



Review

Eustress and Plants: A Synthesis with Prospects for *Cannabis sativa* Cultivation

Roberto Berni ¹, Margaux Thiry ¹, Jean-Francois Hausman ¹, Stanley Lutts ² and Gea Guerriero ^{1,*}

¹ Environmental Research and Innovation Department, Luxembourg Institute of Science and Technology, 5, rue Bommel, L-4940 Hautcharage, Luxembourg; roberto.berni@yahoo.com (R.B.); margaux.thiry@list.lu (M.T.); jean-francois.hausman@list.lu (J.-F.H.)

² Groupe de Recherche en Physiologie Végétale (GRPV), Earth and Life Institute-Agronomy (ELI-A), Université Catholique de Louvain, Croix du Sud 45, boîte L7.07.13, B-1348 Louvain-la-Neuve, Belgium; stanley.lutts@uclouvain.be

* Correspondence: gea.guerriero@list.lu; Tel.: +352-275-888-5096

Abstract: *Cannabis sativa* L. is a species of great economic value. It is a medicinal plant that produces several bioactive phytochemicals, and the stems of the industrial cultivars, commonly referred to as “hemp”, are sources of both cellulosic fibers and hurds used in textiles and bio-composites. Environmental stresses of biotic and abiotic nature affect plant development and metabolism and can, consequently, impact biomass yield and phytochemical content. Stress factors can be divided into eustressors and distressors; while the former stimulate a positive response in terms of growth, productivity, and resistance, the latter impair plant development. Eustressors are factors that, applied at low–moderate doses, can improve plant performance. Several studies have investigated different types of distress in *C. sativa* and evaluated the impact on biomass and phytochemicals, while less attention has been paid to the study of eustress. This review discusses the concept of plant eustress by referring to the recent literature and extrapolates it to applications in *C. sativa* cultivation. The data available on the response of *C. sativa* to exogenous factors are reviewed, and then, salinity eustress applied to hemp cultivation is taken as a proof-of-concept example. The knowledge developed on plant eustress and the results collected so far are discussed in light of future applications to improve the production of biomass and phytochemicals in plants of economic interest. Emphasis is placed on the potential use of eustress in conjunction with other factors shown to impact both the physiological response and metabolism of *Cannabis*, among which there are macronutrients and biofertilizers. Perspectives are also drawn with respect to applying the knowledge developed on the elicitation of whole plants to *Cannabis* cell suspension cultures, which provide a controlled, scalable, and season-independent platform to produce secondary metabolites.

Keywords: eustress; distress; hormesis; *Cannabis sativa*; bast fibers; phytochemicals



Citation: Berni, R.; Thiry, M.; Hausman, J.-F.; Lutts, S.; Guerriero, G. Eustress and Plants: A Synthesis with Prospects for *Cannabis sativa* Cultivation. *Horticulturae* **2024**, *10*, 127. <https://doi.org/10.3390/horticulturae10020127>

Academic Editor: Aisheng Xiong

Received: 16 December 2023

Revised: 23 January 2024

Accepted: 26 January 2024

Published: 30 January 2024



Copyright: © 2024 by the authors. Licensee MDPI, Basel, Switzerland. This article is an open access article distributed under the terms and conditions of the Creative Commons Attribution (CC BY) license (<https://creativecommons.org/licenses/by/4.0/>).

1. Introduction

The term “stress” in plant biology refers to any substance or condition impairing plant growth, metabolism, or development [1]. Plants in the field are exposed to several stress factors (“stressors”) of biotic and abiotic nature and mixtures thereof. As sessile organisms, they have developed both physical and chemical defenses. The former are linked to the structural/tissular features of organs, namely trichomes, prickles, spikes, and thorns, as well as suberization, lignification, silicification, and the accumulation of crystals such as calcium oxalate [2]. The latter involve the production of specialized metabolites via secondary metabolism [3].

Plant stressors can be distinguished by their nature (biotic or abiotic), as well as their effect on plants (positive—eustressors or negative—distressors). The positive or negative outcome is determined by both the dose and duration of a given stress [4]; stressors applied at low–moderate levels can positively affect plant growth via hormesis and act as

eustressors. The plant hormetic stress response is a non-linear, biphasic dose–response with the highest stimulatory effect below the NOAEL (the no observed adverse effect level, i.e., the highest concentration of a stressor with no/negligible effects) [5]. Although hormesis is a phenomenon known since the 19th century [6], its study in relation to plants has gained momentum only in the last few years; a search with the words “plant hormesis” in PubMed in October 2023 during the preparation of the present review showed >60 publications per year only since 2020.

The positive effect that eustressors can have on plant yield has been documented in several species, both economically relevant crop models and those that are not, as detailed in the following paragraphs. More examples are provided in Section 2. For instance, in *Solanum lycopersicum* L., the insecticide acephate applied at a concentration five times lower than the recommended dosage increased the biosynthesis of chlorophyll and stimulated photosynthesis by impacting the antenna complex at the transcriptomic level [7]. Additionally, tomato seedlings treated with AgNPs (nanoparticles) at 5 mg/L showed increased concentrations of nitrogen–phosphorus–potassium (N, P, and K) in the leaves in a hormetic manner [8]. A study on another well-known plant model, *Arabidopsis thaliana*, showed that both young and more mature leaves displayed a hormetic response of the effective quantum yield of PSII to water deprivation; defense responses were activated by reactive oxygen species—ROS at mild water deficit stress, and acclimation occurred at moderate stress [9].

Literature evidence is also available for the hormetic effect exerted by other abiotic stressors, namely ozone and salinity. The application of ozone (120 ppb for 5 h per day and a total of 36 consecutive days) to sage plants induced an accumulation of phenolic compounds and sesquiterpenes; the induction was observed 14 days from the beginning of the exposure and disappeared at the last time point [10]. With respect to salinity, it is worth mentioning the value of halophytes here, which can contribute to a resilient food system with their interesting nutritional profile; this is, for example, the case for *Salicornia europaea*, which can be produced via indoor farming and which showed increased production of carotenoids upon exposure to medium doses of UVB ($2.5 \text{ kJ} \cdot \text{m}^{-2} \cdot \text{s}^{-1}$) [11]. This stress dose did not cause necrosis, chlorosis, or growth impairment but induced the production of abscisic acid—ABA and carotenoids as defense mechanisms to protect the photosystems against the altered oxidative status of the UVB-exposed tissues (increased H_2O_2 levels) [11].

Mechanical stimuli applied in a controlled manner can also trigger eustress in plants with a consequent impact on secondary metabolism. A robotic platform with an arm capable of stroking basil plants at a rate of 100 repetitions per day was used in an experimental set-up aimed at determining the impact on the metabolism and sensory quality of the derived pesto sauce [12]. Among the significantly different metabolites between the control and mechanically stimulated plants, terpenes, benzenoids, amino acids, and organic acids were among the most affected; in particular, linalool glucoside positively correlated with the overall improved taste [12].

Data on hormetic effects also exist for compounds such as allelochemicals and herbicides, although specific experimental conditions and different plant species need to be considered before drawing general conclusions. The natural plant toxin parthenin, a sesquiterpene lactone, showed hormetic effects on *Lactuca sativa* in an experimental condition-dependent manner [13]; under conditions promoting root growth (the exclusion of light, increasing T), the stimulatory effect decreased or disappeared. Seedlings of *Coffea arabica* L. (cv Catuai Vermelho IAC-144) exposed to the herbicide glyphosate showed enhanced growth parameters (i.e., number of leaves, height, and dry biomass) when 14.5–30 g acid equivalents were used per hectare [14]. The use of glyphosate at low doses can have a different hormetic effect in other plants, and while showing anti-fungal activity against some pathogens, it can increase the susceptibility to others [15].

Eustress has also been studied in plants grown in aquaponics; the organically enriched water formed via the waste products of fish and via microorganisms can cause eustress and impact secondary metabolism by acting as a biostimulant. For example, *Cuphea hyssopifolia*

grown in aquaponics showed an increase in apigenin > 60% compared to plants cultivated conventionally, together with higher total phenol content [16]. Studying the impact of eustress on plants and understanding its physiological and molecular implications will be useful in designing successful agricultural practices for different crops.

In the context of bioeconomy, the multi-purpose plant *Cannabis sativa* L. certainly deserves attention; it is a fast-growing herbaceous species supplying industry with cellulosic fibers known as bast fibers [17] for bio-composites, phytochemicals for cosmetics/pharma, oil for food applications, and also biodiesel, bioethanol, biomethane, platform chemicals, biopolymers [18]. Because of their stimulatory effect on plant performance, eustressors hold great potential to boost the production of *C. sativa* biomass and phytochemicals. Hereafter, a synthesis is offered on what is documented in the literature concerning the response of plants to (a)biotic eustressors with a perspective of transferring the current knowledge to *C. sativa* cultivation.

2. Plant Hormesis and Its Links with Priming, Preconditioning, Biostimulation, and Elicitation

The concept of hormesis was formulated in the last decades of the 19th century, but its scientific interest soon decreased and encountered hostility until the late 20th century as it was linked to homeopathy (for a review, see [19]). The linear non-threshold response (also known as the proportionality rule, i.e., linear inhibition with increasing stress dose) and threshold response models (no inhibition observed until a threshold value is reached) started to be questioned in plants when increasing evidence was gathered for the existence of a biphasic dose–response [19].

The terms priming, biostimulation, elicitation, and preconditioning are very often found in publications covering plant hormesis [20,21]. Priming and preconditioning refer to the same concept of pre-activating the plant defenses with low-level stress to help tolerate a subsequent severe exogenous constraint [19]; priming–elicitation [22] and elicitors–biostimulants [19] have been interchangeably employed as synonyms. Therefore, priming, preconditioning, biostimulation, and elicitation all refer to the phenomenon of hormesis and are all manifestations of the beneficial response when a low stress dose is applied (eustress).

