sci Rep* 2018; 8: 5879
- [38] Zhao Q, Li R, Gao Y, Yao Q, Guo X, Wang W. Modeling impacts of climate change on the geographic distribution of medicinal plant *Fritillaria cirrhosa* D. Don. *Plant Biosyst* 2018; 152: 349–355
- [39] Abdelaal M, Fois M, Fenu G, Bacchetta G. Using MaxEnt modeling to predict the potential distribution of the endemic plant *Rosa arabica* Crép. in Egypt. *Ecol Inform* 2019; 50: 68–75
- [40] Lamprecht A, Semenchuk PR, Steinbauer K, Winkler M, Pauli H. Climate change leads to accelerated transformation of high-elevation vegetation in the central Alps. *New Phytol* 2018; 220: 447–459
- [41] Chen IC, Hill JK, Ohlemüller R, Roy DB, Thomas CD. Rapid range shifts of species associated with high levels of climate warming. *Science* 2011; 333: 1024–1026
- [42] Lenoir J, Svenning JC. Latitudinal and elevational Range Shifts under contemporary Climate Change. In: Levin S, ed. *Encyclopedia of Biodiversity*, 2nd edition. Amsterdam: Elsevier; 2013: 599–611
- [43] Kudo G, Ida TY. Early onset of spring increases the phenological mismatch between plants and pollinators. *Ecology* 2013; 94: 2311–2320
- [44] Phondani PC, Bhatt ID, Negi VS, Kothiyari BP, Bhatt A, Maikhuri RK. Promoting medicinal plants cultivation as a tool for biodiversity conservation and livelihood enhancement in Indian Himalaya. *J Asia-Pac Biodiv* 2016; 9: 39–46
- [45] Kharouba HM, Ehrlén J, Gelman A, Bolmgren K, Allen JM, Travers SE, Wolkovich EM. Global shifts in the phenological synchrony of species interactions over recent decades. *Proc Natl Acad Sci U S A* 2018; 115: 5211–5216
- [46] Sánchez-Bayo F, Wyckhuys KAG. Worldwide decline of the entomofauna: A review of its drivers. *Biol Conserv* 2019; 232: 8–27
- [47] Bentz BJ, Régnière J, Fettig CJ, Hansen EM, Hayes JL, Hicke JA, Kelsey RG, Negrón JF, Seybold SJ. Climate change and bark beetles of the western United States and Canada: direct and indirect effects. *Bioscience* 2010; 60: 602–613
- [48] Amberson JT, Keville MP, Nelson CR. Effects of disturbance on tree community dynamics in whitebark pine (*Pinus albicaulis* Engelm.) ecosystems. *Forests* 2018; 9: 566
- [49] Williams DW, Liebhold AM. Climate change and the outbreak ranges of two North American bark beetles. *Agric Forest Entomol* 2002; 4: 87–99
- [50] Bergot M, Cloppet E, Pérarnaud V, Déqué M, Marçais B, Desprez-Loustau ML. Simulation of potential range expansion of oak disease caused by *Phytophthora cinnamomi* under climate change. *Global Change Biol* 2004; 10: 1539–1552
- [51] Bosso L, Di Febraro M, Cristinzio G, Zoina A, Russo D. Shedding light on the effects of climate change on the potential distribution of *Xylella fastidiosa* in the Mediterranean basin. *Biol Invasions* 2016; 18: 1759–1768
- [52] Cudmore TJ, Björklund N, Carroll AL, Lindgren BS. Climate change and range expansion of an aggressive bark beetle: evidence of higher beetle reproduction in naïve host tree populations. *J Appl Ecol* 2010; 47: 1036–1043
- [53] Chertov O, Bhatti JS, Komarov A, Mikhailov A, Bykhovets S. Influence of climate change, fire and harvest on the carbon dynamics of black spruce in Central Canada. *Forest Ecol Manage* 2009; 257: 941–950
- [54] Kurz WA, Stinson G, Rampley GJ, Dymond CC, Neilson ET. Risk of natural disturbances makes future contribution of Canada's forests to the global carbon cycle highly uncertain. *Proc Natl Acad Sci U S A* 2008; 105: 1551–1555