The functional mechanism behind the beneficial effects of eustressors can depend on several factors, namely the species, eustressor types, and experimental conditions used. Three mechanisms are hereafter discussed as examples, focused on different eustressors, but they only provide a partial picture of the mechanisms triggered by eustressors. There is a need to generate more data encompassing different *omic* layers for different species, eustressors, and experimental conditions and to analyze them bioinformatically to identify a common set of genes, gene products, and metabolites [15]. The first example shown concerns the possible impact of eustressors on phytohormone-regulated processes. The hormetic effects of the allelochemical parthenin on irradiated roots of *L. sativa* was suggested to be due to the an auxin-like effect of the sesquiterpene lactone [13]. Experiments conducted using two approaches, i.e., binary interaction of a natural auxin with well-known auxin-related compounds and a genetic screen using *A. thaliana* mutants resistant to auxins or inhibitors of auxin-related processes, showed that the inhibitory effects of parthenin at high doses is not linked to auxin-like activity, while the link between auxin-related processes and hormetic effects at low doses could not be ruled out [23]. The second and third examples are based on a transcriptomic study in response to low-dose applications of UVC irradiation [24] and Cd [25]. The pre-harvest treatment of lettuce with low level doses of UVC followed by inoculation with *Xanthomonas campestris* pv. *vitians* activated genes involved in the return to homeostasis, the resumption of normal growth, and defense response [24]; genes involved in both the production (by interacting with NADPH oxidases) and control of ROS (protein kinases), as well as transcripts involved in primary metabolism, photosynthesis (genes associated with RuBisCo), and cell wall reinforcement, were induced by UVC treatment. These findings suggest the activation of a primed state following low

doses of UVC treatment. Cadmium—Cd applied to young peppermint plants at low doses (1.6 mg/L) enhanced the total content of flavonoids, as well as the transcription of polyphenol oxidase, an enzyme involved in quinone biosynthesis [25]. The enhanced formation of quinones and flavonoids following low-dose Cd treatment suggests the promotion of a non-enzymatic mechanism protecting against oxidative stress [25].

Several literature data sources exist on the effect of eustressors in improving plant performance. Examples are provided in the next paragraph.

2.1. Potentially Toxic Elements and Eustress

The analysis of 18 biomarkers in *Tillandsia ionantha* Planch. exposed to Cd 5 mM showed a hormetic response for seven of them, namely six Cd resistance genes and glutathione—GSH [26]. Another species of *Tillandsia*, *T. usneoides*, showed a predominant biphasic hormetic response at 10 different atmospheric lead—Pb concentrations; the hormetic response was confirmed by the levels of malondialdehyde (MDA) and superoxide anion radical and the superoxide dismutase (SOD) activity after 6–12 h, as well as by GSH and metallothionein—MT content after 12 h [27]. SOD, GSH, and MT also showed a hormetic response in *T. usneoides* exposed to different mercury—Hg atmospheric concentrations [28].

Other evidence of the existence of hormetic responses in plants come from two studies, one on *Lonicera japonica* Thunb. and the other on young peppermint (*Mentha piperita* L.) exposed to Cd. In *L. japonica*, 5 mg/L Cd promoted growth and photosynthesis; interestingly, in the presence of an electric field, a synergistic improvement in leaf and root biomass, as well as photosynthetic pigment content and photosynthetic parameters (i.e., net photosynthetic rate, stomatal conductance, transpiration rate, and intercellular CO₂ concentration), was observed [29]. *M. piperita* treated with Cd 1.6 mg/L showed growth promotion and the induction of genes in the phenylpropanoid pathway and flavonoid biosynthesis; the activities of antioxidant enzymes (peroxidase, catalase, superoxide dismutase, and polyphenol oxidase) also increased [25].

Corn coleoptiles grown in the presence of Pb or Cd and then subsequently excised and grown in the absence of the heavy metals showed increased growth due to higher content of H₂O₂ and indole-3-acetic acid (IAA) [30]. When the experiment was repeated with corn seedlings and different sub-toxic concentrations of Pb and Cd, a significant growth increase compared to the control was observed with 10 µM Cd and 5 µM Pb; this stimulatory effect coincided with a higher content of IAA and flavonols, together with the maintenance of H₂O₂ levels to the control ones [30].

A study performed on three representative annual species commonly found in urban areas, *Cardamine hirsuta* L., *Poa annua* L., and *Stellaria media* (L.) Vill., revealed that all or some plants (depending on the elements) displayed hormetic responses when exposed, in hydroponics, to urban concentrations of Cd (up to 2 µM), Pb (up to 15 µM), and chromium—Cr (up to 100 µM) [31]. This study therefore highlights how urban concentrations of Cd, Pb, and Cr are not harmful but rather stimulatory for plants. It should be highlighted, however, that the results were obtained for plants exposed to the single elements and not their combination, which is a condition likely to occur in real urban environments.

2.2. Nutrient Eustress

Some examples have been reported on the use of nutrient eustress in plants. A recent one studied the application of eustress to closed soilless systems to produce vegetables, which was shown to be effective in boosting bioactive content. This was proven in lettuce, where nutrient eustress (applied in the form of half-strength nutrient solution) led to a remarkable increase in phenolic compounds, as well as carotenoids [32].

Eustress has also been reported in plants supplemented with the non-essential metalloid silicon—Si (nano-forms of it are discussed in Section 2.4). For example, Si applied to pepper plants triggered a hormetic response, with an increase in chlorophyll content, total

free amino acids, and soluble sugars in the range of 60–125 mg/L, while inhibitory effects were observed at a higher dose (250 mg/L) [33].

2.3. Salinity Eustress

Soil salinity is a global ecological issue and one of the most damaging environmental stress factors disturbing physiological, biochemical, and morphological processes in crops [34]. However, the application of salinity in mild-to-moderate doses and during specific phenological states can positively influence the aroma, flavor, taste, and content of antioxidant compounds [35].

For instance, in red lettuce, the application of moderate salt stress (50 mM NaCl) for fifteen days in hydroponics induced the biosynthesis of secondary metabolites (e.g., polyphenols and flavonoids) and also improved their antioxidant activity [36].

In green and red *Perilla frutescens* cultivated in a greenhouse, mild and moderate NaCl (10–20–30 mM) induced an increase in the accumulation of rosmarinic acid, as well as total polyphenols and aromatic volatile compounds [37]. Salinity eustress is thus an effective strategy to boost the nutritional and functional quality of plants grown under controlled conditions.

Mild salinity stress can also be useful in limiting the accumulation of nitrate in leafy vegetables. Some concerns, which are difficult to prove because of inconsistencies in epidemiological studies (referred to in [38]), have indeed been put forward in relation to dietary nitrate and different types of cancer. For instance, salinity eustress (induced with 20 mM NaCl) in hydroponically grown *Valerianella locusta* reduced the nitrate content, without impacting agronomical traits (leaf fresh weight, leaf number, and relative growth rate) or macro–micronutrient content [38].

Increasing the electrical conductivity (EC) by means of controlled salt addition in soilless cultivation systems proved to be an effective way to stimulate the production of bioactive compounds in plants without significant effects on growth (reviewed in [39]); this was the case in tomato, which showed enhanced lycopene, β -carotene, vitamin C, and total phenolic content [40], as well as cauliflower in which a two-fold increase in neoglucobrassicin was measured with a saline nutrient solution [41].

Amaranthus gangeticus exposed to salinity up to 100 mM NaCl showed increased content of phenolic acids and antiradical potential, as well as micro- and macro-elements [42], with 50 and 100 mM NaCl representing the conditions at which the highest ascorbic acid, β -carotene, and pigment (betalain) contents were measured [43]. *A. gangeticus* thus constitutes an excellent example of a substitute crop that can be grown in soils affected by salinity [42].

2.4. Nanoparticle Eustress

A detailed literature review has been recently provided on the hormetic effects of essential metal nanoparticles in plants [44]; the physico-chemical nature of the metal nano-forms, as well as the developmental stage of the plants, dictate the type of response observed. In this paragraph, the focus will be put on recent data (maximum 2 years old) on nanoparticles of the quasi-essential element Si, or derived silica—SiO₂ nano-forms, given their increasingly reported use for agronomical applications [45]. Nano-forms of this element have biotechnological relevance as biocompatible delivery systems to alleviate stress symptoms in plants [46,47]. Hence, it is anticipated that more research will be devoted to their synthesis and the study of their effects *in planta*.

Nano-Si (0.5 ppm, foliar application) positively impacted tomato growth under salt stress and after grafting on two different rootstocks [48]; vitamin C and mineral content, total soluble solid percentage, and fruit firmness increased when nano-Si was applied to plants grafted on the Edkawy rootstock.

Nano-SiO₂ applied for wheat seed priming (at 15 mg/L) improved germination, water uptake, and amylase activity, together with seedling growth, vigor, and drought tolerance [49].

Nano-SiO₂ (either porous, SBA-15, or consisting of hexagonal arrays, SBA-16) applied to chili pepper plants via spraying (at 100 and 50 ppm, respectively) had a positive effect

on seedlings' growth and stimulated the expression of genes involved in defense, namely Mn-superoxide dismutase and peroxidase, as well as transcripts related to the synthesis of phenylpropanoids (phenylalanine ammonia lyase and chalcone synthase) [21]. The induction of these genes was proposed to be related to the higher resistance to cold stress reported for SBA-16.

The paragraphs that follow will be focused on *Cannabis*; the response to exogenous factors will be reviewed first, by referring to recent studies, and then, the prospects of applying eustress in *C. sativa* cultivation will be discussed by providing salinity as an example.

3. Response of *C. sativa* to Exogenous Factors

Several papers have been published on the response of *Cannabis* to exogenous factors, with several angles being studied, namely molecular, physiological, and agricultural angles. Part of this literature is hereafter discussed with a focus on drought, salinity, cold, heavy metals, light, and macronutrients.

3.1. *C. sativa* vs. Drought

An experiment conducted on 47 Iranian ecotypes of *C. sativa* revealed the impact of water stress on dry matter yield and water use efficiency and highlighted a clear distinction between tolerant and susceptible genotypes. This distinction could be determined by analyzing the geometric mean productivity, mean productivity, and stress tolerance index, which are parameters that allow the identification of genotypes suitable for growth in arid environments under both non-stress and stress conditions [50].

The dependence on the genotype of the water stress response in *Cannabis* was confirmed in a study focused on 26 commercial European cultivars [51], as well as two essential oil cultivars, 'Wife' and 'Cherry' [52]. The cultivar 'Wife' responded by adopting a rapid leaf-shedding mechanism; 'Cherry' showed anisohydric behavior, with it maintaining a full canopy and open stomata.

The supplementation of the plant growth retardant uniconazole has been shown to protect *C. sativa* against the injuries caused by drought; the triazole chemical protected chlorophyll against degradation and ameliorated the histological features of the mesophyll (chloroplast and starch grain number), which improved photosynthesis under drought and mitigated the production of ROS [53]. The treatment with uniconazole impacted the expression of several genes involved in porphyrin/chlorophyll, starch/sucrose, and N metabolism, the synthesis of photosynthesis-antenna proteins, and plant hormone signal transduction [54]. Despite the sensitivity of *Cannabis* to water deprivation, studies have shown that some cultivars can complete their life cycle and produce seeds even when growing in soils with very low water content. For example, the hemp cultivar 'Black Label' grown under well-watered, moderately watered, or water stressed conditions showed a reduction in biomass (roots and shoots), plant height, leaf area, and water potential but produced seeds in all conditions, which were lower in number but with comparable size and weight to those produced under non-stress conditions [55]. Hemp plants are thus able to prioritize quality seed production over quantity under drought.

Drought applied in a controlled manner can be used as a stimulator of secondary metabolite biosynthesis in medicinally important plants such as *Cannabis*. A study investigating the effects of water deprivation in the flowering stage revealed that despite the significant decrease in net photosynthetic rate and plant water potential, the yield of cannabinoids increased after drought, together with an increased yield of inflorescence dry weight [56]. The response to drought of different cultivars needs to be determined, however, since at least one other study has shown that drought does not lead to an increase in THC and CBD content [52].

3.2. *C. sativa* vs. Salinity

Salinity is known to affect *Cannabis* development both in soil and hydroponics. For instance, after 150 mM or 200 mM of NaCl, the seed germination percentage decreased in the

four different industrial hemp varieties ‘CFX-2’, ‘Joey’, ‘Bialobrzieskie’, and ‘Henola’; ‘CFX-2’ and ‘Bialobrzieskie’ tolerated up to 100 mM of salt by maintaining a high seed germination percentage and increasing the activities of ROS-scavenging enzymes in the roots [57].

Concentrations ≥ 200 mM impact both young and adult plants with effects on the vascular tissue anatomy in the hypocotyl and leaves (smaller xylem vessels [58]), leaf biomass accumulation, and drooping with the loss of turgidity [46].

A transcriptome analysis coupled to metabolomics performed on the leaves of Longma #3 and #9 revealed a >10-fold increase in glutamic, succinic, and gamma-aminobutyric acids under salinity, accompanied by the activation of genes related to the tricarboxylic acid cycle and the MAPK pathway [59]. The involvement of the MAPK pathway was further confirmed in two additional varieties, ‘W20’, widely cultivated in China, and ‘K94’, cultivated in Russia [60]. Transcriptomics also revealed that salinity had an impact on genes involved in the phenylpropanoid pathway and plant hormone signal transduction.

NaCl at 40 mM was shown to be phytotoxic for a drug-type cultivar of *C. sativa* grown in hydroponics with negative effects on reproductive parameters already evident at 5 mM [61]. Both the inflorescence dry mass and potency (content of THC, CBD, CBC, and CBG) decreased with salinity; however, aquaponics mitigated the adverse effects of salinity probably by providing Si, organic particles, and bacteria acting as PGPMs (plant growth-promoting microorganisms).

A study comparing seedlings of seed- and fiber-type hemp revealed different sensitivity to salinity, which was reflected in the different gene expression trends for transcripts involved in stress response (encoding the chloroplast protein CP12, polyphenol oxidase glutathione *S*-transferase, and peroxiredoxins); notably, when comparing alkali to salinity stress, hemp was found to be more sensitive to the former [62]. The transcriptomic signature of hemp growing in the presence of alkali stress provided the molecular explanation of its sensitivity to alkali stress; research performed on plants in hydroponics revealed the differential expression of genes involved in phytohormone signal transduction and synthesis, as well as pathways connected to the metabolism of starch, sucrose, nitrogen, and amino acids [63].

3.3. *C. sativa* vs. Cold

Some literature is available on the impact of cold stress on *C. sativa*. A study was conducted on two different cultivars, ‘AutoCBD’ and ‘Finola’, to investigate the effect of temperature on plant health and cannabinoid levels. This experiment consisted of three different age groups, old–middle age–young (seeds sown at 14-day intervals), with half of the plants exposed to cold acclimation for 10 days at 10 °C. Then, four treatment groups were studied: group 1 corresponded to the control (no cold treatment), group 2 was subjected to one cold exposure, group 3 was exposed to two consecutive exposures, and group 4 was exposed to three consecutive exposures. The consecutive cold exposures took place within an interval of 24 h [64]. The content of cannabinoids in the variety ‘AutoCBD’ decreased in non-acclimated plants exposed to cold, with the old group showing the most dramatic effect after two consecutive exposures; the plants of the same age that were cold acclimated showed lower cannabinoid content, but the differences in content were mitigated upon cold exposure compared to the non-acclimated groups [64].

From a molecular point of view, the *CsDGAT* genes (diacylglycerol acyltransferases) were shown to be involved in the response to cold stress in *C. sativa* [65]. Membrane lipid composition is indeed important in low T stress tolerance. Of the members composing the DGAT family, *CsDGAT1*, *CsDGAT2*, and *CsDGAT3* were upregulated both in the leaves and roots upon cold stress, while others showed a tissue- and time-specific response [65].

3.4. *C. sativa* vs. Heavy Metals

Several studies have addressed the impact of Cd pollution on *C. sativa* growth. Among those, it is worthwhile commenting on the transcriptomic investigation performed on two varieties differing in their tolerance to Cd, ‘Ym’ (tolerant) and ‘Nx’ (sensitive) [66].

The tolerant variety could activate, at the transcriptomic level, the pathways involved in phytohormone signaling, enzymatic ROS scavenging, and cell wall remodeling. MYB genes were also correlated to the response of *C. sativa* to Cd stress and cannabinoid biosynthesis (upon Cd stress, CBD/CBDA levels increased in flowers but decreased in leaves) [67]. Seven MYBs were proposed to be key regulators of the response: MYB016, MYB067, MYB045, and MYB098, which were upregulated, and MYB005, MYB061, and MYB010, which were downregulated instead. Three MYBs, MYB024, MYB048, and MYB062, were highly expressed in the variety with higher CBD content, with MYB024 likely mediating the increased CBD biosynthesis under Cd stress in flowers [67].

3.5. The Impact of Light on *C. sativa* Development and Secondary Metabolism

Light quality has been studied in relation to cannabinoid production in plants growing under controlled conditions [68]. Increasing light intensity increased the density of the apical inflorescence and the harvest index but not the cannabinoid potency [69], while long-term exposure to short-wavelength UV negatively impacted growth and inflorescence quality. The commercial benefit of applying UV stress to *C. sativa* remains to be unequivocally proven [70], although exposure to UVA+UVB was reported to increase the density of trichomes on the sugar leaves [71].

An experiment comparing different light regimes (natural light, white light, and different combinations of red–blue–green–far red–UV light) showed that the combination red + blue + green at 70:20:10 produced all of the cannabinoids at higher concentrations in aeroponic-grown plants and led to a lower stress response and that green light plays a significant role in CBD/CBDA synthesis [68].

Cultivar-dependent as well as light spectra-dependent responses have been observed with respect to inflorescence yield and cannabinoid content [72]. A 1:1 ratio of red:blue light resulted in the highest inflorescence yield, and blue light stimulated cannabigerolic acid content (CBGA), as well as impacting the architecture of the plants, which were compact. With respect to architecture, *C. sativa* plants' shape has relevant consequences for secondary metabolite production; for example, manipulations of the plant architecture such as pruning can improve light penetration and result in uniformity of cannabinoid content (by increasing the concentration in the bottom parts which normally have lower abundance compared to the top) and biomass yield [73,74].

3.6. The Impact of Macronutrients on *C. sativa* Growth and Metabolism

Studies have investigated the impact of macronutrients on *Cannabis* growth and the production of secondary metabolites by investigating the effect of different ranges of concentration.

Increasing N supply showed that while biomass increased, the content of terpenoids and cannabinoids decreased. More specifically, although a N concentration of 30 mg/L led to the highest amount of secondary metabolites, below 160 mg/L, plant development was impaired; a N concentration of 160 mg/L was shown to be the most appropriate to achieve both high biomass yield and relatively high content of secondary metabolites [75]. Increased N supply was shown to have an impact on both primary and secondary metabolism of *Cannabis* by affecting the plant C:N ratio [76]; chlorophyll and amino acids increased in content, while sugars and phosphates decreased, with a concomitant decrease in flavonoids, olivetolic acid, and phenols, besides cannabinoids and terpenoids. Under the condition of high N supply, phenylalanine (the precursor of flavonoid biosynthesis) is shunted towards the synthesis of proteins to sustain growth. *Cannabis* inflorescences are a stronger sink for N than leaves and draw, from these, N, C skeletons and energy; this process is enhanced with higher N input due to increased photosynthesis in the leaves, with the resulting higher accumulation of most amino acids at the expense of C metabolites [76].

P supply > 5 mg/L reduced the contents of THCA and CBDA, but concentrations lower than 15 mg/L were insufficient to sustain optimal plant development and physiology [77]. K inputs < 60 mg/L induce *Cannabis* secondary metabolism, while an

increasing K concentration negatively affects cannabinoid and terpenoid content; K input of 60 mg/L is optimal to maintain both high yield and secondary metabolite content [78].

Mg has also been shown to impact *C. sativa* growth [79]; between 2–20 mg/L, plants showed clear signs of deficiency, with older leaves impacted first, while concentrations of 35–70 mg/L were optimal for development during the vegetative stage.

4. Prospects of Applying Eustress for *C. sativa* Cultivation: Salinity as a Proof-of-Concept

C. sativa is a valuable medicinal plant and a source of fibers; hence, improving its cultivation is relevant in boosting the yield of phytochemicals and biomass, as well as their quality (e.g., the presence of different secondary metabolites and the mechanical properties of the fibers). Eustress applied to hemp in the field would be an ideal way to reach this goal without consequences on the environment and could also be a strategy used in vitro to elicit micro-propagated plants. Micro-propagated *C. sativa* plants have the advantage of being totally free from pathogens, they occupy less space than pot-grown plants, and their propagation can be easily scaled up. The prospects of eustress in *C. sativa* cultivation will be discussed herein with respect to applications for field-grown and micro-propagated plants.

Preliminary proof-of-concept data were gathered by the authors in support of the existence of a stimulatory effect of salt stress applied at low doses (Figure 1). NaCl at the concentrations of 12.5–25–50–100 mM positively impacted germination, shoot and root length, and growth of the plantlets ('Santhica 27' fiber variety) 2 weeks after sowing. In this respect, comparing different industrial varieties bred for different traits (fibers, grains, or both) is relevant in understanding whether common molecular mechanisms exist in response to eustress.