- [55] Nobre CA, Borma LDS. 'Tipping points' for the Amazon forest. *Curr Opin Environ Sust* 2009; 1: 28–36
- [56] Allen CD, Macalady AK, Chenchouni H, Bachelet D, McDowell N, Vennetier M, Kitzberger T, Rigling A, Breshears DD, Hogg EH, Gonzalez P, Fensham R, Zhang Z, Castro J, Demidova N, Lim JH, Allard G, Running SW, Semerci A, Cobb N. A global overview of drought and heat-induced tree mortality reveals emerging climate change risks for forests. *Forest Ecol Manage* 2010; 259: 660–684
- [57] Anderegg WRL, Schwalm C, Biondi F, Camarero JJ, Koch G, Litvak M, Ogle K, Shaw JD, Shevliakova E, Williams AP, Wolf A, Ziaco E, Pacala S. Pervasive drought legacies in forest ecosystems and their implications for carbon cycle models. *Science* 2015; 349: 528–532
- [58] Zhang JZ, Zhu RW, Zhong DL, Zhang JQ. Nunataks or massif de refuge? A phylogeographic study of *Rhodiola crenulata* (Crassulaceae) on the world's highest sky islands. *BMC Evol Biol* 2018; 18: 154
- [59] Khanum R, Mumtaz AS, Kumar S. Predicting impacts of climate change on medicinal asclepiads of Pakistan using Maxent modeling. *Acta Oecol* 2013; 49: 23–31
- [60] Cavaliere C. The effects of climate change on medicinal and aromatic plants. *HerbalGram* 2008; 81: 44–57
- [61] Turner NJ, Clifton H. "It's so different today": Climate change and indigenous lifeways in British Columbia, Canada. *Global Environ Change* 2009; 19: 180–190
- [62] Ruelle ML, Kassam KAS. Diversity of plant knowledge as an adaptive asset: a case study with Standing Rock elders. *Econ Bot* 2011; 65: 295–307
- [63] Grabherr G. Biodiversity in the high ranges of the Alps: ethnobotanical and climate change perspectives. *Global Environ Change* 2009; 19: 167–172
- [64] Nogués-Bravo D, Araújo MB, Errea MP, Martínez-Rica JP. Exposure of global mountain systems to climate warming during the 21st Century. *Global Environ Change* 2007; 17: 420–428
- [65] Salick J, Fang Z, Byg A. Eastern Himalayan alpine plant ecology, Tibetan ethnobotany, and climate change. *Global Environ Change* 2009; 19: 147–155
- [66] Salick J, Ghimire SK, Fang Z, Dema S, Konchar KM. Himalayan alpine vegetation, climate change and mitigation. *J Ethnobiol* 2014; 34: 276–293
- [67] Brandt JS, Haynes MA, Kuemmerle T, Waller DM, Radeloff VC. Regime shift on the roof of the world: Alpine meadows converting to shrublands in the southern Himalayas. *Biol Conserv* 2013; 158: 116–127
- [68] Loarie SR, Duffy PB, Hamilton H, Asner GP, Field CB, Ackerly DD. The velocity of climate change. *Nature* 2009; 462: 1052–1055
- [69] Huang J, Wang P, Niu Y, Yu H, Ma F, Xiao G, Xu X. Changes in C:N:P stoichiometry modify N and P conservation strategies of a desert steppe species *Glycyrrhiza uralensis*. *Sci Rep* 2018; 8: 12668

- [70] Zhang JT, Xu B, Li M. Diversity of communities dominated by *Glycyrrhiza uralensis*, an endangered medicinal plant species, along a precipitation gradient in China. *Bot Stud* 2011; 52: 493–501
- [71] Brinckmann JA. Geographical indications for medicinal plants: globalization, climate change, quality and market implications for geo-authentic botanicals. *World J Tradit Chin Med* 2015; 1: 16–23
- [72] Chen KZ, Song H, Chen R. Licorice Industry in China: Implications for licorice Producers in Uzbekistan. Beijing: International Food Policy Research Institute; 2014
- [73] Ogbazghi W, Rijkers AJM, Wessel M, Bongers FJJM. The distribution of the frankincense tree *Boswellia papyrifera* in Eritrea: the role of environment and land use. *J Biogeogr* 2006; 33: 524–535