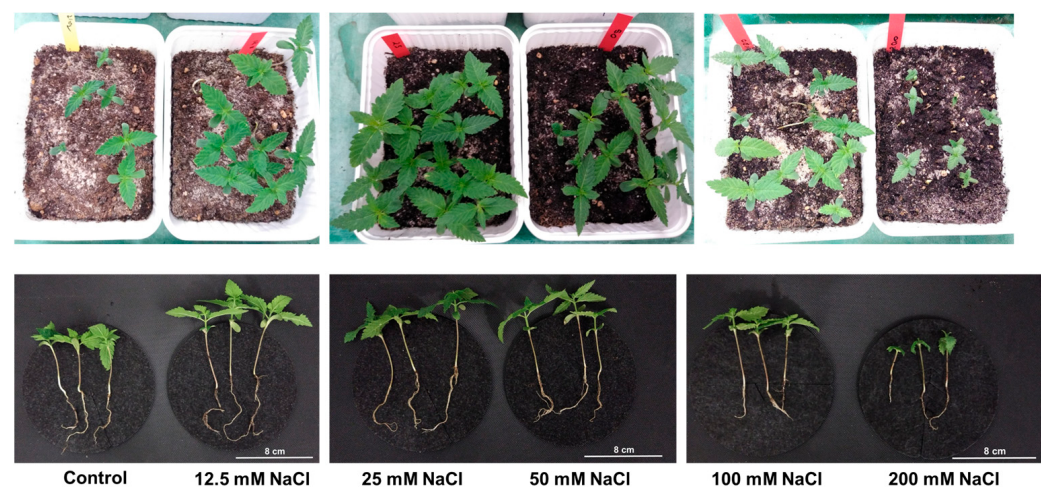


Figure 1. Stimulatory effect of NaCl at low doses on the germination and growth of *C. sativa* 'Santhica' 27.

In connection with salinity eustress, it would be interesting to study, from an agronomical, physiological, and molecular perspective, the response of *C. sativa* to growth when irrigated with diluted seawater. This could be especially interesting for coastal areas. Alternatives to freshwater irrigation are becoming urgent in light of climate change, and the prospect of using diluted seawater would not further aggravate the problem of soil salinization [80]. For example, cherry tomatoes were shown to benefit from irrigation with 12% seawater (corresponding to 10 mS/cm), with berries characterized by higher nutritional value (i.e., higher amounts of vitamin C and E and dihydrolipoic and chlorogenic acids [81]).

The authors of this review preliminarily experimented with the use of diluted Mediterranean seawater at 5 and 10% v/v (corresponding to soil conductivity of 3.78 and 6.66 mS/cm and pH values of pH 7.88 and 7.80, respectively) to irrigate pot-grown hemp ('Santhica 27') for 3 weeks (Figure 2). More research will have to be performed to understand the impact on the fibers, but the preliminary results indicate that the use of diluted seawater

at 5% *v/v* led to thicker and more abundant secondary fibers and primary bast fibers with wider lumens, while 10% seawater had a negative impact on both the number and cell wall thickness of primary and secondary bast fibers (Figure 2b,c).

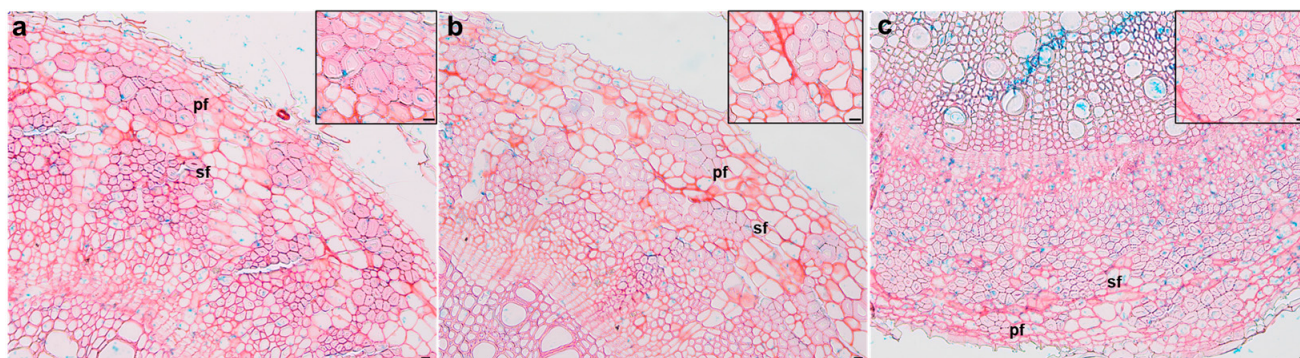


Figure 2. Microscope observations after FASGA staining of 10 μm cross-sections obtained for hemp hypocotyls ('Santhica 27') irrigated with tap water (a), seawater 5% *v/v* (b), and seawater 10% *v/v* (c). pf: primary bast fibers; sf: secondary bast fibers. Bars indicate 10 μm . The seawater was autoclaved and filtered before use. The plants were irrigated with 100 mL diluted seawater or water twice a week for 3 weeks.

Although unwanted for textile applications or the manufacture of high-performance bio-composites, hemp secondary bast fibers can be used as a source of nanocellulose (to manufacture nano-papers or nano-composites) [82]. The disordered decortication method could be applied and, given the lower content of lignin with respect to woody fibers, milder delignification treatments can be used with lower impact on the environment.

The use of diluted seawater could also induce higher content of secondary metabolites in *C. sativa* via a hormetic response; it will therefore be interesting to evaluate the impact of irrigation with diluted seawater on the metabolome of leaves and flowers. Irrigation with diluted seawater or, more generally, the application of salinity eustress to *C. sativa* could be coupled with the supplementation of beneficial elements known to exert a priming action on plants, for example Si, which was demonstrated to be taken up by hemp [83] and to be effective in mitigating the negative effects caused by distress [58,84].

With respect to the soil cultivation of *C. sativa*, it will be interesting to explore the interaction between salinity eustress and organic substrates. In cucumber, the combination of nutrient solution with high electrical conductivity and lignite substrate resulted in fruits with high content of β -carotene and lutein [85]. The combination of abiotic eustress and growth in the presence of humic acids (HAs) is also worth future investigation; HAs indeed act as chemical eustressors, since they can interact as aggregates with the root surface and cause a rise in ROS, which in turn activate scavenging enzymes by working as signaling molecules [86]. The mechanisms leading to the bioactivity of HAs is still a matter of discussion, but among the possible mechanisms, there is the dissociation of the HA superstructure into fractions able to mimic phytohormones [86,87]. As an example of the eustress effect generated by HAs, a study on rice is hereafter reported. The addition of HAs extracted from vermicompost, soil, and sediments of the Negro River to rice plants resulted in a decrease in photosynthetic performance after 96 h followed by an increase after 144 h; this positive effect was accompanied by an increase in chlorophyll *a* and an impact on carotenoid content which depended on the source of HAs (higher with HAs from sediments of the Negro River) [86]. HAs also increased soluble sugars in the roots, and HAs from vermicompost significantly increased the root volume in rice plants [86]. The positive impact of HAs on plant height, chlorophyll content, and photosynthetic efficiency was demonstrated in *C. sativa* subjected to moderate water stress when applied alone or together with a biofertilizer (composed of active and dormant cells of yeast, algae, bacteria, and filamentous fungi) [88]. Additionally, HA application to *C. sativa* resulted, on one hand,

in a reduction in THC levels from 11.8 to 7.4% in the top flowers, but, on the other, less spatial variability in cannabinoid content [89].

Eustress can be applied to *Cannabis* plants that are micro-propagated; micro-propagation is a cost-effective and rapid procedure to mass-propagate, in a standardized manner, pathogen-free plants, and it has been effectively used in conjunction with elicitation or precursor feeding to produce rare and added-value phytochemicals [90,91]. Micro-propagated *Cannabis* could be exposed to different eustressors in vitro or even their combination; salinity could be combined with nutrient eustress, for example, as well as the supplementation of Si and/or biotic elicitors. The possibilities are many, and the space-saving advantage of micro-propagation provides the possibility of screening several conditions at the same time in biological replicates.

5. Future Avenues of Research and Conclusions

5.1. Future Research Avenues

Some of the research avenues related to eustress deserving future efforts are (1) understanding the impact of eustress on epigenetic mechanisms and (2) the activation of a trans-generational memory [92]. Eustress could be used as a tool for breeding once the epigenetic marks linked to the improved stress response are identified and their stability and heritability proven and understood [92].

The study of eustress can have even broader implications which go beyond Earth applications and concern space farming [93]; even when reducing to a minimum the occurrence of stressors in set-ups for plant cultivation on orbiting stations or future settlements on the Moon and Mars, it will be impossible to recreate an environment like the one on Earth, and stressors will be largely unpredictable in space. However, there could be the possibility of utilizing some of the known space stressors as eustressors, provided some crucial growth conditions can be ensured and maintained. Such an example is radiation; instead of shielding the plant cultures completely, it could be envisaged to filter out the detrimental components and leave those that could be stimulatory and, ultimately, beneficial to growth [93].

Research on eustress using stressors known to occur in space can not only help understand the response of different species from a physiological and molecular angle but also identify the stress ranges that can be tolerated by plants with minimal impacts, as well as those that can instead stimulate their physiology. This knowledge can, in turn, help in designing the equipment needed for the space cultivation of the selected species.

Studies on Earth will be needed to understand and create predictive models of space farming; the use of artificial intelligence tools such as deep learning to process and interpret different sets of data (genomics, proteomics, metabolomics, and phenomics) will offer great help in constructing models and predicting eustress response in plants [94].

5.2. Conclusions

There is much potential in studying the response of *C. sativa* (Figure 3) and, more generally, multi-purpose plants to eustress for different applications, e.g., pharmaceuticals, nutraceuticals, and biomaterials. Coupling eustress application to NPK inputs optimized according to the desired production purpose can have significant results in terms of biomass accumulation or secondary metabolite content in *Cannabis* (see Section 3).