- [74] Tolera M, Sass-Klaassen U, Eshete A, Bongers F, Sterck FJ. Frankincense tree recruitment failed over the past half century. *Forest Ecol Manage* 2013; 304: 65–72
- [75] Bongers F, Groenendijk P, Bekele T, Birhane E, Damtew A, Decuyper M, Eshete A, Gezahgne A, Girma A, Khamis MA, Lemenih M, Mengistu T, Ogbazghi W, Sass-Klaassen U, Tadesse W, Teshome M, Tolera M, Sterck FJ, Zuidema PA. Frankincense in peril. *Nat Sustain* 2019; 2: 602–610
- [76] Groenendijk P, Eshete A, Sterck FJ, Zuidema PA, Bongers F. Limitations to sustainable frankincense production: blocked regeneration, high adult mortality and declining populations. *J Appl Ecol* 2012; 49: 164–173
- [77] Lemenih M, Arts B, Wiersum K, Bongers F. Modelling the future of *Boswellia papyrifera* population and its frankincense production. *J Arid Environ* 2014; 105: 33–40
- [78] Govender N, Trollope WS, Van Wilgen BW. The effect of fire season, fire frequency, rainfall and management on fire intensity in savanna vegetation in South Africa. *J Appl Ecol* 2006; 43: 748–758
- [79] Rodríguez MA, Angueyra A, Cleef AM, van Andel TR. Ethnobotany of the Sierra Nevada del Cocuy-Güicán: climate change and conservation strategies in the Colombian Andes. *J Ethnobiol Ethnomed* 2018; 14: 34
- [80] De Cauwer V, Knox N, Kobue-Lekalake R, Lepetu JP, Ompelele M, Naidoo S, Nott A, Parduhn D, Sichone P, Tshwenyane S, Elizabeth Y, Revermann R. Woodland Resources and Management in southern Africa. In: Revermann R, Krewenka KM, Schmiedel U, Olwoch JM, Helmschrot J, Jürgens N, eds. *Climate Change and adaptive Land Management in southern Africa – Assessments, Changes, Challenges, and Solutions*. Göttingen & Windhoek: Klaus Hess Publishers; 2018: 296–308
- [81] De Cauwer V, Muys B, Revermann R, Trabucco A. Potential, realised, future distribution and environmental suitability for *Pterocarpus angolensis* DC in southern Africa. *Forest Ecol Manage* 2014; 315: 211–226
- [82] Mehl JW, Slippers B, Roux J, Wingfield MJ. Botryosphaeriaceae associated with *Pterocarpus angolensis* (kiaat) in South Africa. *Mycologia* 2011; 103: 534–553
- [83] Schmidhuber J, Tubiello FN. Global food security under climate change. *Proc Natl Acad Sci U S A* 2007; 104: 19703–19708
- [84] IPCC. *Climate Change 2014: Synthesis Report*. Contribution of Working Groups I, II and III to the Fifth Assessment Report of the Intergovernmental Panel on Climate Change [Core Writing Team, Pachauri RK, and Meyer LA, editors]. Geneva: IPCC; 2014
- [85] Ren Z, Wang D, Ma A, Hwang J, Bennett A, Sturrock HJW, Fan J, Zhang W, Yang D, Feng X, Xia Z, Zhou XN, Wang J. Predicting malaria vector distribution under climate change scenarios in China: Challenges for malaria elimination. *Sci Rep* 2016; 6: 20604
- [86] Wayne P, Foster S, Connolly J, Bazzaz F, Epstein P. Production of allergenic pollen by ragweed (*Ambrosia artemisiifolia* L.) is increased in CO₂-enriched atmospheres. *Ann Allergy Asthma Immunol* 2002; 8: 279–282
- [87] Chapman DS, Makra L, Albertini R, Bonini M, Páldy A, Rodinkova V, Šikoparija B, Weryszko-Chmielewska E, Bullock JM. Modelling the introduction and spread of non-native species: international trade and climate change drive ragweed invasion. *Global Change Biol* 2016; 22: 3067–3079
- [88] Frei T. The effects of climate change in Switzerland 1969–1996 on airborne pollen quantities from hazel, birch and grass. *Grana* 1998; 37: 172–179