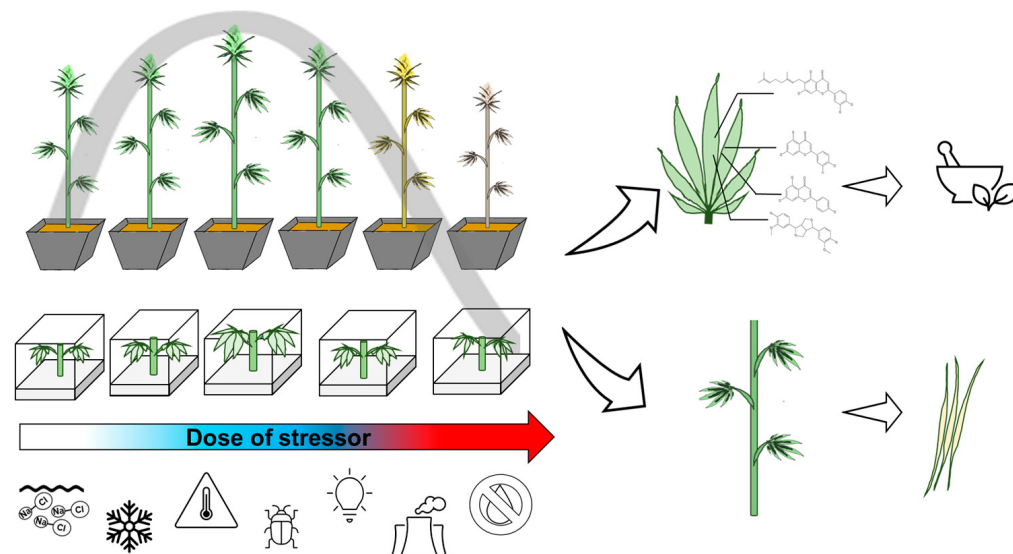


Figure 3. Prospects of applying eustress (here, salinity, cold, heat, biotic stress, light, and potentially toxic elements derived from anthropogenic activities and drought stress are schematically represented) to *C. sativa* cultivation in soil or in vitro to produce phytochemicals and/or biomass for fibers.

The use of biofertilizers also constitutes an interesting line of research, in light of the positive effects against stress and their role in promoting sustainable agriculture. The application of PGPMs and arbuscular mycorrhizae to *Cannabis* and their positive impact on yield and the mitigation of stress symptoms have already been investigated in the literature in conjunction with both abiotic and biotic stresses [95–97].

Exploring the connection between stress and phytochemistry through elicitation is also worthwhile to increase the content of bioactive substances and the therapeutic potential of medicinal plants [98]. Salicylic acid and γ -aminobutyric acid have already been shown to positively impact the expression of THC biosynthetic genes and the content of THC in plants grown under controlled conditions [99]. Methyl jasmonate and salicylic acid applied at 0.1 mM were effective in increasing THCA and CBDA concentrations both in inflorescences and leaves [100]. However, genotype and environmental conditions, as well as pests (shown to impact cannabinoid and terpene content [101]), pose a challenge to the application of *C. sativa* plants' elicitation on a large scale, i.e., under field conditions, as these factors can contribute to a great variability in secondary metabolite content. Elicitors' type, concentration, duration, synergistic action, and cost, as well as the complexity of the shoot–root feedback mechanism, the impact on the synthesis of the target molecules and effect on other pathways leading to undesired effects need to be considered before applying *C. sativa* elicitation at a large scale [98,102].

Besides applications to whole plants, it is also worth mentioning the application of eustress to plant cell culture-based bioprocesses here; the scalability of this technology coupled with standardization, good manufacturing practice compliance, and the absence of contaminants make it very powerful to produce high-added-value compounds. A few studies have started investigating the cultivation of *C. sativa* cell suspension cultures [103,104], and the increasing interest that plant cell culture technology is attracting for cosmetics, nutraceuticals, and pharmaceuticals will, in the coming years, further promote its use [105,106].

Author Contributions: Conceptualization, R.B. and G.G.; investigation, R.B., M.T., J.-F.H., S.L. and G.G.; resources, J.-F.H., S.L. and G.G.; writing—original draft preparation, R.B., M.T. and G.G.; writing—review and editing, R.B., M.T., J.-F.H., S.L. and G.G.; supervision, J.-F.H., S.L. and G.G.; project administration, G.G.; funding acquisition, G.G. All authors have read and agreed to the published version of the manuscript.

Funding: This research was funded by the Luxembourg National Research Fund, project “HEMPHASE” and grant number O21/16231453.

Data Availability Statement: All data are available in the published paper.

Conflicts of Interest: The authors declare no conflicts of interest.

References

1. Lichtenthaler, H.K. The Stress Concept in Plants: An Introduction. *Ann. N. Y. Acad. Sci.* **1998**, *851*, 187–198. [[CrossRef](#)] [[PubMed](#)]
2. Barton, K.E. Tougher and Thornier: General Patterns in the Induction of Physical Defence Traits. *Funct. Ecol.* **2016**, *30*, 181–187. [[CrossRef](#)]
3. Mithöfer, A.; Boland, W. Plant Defense Against Herbivores: Chemical Aspects. *Annu. Rev. Plant Biol.* **2012**, *63*, 431–450. [[CrossRef](#)] [[PubMed](#)]
4. Vázquez-Hernández, M.C.; Parola-Contreras, I.; Montoya-Gómez, L.M.; Torres-Pacheco, I.; Schwarz, D.; Guevara-González, R.G. Eustressors: Chemical and Physical Stress Factors Used to Enhance Vegetables Production. *Sci. Hortic.* **2019**, *250*, 223–229. [[CrossRef](#)]
5. Agathokleous, E.; Saitanis, C.; Markouizou, A. Hormesis Shifts the No-Observed-Adverse-Effect Level (NOAEL). *Dose Response* **2021**, *19*, 15593258211001667. [[CrossRef](#)] [[PubMed](#)]
6. Henschler, D. The Origin of Hormesis: Historical Background and Driving Forces. *Hum. Exp. Toxicol.* **2006**, *25*, 347–351. [[CrossRef](#)]
7. Xu, N.; Sun, Y.; Wang, Y.; Cui, Y.; Jiang, Y.; Zhang, C. Hormesis Effects in Tomato Plant Growth and Photosynthesis Due to Acephate Exposure Based on Physiology and Transcriptomic Analysis. *Pest Manag. Sci.* **2023**, *79*, 2029–2039. [[CrossRef](#)] [[PubMed](#)]
8. Guzmán-Báez, G.A.; Trejo-Téllez, L.I.; Ramírez-Olvera, S.M.; Salinas-Ruiz, J.; Bello-Bello, J.J.; Alcántar-González, G.; Hidalgo-Contreras, J.V.; Gómez-Merino, F.C. Silver Nanoparticles Increase Nitrogen, Phosphorus, and Potassium Concentrations in Leaves and Stimulate Root Length and Number of Roots in Tomato Seedlings in a Hormetic Manner. *Dose Response* **2021**, *19*, 15593258211044576. [[CrossRef](#)]
9. Sperdoui, I.; Ouzounidou, G.; Moustakas, M. Hormesis Responses of Photosystem II in *Arabidopsis thaliana* under Water Deficit Stress. *Int. J. Mol. Sci.* **2023**, *24*, 9573. [[CrossRef](#)]
10. Marchica, A.; Ascrizzi, R.; Flamini, G.; Cotrozzi, L.; Tonelli, M.; Lorenzini, G.; Nali, C.; Pellegrini, E. Ozone as Eustress for Enhancing Secondary Metabolites and Bioactive Properties in *Salvia officinalis*. *Ind. Crops Prod.* **2021**, *170*, 113730. [[CrossRef](#)]
11. Fitzner, M.; Schreiner, M.; Baldermann, S. Between Eustress and Distress: UVB Induced Changes in Carotenoid Accumulation in Halophytic *Salicornia europaea*. *J. Plant Physiol.* **2023**, *291*, 154124. [[CrossRef](#)] [[PubMed](#)]
12. Seeburger, P.; Herdenstam, A.; Kurtser, P.; Arunachalam, A.; Castro-Alves, V.C.; Hyötyläinen, T.; Andreasson, H. Controlled Mechanical Stimuli Reveal Novel Associations between Basil Metabolism and Sensory Quality. *Food Chem.* **2023**, *404*, 134545. [[CrossRef](#)] [[PubMed](#)]
13. Belz, R.G.; Cedergreen, N. Parthenin Hormesis in Plants Depends on Growth Conditions. *Environ. Exp. Bot.* **2010**, *69*, 293–301. [[CrossRef](#)]
14. Costa, R.N.; Bevilacqua, N.d.C.; Krenchinski, F.H.; Giovanelli, B.F.; Pereira, V.G.C.; Velini, E.D.; Carbonari, C.A. Hormetic Effect of Glyphosate on the Morphology, Physiology and Metabolism of Coffee Plants. *Plants* **2023**, *12*, 2249. [[CrossRef](#)] [[PubMed](#)]
15. Gressel, J.; Dodds, J. Commentary: Hormesis Can Be Used in Enhancing Plant Productivity and Health; but Not as Previously Envisaged. *Plant Sci.* **2013**, *213*, 123–127. [[CrossRef](#)] [[PubMed](#)]
16. Flores-Aguilar, P.S.; Rico-Chávez, A.K.; Rodríguez-deLeón, E.; Aguirre-Becerra, H.; Zamora-Castro, S.A.; Soto-Zarazúa, G.M. Bioactive Compounds of Endemic Medicinal Plants (*Cuphea* spp.) Cultured in Aquaponic Systems: A Short Study. *Agriculture* **2023**, *13*, 2018. [[CrossRef](#)]
17. Andre, C.M.; Hausman, J.-F.; Guerriero, G. *Cannabis sativa*: The Plant of the Thousand and One Molecules. *Front. Plant Sci.* **2016**, *7*, 19. [[CrossRef](#)]
18. Moscariello, C.; Matassa, S.; Esposito, G.; Papirio, S. From Residue to Resource: The Multifaceted Environmental and Bioeconomy Potential of Industrial Hemp (*Cannabis sativa* L.). *Resour. Conserv. Recycl.* **2021**, *175*, 105864. [[CrossRef](#)]
19. Agathokleous, E.; Kitao, M.; Calabrese, E.J. Hormesis: A Compelling Platform for Sophisticated Plant Science. *Trends Plant Sci.* **2019**, *24*, 318–327. [[CrossRef](#)]
20. Vargas-Hernandez, M.; Macias-Bobadilla, I.; Guevara-Gonzalez, R.G.; Romero-Gomez, S.d.J.; Rico-Garcia, E.; Ocampo-Velazquez, R.V.; Alvarez-Arquieta, L.d.L.; Torres-Pacheco, I. Plant Hormesis Management with Biostimulants of Biotic Origin in Agriculture. *Front. Plant Sci.* **2017**, *8*, 1762. [[CrossRef](#)]
21. Magaña-López, E.; Palos-Barba, V.; Zuverza-Mena, N.; Vázquez-Hernández, M.C.; White, J.C.; Nava-Mendoza, R.; Feregrino-Pérez, A.A.; Torres-Pacheco, I.; Guevara-González, R.G. Nanostructured Mesoporous Silica Materials Induce Hormesis on Chili Pepper (*Capsicum annuum* L.) under Greenhouse Conditions. *Heliyon* **2022**, *8*, e09049. [[CrossRef](#)]
22. Godínez-Mendoza, P.L.; Rico-Chávez, A.K.; Ferrusquía-Jimenez, N.I.; Carbajal-Valenzuela, I.A.; Villagómez-Aranda, A.L.; Torres-Pacheco, I.; Guevara-González, R.G. Plant Hormesis: Revising of the Concepts of Biostimulation, Elicitation and Their Application in a Sustainable Agricultural Production. *Sci. Total Environ.* **2023**, *894*, 164883. [[CrossRef](#)]
23. Belz, R.G. Investigating a Potential Auxin-Related Mode of Hormetic/Inhibitory Action of the Phytotoxin Parthenin. *J. Chem. Ecol.* **2016**, *42*, 71–83. [[CrossRef](#)] [[PubMed](#)]

24. Sidibé, A.; Charles, M.T.; Lucier, J.-F.; Xu, Y.; Beaulieu, C. Preharvest UV-C Hormesis Induces Key Genes Associated with Homeostasis, Growth and Defense in Lettuce Inoculated with *Xanthomonas campestris* P.v. *Vitians*. *Front. Plant Sci.* **2022**, *12*, 793989. [[CrossRef](#)] [[PubMed](#)]
25. Wang, B.; Lin, L.; Yuan, X.; Zhu, Y.; Wang, Y.; Li, D.; He, J.; Xiao, Y. Low-Level Cadmium Exposure Induced Hormesis in Peppermint Young Plant by Constantly Activating Antioxidant Activity Based on Physiological and Transcriptomic Analyses. *Front. Plant Sci.* **2023**, *14*, 1088285. [[CrossRef](#)] [[PubMed](#)]
26. Zhang, J.; Tang, Z.; Agathokleous, E.; Zheng, G.; Xu, L.; Li, P. Hormesis in the Heavy Metal Accumulator Plant *Tillandsia ionantha* under Cd Exposure: Frequency and Function of Different Biomarkers. *Sci. Total Environ.* **2023**, *889*, 164328. [[CrossRef](#)]
27. Li, P.; Zhang, J.; Sun, X.; Agathokleous, E.; Zheng, G. Atmospheric Pb Induced Hormesis in the Accumulator Plant *Tillandsia usneoides*. *Sci. Total Environ.* **2022**, *811*, 152384. [[CrossRef](#)] [[PubMed](#)]
28. Sun, X.; Li, P.; Zheng, G. Biomarker Responses of Spanish Moss *Tillandsia usneoides* to Atmospheric Hg and Hormesis in This Species. *Front. Plant Sci.* **2021**, *12*, 625799. [[CrossRef](#)] [[PubMed](#)]
29. Liu, Z.; Tian, L.; Chen, M.; Zhang, L.; Lu, Q.; Wei, J.; Duan, X. Hormesis Responses of Growth and Photosynthetic Characteristics in *Lonicera japonica* Thunb. to Cadmium Stress: Whether Electric Field Can Improve or Not? *Plants* **2023**, *12*, 933. [[CrossRef](#)]
30. Małkowski, E.; Sitko, K.; Szopiński, M.; Gieroń, Ż.; Pogrzeba, M.; Kalaji, H.M.; Zieleźnik-Rusinowska, P. Hormesis in Plants: The Role of Oxidative Stress, Auxins and Photosynthesis in Corn Treated with Cd or Pb. *Int. J. Mol. Sci.* **2020**, *21*, 2099. [[CrossRef](#)]
31. Salinitro, M.; Mattarello, G.; Guardigli, G.; Odajiu, M.; Tassoni, A. Induction of Hormesis in Plants by Urban Trace Metal Pollution. *Sci. Rep.* **2021**, *11*, 20329. [[CrossRef](#)] [[PubMed](#)]
32. El-Nakhel, C.; Pannico, A.; Kyriacou, M.C.; Giordano, M.; De Pascale, S.; Rouphael, Y. Macronutrient Deprivation Eustress Elicits Differential Secondary Metabolites in Red and Green-Pigmented Butterhead Lettuce Grown in a Closed Soilless System. *J. Sci. Food Agric.* **2019**, *99*, 6962–6972. [[CrossRef](#)] [[PubMed](#)]
33. Trejo-Téllez, L.I.; García-Jiménez, A.; Escobar-Sepúlveda, H.F.; Ramírez-Olvera, S.M.; Bello-Bello, J.J.; Gómez-Merino, F.C. Silicon Induces Hormetic Dose-Response Effects on Growth and Concentrations of Chlorophylls, Amino Acids and Sugars in Pepper Plants during the Early Developmental Stage. *PeerJ* **2020**, *8*, e9224. [[CrossRef](#)] [[PubMed](#)]
34. Machado, R.M.A.; Serralheiro, R.P. Soil Salinity: Effect on Vegetable Crop Growth. Management Practices to Prevent and Mitigate Soil Salinization. *Horticulturae* **2017**, *3*, 30. [[CrossRef](#)]
35. Rouphael, Y.; Petropoulos, S.A.; Cardarelli, M.; Colla, G. Salinity as Eustressor for Enhancing Quality of Vegetables. *Sci. Hortic.* **2018**, *234*, 361–369. [[CrossRef](#)]
36. Santander, C.; Vidal, G.; Ruiz, A.; Vidal, C.; Cornejo, P. Salinity Eustress Increases the Biosynthesis and Accumulation of Phenolic Compounds That Improve the Functional and Antioxidant Quality of Red Lettuce. *Agronomy* **2022**, *12*, 598. [[CrossRef](#)]
37. Rouphael, Y.; Kyriacou, M.C.; Carillo, P.; Pizzolongo, F.; Romano, R.; Sifola, M.I. Chemical Eustress Elicits Tailored Responses and Enhances the Functional Quality of Novel Food *Perilla frutescens*. *Molecules* **2019**, *24*, 185. [[CrossRef](#)] [[PubMed](#)]
38. Voutsinos-Frantzis, O.; Karavidas, I.; Petropoulos, D.; Zioviris, G.; Fortis, D.; Ntanasi, T.; Ropokis, A.; Karkanis, A.; Sabatino, L.; Savvas, D.; et al. Effects of NaCl and CaCl₂ as Eustress Factors on Growth, Yield, and Mineral Composition of Hydroponically Grown *Valerianella locusta*. *Plants* **2023**, *12*, 1454. [[CrossRef](#)]
39. Rouphael, Y.; Kyriacou, M.C. Enhancing Quality of Fresh Vegetables Through Salinity Eustress and Biofortification Applications Facilitated by Soilless Cultivation. *Front. Plant Sci.* **2018**, *9*, 1254. [[CrossRef](#)]
40. Moya, C.; Oyanedel, E.; Verdugo, G.; Flores, M.F.; Urrestarazu, M.; Álvaro, J.E. Increased Electrical Conductivity in Nutrient Solution Management Enhances Dietary and Organoleptic Qualities in Soilless Culture Tomato. *HortScience* **2017**, *52*, 868–872. [[CrossRef](#)]
41. Giuffrida, F.; Cassaniti, C.; Malvuccio, A.; Leonardi, C. Effects of Salt Stress Imposed during Two Growth Phases on Cauliflower Production and Quality. *J. Sci. Food Agric.* **2017**, *97*, 1552–1560. [[CrossRef](#)]
42. Sarker, U.; Ercisli, S. Salt Eustress Induction in Red Amaranth (*Amaranthus gangeticus*) Augments Nutritional, Phenolic Acids and Antiradical Potential of Leaves. *Antioxidants* **2022**, *11*, 2434. [[CrossRef](#)] [[PubMed](#)]
43. Sarker, U.; Hossain, M.N.; Oba, S.; Ercisli, S.; Marc, R.A.; Golokhvast, K.S. Salinity Stress Ameliorates Pigments, Minerals, Polyphenolic Profiles, and Antiradical Capacity in Lalshak. *Antioxidants* **2023**, *12*, 173. [[CrossRef](#)] [[PubMed](#)]
44. Kolbert, Z.; Szöllösi, R.; Rónavári, A.; Molnár, Á. Nanoforms of Essential Metals: From Hormetic Phytoeffects to Agricultural Potential. *J. Exp. Bot.* **2022**, *73*, 1825–1840. [[CrossRef](#)] [[PubMed](#)]
45. Pan, W.; Zhang, H.-J.; Zhang, Y.-F.; Wang, M.; Tsui, M.T.-K.; Yang, L.; Miao, A.-J. Silica Nanoparticle Accumulation in Plants: Current State and Future Perspectives. *Nanoscale* **2023**, *15*, 15079–15091. [[CrossRef](#)] [[PubMed](#)]
46. Guerriero, G.; Sutura, F.M.; Torabi-Pour, N.; Renaut, J.; Hausman, J.-F.; Berni, R.; Pennington, H.C.; Welsh, M.; Dehsorkhi, A.; Zancan, L.R.; et al. Phyto-Courier, a Silicon Particle-Based Nano-Biostimulant: Evidence from *Cannabis sativa* Exposed to Salinity. *ACS Nano* **2021**, *15*, 3061–3069. [[CrossRef](#)]
47. Guerriero, G.; Sutura, F.M.; Hoffmann, J.; Leclercq, C.C.; Planchon, S.; Berni, R.; Hausman, J.-F.; Renaut, J.; Torabi-Pour, N.; Pennington, H.C.; et al. Nanoporous Quercetin-Loaded Silicon-Stabilized Hybrid Lipid Nanoparticles Alleviate Salt Stress in Tomato Plants. *ACS Appl. Nano Mater.* **2023**, *6*, 3647–3660. [[CrossRef](#)]
48. Sayed, E.G.; Mahmoud, A.W.M.; El-Mogy, M.M.; Ali, M.A.A.; Fahmy, M.A.M.; Tawfic, G.A. The Effective Role of Nano-Silicon Application in Improving the Productivity and Quality of Grafted Tomato Grown under Salinity Stress. *Horticulturae* **2022**, *8*, 293. [[CrossRef](#)]