- [89] Ziello C, Sparks TH, Estrella N, Belmonte J, Bergmann KC, Bucher E, Brighetti MA, Damialis A, Detandt M, Galán C, Gehrig R, Grewling L, Gutiérrez Bustillo AM, Hallsdóttir M, Kockhans-Bieda MC, De Linares C, Myszkowska D, Páldy A, Sánchez A, Smith M, Thibaudon M, Travaglini A, Uruska A, Valencia-Barrera RM, Vokou D, Wachter R, de Weger LA, Menzel A. Changes to airborne pollen counts across Europe. *PLoS One* 2012; 7: e34076
- [90] Zhang Y, Bielory L, Georgopoulos PG. Climate change effect on *Betula* (birch) and *Quercus* (oak) pollen seasons in US. *Int J Biometeorol* 2014; 58: 909–919
- [91] McLachlan JS, Hellmann JJ, Schwartz MW. A framework for debate of assisted migration in an era of climate change. *Conserv Biol* 2007; 21: 297–302
- [92] Williams MI, Dumroese RK. Preparing for climate change: forestry and assisted migration. *J Forest* 2013; 111: 287–297
- [93] Welch RM, Graham RD. Breeding for micronutrients in staple food crops from a human nutrition perspective. *J Exp Bot* 2004; 55: 353–364
- [94] Davis DR. Declining fruit and vegetable nutrient composition: What is the evidence? *HortScience* 2009; 44: 15–19
- [95] Bøhn T, Cuhra M, Traavik T, Sanden M, Fagan J, Primicerio R. Compositional differences in soybeans on the market: glyphosate accumulates in Roundup Ready GM soybeans. *Food Chem* 2014; 153: 207–215
- [96] Figàs MR, Prohens J, Raigón MD, Fita A, Garcia-Martinez MD, Casanova C, Borràs D, Plazas M, Andújar I, Soler S. Characterization of composition traits related to organoleptic and functional quality for the differentiation, selection and enhancement of local varieties of tomato from different cultivar groups. *Food Chem* 2015; 187: 517–524
- [97] Mountain Research Initiative EDW Working Group. Elevation-dependent warming in mountain regions of the world. *Nat Clim Chang* 2015; 5: 424–430
- [98] Turner NJ, Deur D, Mellott CR. “Up on the mountain”: Ethnobotanical importance of montane sites in Pacific coastal North America. *J Ethnobiol* 2011; 31: 4–43
- [99] Nchabeleng L, Mudau FN, Mariga IK. Effects of chemical composition of wild bush tea (*Ahrixia phyllicoides* DC.) growing at locations differing in altitude, climate and edaphic factors. *Med Plants Res* 2012; 6: 1662–1666
- [100] Ganzera M, Guggenberger M, Stuppner H, Zidorn C. Altitudinal variation of secondary metabolite profiles in flowering heads of *Matricaria chamomilla* cv. BONA. *Planta Med* 2008; 74: 453–457
- [101] Spitaler R, Winkler A, Lins I, Yanar S, Stuppner H, Zidorn C. Altitudinal variation of phenolic contents in flowering heads of *Arnica montana* cv. ARBO: a 3-year comparison. *J Chem Ecol* 2008; 34: 369–375
- [102] Albert A, Sareedenchai V, Heller W, Seidlitz HK, Zidorn C. Temperature is the key to altitudinal variation of phenolics in *Arnica montana* L. cv. ARBO. *Oecologia* 2009; 160: 1–8
- [103] Selmar D, Kleinwächter M. Influencing the product quality by deliberately applying drought stress during the cultivation of medicinal plants. *Ind Crops Prod* 2013; 42: 558–566
- [104] Al-Gabbies A, Kleinwächter M, Selmar D. Influencing the contents of secondary metabolites in spice and medicinal plants by deliberately applying drought stress during their cultivation. *Jordan J Biol Sci* 2015; 8: 1–10
- [105] Maranz S, Wiesman Z. Influence of climate on the tocopherol content of shea butter. *J Agric Food Chem* 2004; 52: 2934–2937