49. Rai-Kalal, P.; Tomar, R.S.; Jajoo, A.; Rai-Kalal, P.; Tomar, R.S.; Jajoo, A. Seed Nanoprimering by Silicon Oxide Improves Drought Stress Alleviation Potential in Wheat Plants. *Funct. Plant Biol.* **2021**, *48*, 905–915. [\[CrossRef\]](#)
50. Babaei, M.; Ajdarian, L. Screening of Different Iranian Ecotypes of Cannabis under Water Deficit Stress. *Sci. Hortic.* **2020**, *260*, 108904. [\[CrossRef\]](#)
51. Blandinières, H.; Leoni, M.; Ferrarini, A.; Amaducci, S. Ranking 26 European Hemp (*Cannabis sativa* L.) Cultivars for Osmotic Stress Tolerance and Transpiration Efficiency. *Ind. Crops Prod.* **2021**, *170*, 113774. [\[CrossRef\]](#)
52. Duong, H.; Pearson, B.; Anderson, S.; Berthold, E.; Kjellgren, R. Variation in Hydric Response of Two Industrial Hemp Varieties (*Cannabis sativa*) to Induced Water Stress. *Horticulturae* **2023**, *9*, 431. [\[CrossRef\]](#)
53. Jiang, Y.; Feng, N.; Sun, Y.; Zheng, D.; Han, C.; Wang, X.; Cao, K.; Xu, L.; Liu, S. Uniconazole Mitigates Disadvantageous Effects of Drought Stress on *Cannabis sativa* L. Seedlings. *Pak. J. Bot.* **2022**, *54*, 83–93. [\[CrossRef\]](#) [\[PubMed\]](#)
54. Jiang, Y.; Sun, Y.; Zheng, D.; Han, C.; Cao, K.; Xu, L.; Liu, S.; Cao, Y.; Feng, N. Physiological and Transcriptome Analyses for Assessing the Effects of Exogenous Uniconazole on Drought Tolerance in Hemp (*Cannabis sativa* L.). *Sci. Rep.* **2021**, *11*, 14476. [\[CrossRef\]](#) [\[PubMed\]](#)
55. Gill, A.R.; Loveys, B.R.; Cowley, J.M.; Hall, T.; Cavagnaro, T.R.; Burton, R.A. Physiological and Morphological Responses of Industrial Hemp (*Cannabis sativa* L.) to Water Deficit. *Ind. Crops Prod.* **2022**, *187*, 115331. [\[CrossRef\]](#)
56. Caplan, D.; Dixon, M.; Zheng, Y. Increasing Inflorescence Dry Weight and Cannabinoid Content in Medical Cannabis Using Controlled Drought Stress. *HortScience* **2019**, *54*, 964–969. [\[CrossRef\]](#)
57. Dixit, N. Salinity Induced Antioxidant Defense in Roots of Industrial Hemp (IH: *Cannabis sativa* L.) for Fiber during Seed Germination. *Antioxidants* **2022**, *11*, 244. [\[CrossRef\]](#) [\[PubMed\]](#)
58. Berni, R.; Mandlik, R.; Hausman, J.-F.; Guerriero, G. Silicon-Induced Mitigatory Effects in Salt-Stressed Hemp Leaves. *Physiol. Plant.* **2020**, *171*, 476–482. [\[CrossRef\]](#)
59. Zhang, M.; Zhang, L.; Wang, G.; Huang, X.; Guo, Z. Comprehensive Transcriptome and Metabolome Analysis of Hemp (*Cannabis sativa* L.) in Soil Under NaCl Stress. *J. Nat. Fibers* **2023**, *20*, 2170948. [\[CrossRef\]](#)
60. Zhang, J.; Zhang, C.; Huang, S.; Chang, L.; Li, J.; Tang, H.; Dey, S.; Biswas, A.; Du, D.; Li, D.; et al. Key Cannabis Salt-Responsive Genes and Pathways Revealed by Comparative Transcriptome and Physiological Analyses of Contrasting Varieties. *Agronomy* **2021**, *11*, 2338. [\[CrossRef\]](#)
61. Yep, B.; Gale, N.V.; Zheng, Y. Aquaponic and Hydroponic Solutions Modulate NaCl-Induced Stress in Drug-Type *Cannabis sativa* L. *Front. Plant Sci.* **2020**, *11*, 1169. [\[CrossRef\]](#) [\[PubMed\]](#)
62. Hu, H.; Liu, H.; Du, G.; Fei, Y.; Deng, G.; Yang, Y.; Feihu, L. Fiber and Seed Type of Hemp (*Cannabis sativa* L.) Responded Differently to Salt-Alkali Stress in Seedling Growth and Physiological Indices. *Ind. Crops Prod.* **2019**, *129*, 624–630. [\[CrossRef\]](#)
63. Cao, K.; Sun, Y.; Han, C.; Zhang, X.; Zhao, Y.; Jiang, Y.; Jiang, Y.; Sun, X.; Guo, Y.; Wang, X. The Transcriptome of Saline-Alkaline Resistant Industrial Hemp (*Cannabis sativa* L.) Exposed to NaHCO₃ Stress. *Ind. Crops Prod.* **2021**, *170*, 113766. [\[CrossRef\]](#)
64. Galic, A.; Grab, H.; Kaczmar, N.; Maser, K.; Miller, W.B.; Smart, L.B. Effects of Cold Temperature and Acclimation on Cold Tolerance and Cannabinoid Profiles of *Cannabis sativa* L. (Hemp). *Horticulturae* **2022**, *8*, 531. [\[CrossRef\]](#)
65. Yan, B.; Chang, C.; Gu, Y.; Zheng, N.; Fang, Y.; Zhang, M.; Wang, G.; Zhang, L. Genome-Wide Identification, Classification, and Expression Analyses of the CsDGAT Gene Family in *Cannabis sativa* L. and Their Response to Cold Treatment. *Int. J. Mol. Sci.* **2023**, *24*, 4078. [\[CrossRef\]](#) [\[PubMed\]](#)
66. Huang, Y.; Li, D.; Zhao, L.; Chen, A.; Li, J.; Tang, H.; Pan, G.; Chang, L.; Deng, Y.; Huang, S. Comparative Transcriptome Combined with Physiological Analyses Revealed Key Factors for Differential Cadmium Tolerance in Two Contrasting Hemp (*Cannabis sativa* L.) Cultivars. *Ind. Crops Prod.* **2019**, *140*, 111638. [\[CrossRef\]](#)
67. Yin, M.; Pan, G.; Tao, J.; Doblin, M.S.; Zeng, W.; Pan, L.; Zhao, L.; Li, Z.; Jiang, H.; Chang, L.; et al. Identification of MYB Genes Reveals Their Potential Functions in Cadmium Stress Response and the Regulation of Cannabinoid Biosynthesis in Hemp. *Ind. Crops Prod.* **2022**, *180*, 114607. [\[CrossRef\]](#)
68. Islam, M.J.; Ryu, B.R.; Azad, M.O.K.; Rahman, M.H.; Cheong, E.J.; Lim, J.-D.; Lim, Y.-S. Cannabinoids Accumulation in Hemp (*Cannabis sativa* L.) Plants under LED Light Spectra and Their Discrete Role as a Stress Marker. *Biology* **2021**, *10*, 710. [\[CrossRef\]](#)
69. Rodriguez-Morrison, V.; Llewellyn, D.; Zheng, Y. Cannabis Yield, Potency, and Leaf Photosynthesis Respond Differently to Increasing Light Levels in an Indoor Environment. *Front. Plant Sci.* **2021**, *12*, 646020. [\[CrossRef\]](#)
70. Rodriguez-Morrison, V.; Llewellyn, D.; Zheng, Y. Cannabis Inflorescence Yield and Cannabinoid Concentration Are Not Increased with Exposure to Short-Wavelength Ultraviolet-B Radiation. *Front. Plant Sci.* **2021**, *12*, 725078. [\[CrossRef\]](#)
71. Llewellyn, D.; Golem, S.; Foley, E.; Dinka, S.; Jones, A.M.P.; Zheng, Y. Indoor Grown Cannabis Yield Increased Proportionally with Light Intensity, but Ultraviolet Radiation Did Not Affect Yield or Cannabinoid Content. *Front. Plant Sci.* **2022**, *13*, 974018. [\[CrossRef\]](#) [\[PubMed\]](#)
72. Danziger, N.; Bernstein, N. Light Matters: Effect of Light Spectra on Cannabinoid Profile and Plant Development of Medical Cannabis (*Cannabis sativa* L.). *Ind. Crops Prod.* **2021**, *164*, 113351. [\[CrossRef\]](#)
73. Danziger, N.; Bernstein, N. Shape Matters: Plant Architecture Affects Chemical Uniformity in Large-Size Medical Cannabis Plants. *Plants* **2021**, *10*, 1834. [\[CrossRef\]](#) [\[PubMed\]](#)
74. Danziger, N.; Bernstein, N. Plant Architecture Manipulation Increases Cannabinoid Standardization in ‘Drug-Type’ Medical Cannabis. *Ind. Crops Prod.* **2021**, *167*, 113528. [\[CrossRef\]](#)

75. Saloner, A.; Bernstein, N. Nitrogen Supply Affects Cannabinoid and Terpenoid Profile in Medical Cannabis (*Cannabis sativa* L.). *Ind. Crops Prod.* **2021**, *167*, 113516. [\[CrossRef\]](#)
76. Song, C.; Saloner, A.; Fait, A.; Bernstein, N. Nitrogen Deficiency Stimulates Cannabinoid Biosynthesis in Medical Cannabis Plants by Inducing a Metabolic Shift towards Production of Low-N Metabolites. *Ind. Crops Prod.* **2023**, *202*, 116969. [\[CrossRef\]](#)
77. Shiponi, S.; Bernstein, N. The Highs and Lows of P Supply in Medical Cannabis: Effects on Cannabinoids, the Ionome, and Morpho-Physiology. *Front. Plant Sci.* **2021**, *12*, 657323. [\[CrossRef\]](#)
78. Saloner, A.; Bernstein, N. Effect of Potassium (K) Supply on Cannabinoids, Terpenoids and Plant Function in Medical Cannabis. *Agronomy* **2022**, *12*, 1242. [\[CrossRef\]](#)
79. Morad, D.; Bernstein, N. Response of Medical Cannabis to Magnesium (Mg) Supply at the Vegetative Growth Phase. *Plants* **2023**, *12*, 2676. [\[CrossRef\]](#)
80. Javeed, H.M.R.; Wang, X.; Ali, M.; Nawaz, F.; Qamar, R.; Rehman, A.U.; Shehzad, M.; Mubeen, M.; Shabbir, R.; Javed, T.; et al. Potential Utilization of Diluted Seawater for the Cultivation of Some Summer Vegetable Crops: Physiological and Nutritional Implications. *Agronomy* **2021**, *11*, 1826. [\[CrossRef\]](#)
81. Sgherri, C.; Kadlecová, Z.; Pardossi, A.; Navari-Izzo, F.; Izzo, R. Irrigation with Diluted Seawater Improves the Nutritional Value of Cherry Tomatoes. *J. Agric. Food Chem.* **2008**, *56*, 3391–3397. [\[CrossRef\]](#) [\[PubMed\]](#)
82. Dalle Vacche, S.; Karunakaran, V.; Patrucco, A.; Zoccola, M.; Douard, L.; Ronchetti, S.; Gallo, M.; Schreier, A.; Leterrier, Y.; Bras, J.; et al. Valorization of Byproducts of Hemp Multipurpose Crop: Short Non-Aligned Bast Fibers as a Source of Nanocellulose. *Molecules* **2021**, *26*, 4723. [\[CrossRef\]](#) [\[PubMed\]](#)
83. Guerriero, G.; Deshmukh, R.; Sonah, H.; Sergeant, K.; Hausman, J.-F.; Lentzen, E.; Valle, N.; Siddiqui, K.S.; Exley, C. Identification of the Aquaporin Gene Family in *Cannabis sativa* and Evidence for the Accumulation of Silicon in Its Tissues. *Plant Sci.* **2019**, *287*, 110167. [\[CrossRef\]](#) [\[PubMed\]](#)
84. Luyckx, M.; Hausman, J.-F.; Blanquet, M.; Guerriero, G.; Lutts, S. Silicon Reduces Cadmium Absorption and Increases Root-to-Shoot Translocation without Impacting Growth in Young Plants of Hemp (*Cannabis sativa* L.) on a Short-Term Basis. *Environ. Sci. Pollut. Res. Int.* **2021**, *28*, 37963–37977. [\[CrossRef\]](#) [\[PubMed\]](#)
85. Łażny, R.; Mirgos, M.; Przybył, J.L.; Niedzińska, M.; Gajc-Wolska, J.; Kowalczyk, W.; Nowak, J.S.; Kalisz, S.; Kowalczyk, K. Lignite Substrate and EC Modulates Positive Eustress in Cucumber at Hydroponic Cultivation. *Agronomy* **2022**, *12*, 608. [\[CrossRef\]](#)
86. van Tol de Castro, T.A.; Berbara, R.L.L.; Tavares, O.C.H.; Mello, D.F.d.G.; Pereira, E.G.; Souza, C.d.C.B.d.; Espinosa, L.M.; García, A.C. Humic Acids Induce a Eustress State via Photosynthesis and Nitrogen Metabolism Leading to a Root Growth Improvement in Rice Plants. *Plant Physiol. Biochem.* **2021**, *162*, 171–184. [\[CrossRef\]](#)
87. Muscolo, A.; Sidari, M.; Francioso, O.; Tugnoli, V.; Nardi, S. The Auxin-like Activity of Humic Substances Is Related to Membrane Interactions in Carrot Cell Cultures. *J. Chem. Ecol.* **2007**, *33*, 115–129. [\[CrossRef\]](#) [\[PubMed\]](#)
88. Da Cunha Leme Filho, J.F.; Thomason, W.E.; Evanylo, G.K.; Zhang, X.; Strickland, M.S.; Chim, B.K.; Diatta, A.A. Biochemical and Physiological Responses of *Cannabis sativa* to an Integrated Plant Nutrition System. *Agron. J.* **2020**, *112*, 5237–5248. [\[CrossRef\]](#)
89. Bernstein, N.; Gorelick, J.; Zerahia, R.; Koch, S. Impact of N, P, K, and Humic Acid Supplementation on the Chemical Profile of Medical Cannabis (*Cannabis sativa* L.). *Front. Plant Sci.* **2019**, *10*, 736. [\[CrossRef\]](#)
90. Thiem, B.; Kikowska, M.; Maliński, M.P.; Kruszka, D.; Napierała, M.; Florek, E. Ecdysteroids: Production in Plant In Vitro Cultures. *Phytochem. Rev.* **2017**, *16*, 603–622. [\[CrossRef\]](#)
91. Ghaderi, S.; Nejad Ebrahimi, S.; Ahadi, H.; Eslambolchi Moghadam, S.; Mirjalili, M.H. In Vitro Propagation and Phytochemical Assessment of *Perovskia abrotanoides* Karel. (Lamiaceae)—A Medicinally Important Source of Phenolic Compounds. *Biocatal. Agric. Biotechnol.* **2019**, *19*, 101113. [\[CrossRef\]](#)
92. Villagómez-Aranda, A.L.; Feregrino-Pérez, A.A.; García-Ortega, L.F.; González-Chavira, M.M.; Torres-Pacheco, I.; Guevara-González, R.G. Activating Stress Memory: Eustressors as Potential Tools for Plant Breeding. *Plant Cell Rep.* **2022**, *41*, 1481–1498. [\[CrossRef\]](#) [\[PubMed\]](#)
93. Hessel, V.; Liang, S.; Tran, N.N.; Escribà-Gelonch, M.; Zeckovic, O.; Knowling, M.; Rebrov, E.; This, H.; Westra, S.; Fisk, I.; et al. Eustress in Space: Opportunities for Plant Stressors Beyond the Earth Ecosystem. *Front. Astron. Space Sci.* **2022**, *9*, 841211. [\[CrossRef\]](#)
94. Rico-Chávez, A.K.; Franco, J.A.; Fernandez-Jaramillo, A.A.; Contreras-Medina, L.M.; Guevara-González, R.G.; Hernandez-Escobedo, Q. Machine Learning for Plant Stress Modeling: A Perspective towards Hormesis Management. *Plants* **2022**, *11*, 970. [\[CrossRef\]](#) [\[PubMed\]](#)
95. Berni, R.; Hausman, J.-F.; Villas-Boas, S.; Guerriero, G. Impact of *Pseudomonas* Sp. SVB-B33 on Stress- and Cell Wall-Related Genes in Roots and Leaves of Hemp under Salinity. *Horticulturae* **2022**, *8*, 336. [\[CrossRef\]](#)
96. Lyu, D.; Backer, R.; Robinson, W.G.; Smith, D.L. Plant Growth-Promoting Rhizobacteria for Cannabis Production: Yield, Cannabinoid Profile and Disease Resistance. *Front. Microbiol.* **2019**, *10*, 1761. [\[CrossRef\]](#) [\[PubMed\]](#)
97. Sun, S.; Feng, Y.; Huang, G.; Zhao, X.; Song, F. *Rhizophagus irregularis* Enhances Tolerance to Cadmium Stress by Altering Host Plant Hemp (*Cannabis sativa* L.) Photosynthetic Properties. *Environ. Pollut.* **2022**, *314*, 120309. [\[CrossRef\]](#) [\[PubMed\]](#)
98. Gorelick, J.; Bernstein, N. Chapter Five—Elicitation: An Underutilized Tool in the Development of Medicinal Plants as a Source of Therapeutic Secondary Metabolites. In *Advances in Agronomy*; Sparks, D.L., Ed.; Academic Press: Cambridge, MA, USA, 2014; Volume 124, pp. 201–230.

99. Jalali, S.; Salami, S.A.; Sharifi, M.; Sohrabi, S. Signaling Compounds Elicit Expression of Key Genes in Cannabinoid Pathway and Related Metabolites in Cannabis. *Ind. Crops Prod.* **2019**, *133*, 105–110. [[CrossRef](#)]
100. Garrido, J.; Rico, S.; Corral, C.; Sánchez, C.; Vidal, N.; Martínez-Quesada, J.J.; Ferreiro-Vera, C. Exogenous Application of Stress-Related Signaling Molecules Affect Growth and Cannabinoid Accumulation in Medical Cannabis (*Cannabis sativa* L.). *Front. Plant Sci.* **2022**, *13*, 1082554. [[CrossRef](#)]
101. Kostanda, E.; Khatib, S. Biotic Stress Caused by Tetranychus Urticae Mites Elevates the Quantity of Secondary Metabolites, Cannabinoids and Terpenes, in *Cannabis sativa* L. *Ind. Crops Prod.* **2022**, *176*, 114331. [[CrossRef](#)]
102. Gorelick, J.; Bernstein, N. Chemical and Physical Elicitation for Enhanced Cannabinoid Production in Cannabis. In *Cannabis sativa* L.—*Botany and Biotechnology*; Chandra, S., Lata, H., ElSohly, M.A., Eds.; Springer International Publishing: Cham, Switzerland, 2017; pp. 439–456. ISBN 978-3-319-54564-6.
103. Flores-Sanchez, I.J.; Pec, J.; Fei, J.; Choi, Y.H.; Dusek, J.; Verpoorte, R. Elicitation Studies in Cell Suspension Cultures of *Cannabis sativa* L. *J. Biotechnol.* **2009**, *143*, 157–168. [[CrossRef](#)] [[PubMed](#)]
104. Gabotti, D.; Locatelli, F.; Cusano, E.; Baldoni, E.; Genga, A.; Pucci, L.; Consonni, R.; Mattana, M. Cell Suspensions of *Cannabis sativa* (Var. Futura): Effect of Elicitation on Metabolite Content and Antioxidant Activity. *Molecules* **2019**, *24*, 4056. [[CrossRef](#)] [[PubMed](#)]
105. Gubser, G.; Vollenweider, S.; Eibl, D.; Eibl, R. Food Ingredients and Food Made with Plant Cell and Tissue Cultures: State-of-the Art and Future Trends. *Eng. Life Sci.* **2021**, *21*, 87–98. [[CrossRef](#)] [[PubMed](#)]
106. Krasteva, G.; Georgiev, V.; Pavlov, A. Recent Applications of Plant Cell Culture Technology in Cosmetics and Foods. *Eng. Life Sci.* **2021**, *21*, 68–76. [[CrossRef](#)]

Disclaimer/Publisher’s Note: The statements, opinions and data contained in all publications are solely those of the individual author(s) and contributor(s) and not of MDPI and/or the editor(s). MDPI and/or the editor(s) disclaim responsibility for any injury to people or property resulting from any ideas, methods, instructions or products referred to in the content.