- [106] Chung IM, Kim JJ, Lim JD, Yu CY, Kim SH, Hahn SJ. Comparison of resveratrol, SOD activity, phenolic compounds and free amino acids in *Rehmannia glutinosa* under temperature and water stress. *Environ Exp Bot* 2006; 56: 44–53

- [107] Jochum GM, Mudge KW, Thomas RB. Elevated temperatures increase leaf senescence and root secondary metabolite concentrations in the understory herb *Panax quinquefolius* (Araliaceae). *Am J Bot* 2007; 94: 819–826
- [108] Nowak M, Manderscheid R, Weigel JJ, Kleinwächter M, Selmar D. 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* 2010; 83: 133–136
- [109] Ghasemzadeh A, Jaafar HZE, Rahmat A. Elevated carbon dioxide increases contents of flavonoids and phenolic compounds, and antioxidant activities in Malaysian young ginger (*Zingiber officinale* Roscoe) varieties. *Molecules* 2010; 15: 7907–7922
- [110] Zhu C, Zeng Q, McMichael A, Ebi KL, Ni K, Khan AS, Zhu J, Liu G, Zhang X, Cheng L, Ziska LH. Historical and experimental evidence for enhanced concentration of artemisinin, a global anti-malarial treatment, with recent and projected increases in atmospheric carbon dioxide. *Clim Change* 2015; 132: 295–306
- [111] Briske DD, Camp BJ. Water stress increases alkaloid concentrations in threadleaf groundsel (*Senecio longilobus*). *Weed Sci* 1982; 30: 106–108
- [112] Kirk H, Vrieling K, van der Meijden E, Klinkhamer PGL. Species by environment interactions affect pyrrolizidine alkaloid expression in *Senecio jacobaea*, *Senecio aquaticus*, and their hybrids. *J Chem Ecol* 2010; 36: 378–387
- [113] Caldwell CR, Britz SJ, Mirecki RM. Effect of temperature, elevated carbon dioxide, and drought during seed development on the isoflavone content of dwarf soybean [*Glycine max* (L) Merrill] grown in controlled environments. *J Agric Food Chem* 2005; 53: 1125–1129
- [114] Canvin DT. The effect of temperature on the oil content and fatty acid composition of the oils from several oil seed crops. *Can J Bot* 1965; 43: 63–69
- [115] Thomas JMG, Boote KJ, Allen LH jr., Gallo-Meagher M, Davis JM. Elevated temperature and carbon dioxide effects on soybean seed composition and transcript abundance. *Crop Sci* 2003; 43: 1548–1557
- [116] Mozaffarian D, Micha R, Wallace S. Effects on coronary heart disease of increasing polyunsaturated fat in place of saturated fat: a systematic review and meta-analysis of randomized controlled trials. *PLoS Med* 2010; 7: e1000252
- [117] Dawczynski C, Kleber ME, März W, Jahreis G, Lorkowski S. Saturated fatty acids are not off the hook. *Nutr Metab Cardiovasc Dis* 2015; 25: 1071–1078
- [118] Wang Q, Afshin A, Yakoob MY, Singh GM, Rehm CD, Khatibzadeh S, Micha R, Shi P, Mozaffarian D; Global Burden of Diseases Nutrition and Chronic Diseases Expert Group (NutriCoDE). Impact of nonoptimal intakes of saturated, polyunsaturated, and trans fat on global burdens of coronary heart disease. *J Am Heart Assoc* 2016; 5: e002891
- [119] Chakraborty S, Newton AC. Climate change, plant diseases and food security: an overview. *Plant Pathol* 2011; 60: 2–14
- [120] Magan N, Medina A, Aldred D. Possible climate-change effects on mycotoxin contamination of food crops pre- and postharvest. *Plant Pathol* 2011; 60: 150–163
- [121] Bebbler DP, Ramotowski MAT, Gurr SJ. Crop pests and pathogens move polewards in a warming world. *Nat Clim Chang* 2013; 3: 985–988
- [122] Van der Fels-Klerx HJ, Liu C, Battilani P. Modelling climate change impacts on mycotoxin contamination. *World Mycotoxin J* 2016; 9: 717–726