agronomy

Review

Hemp Agronomy: Current Advances, Questions, Challenges, and Opportunities

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Abstract: Hemp (*Cannabis sativa* L. ssp. *sativa*) has a long history of domestication due to its versatile use. Recently, different sectors in the economy are investigating hemp cultivation to increase agronomic production and to limit delta-9-tetrahydrocannabinol (THC). Despite the rapid growth of hemp literature in recent years, it is still uncertain whether the knowledge gained from higher latitude regions is applicable to low latitude and tropical regions where hemp has not been grown traditionally. This review provides a comprehensive and updated survey of hemp agronomy, focusing on environmental and management factors influencing the growth and yield of hemp, methods of cannabinoids detection and quantification, and hemp breeding. This review suggests that some previous claims about hemp as a low input crop may not hold true in low-latitude regions. Additional research strategies, such as the integration of experimentation and modeling efforts, are encouraged to hasten new discoveries. Furthermore, to effectively increase the outputs of value products (cannabinoids, seeds, fiber and biomass, etc.) while limiting the THC level, new collaborations between hemp agronomists and economists may streamline the production process by increasing the efficiency of the total production system of hemp as a multifaceted crop.

Keywords: *Cannabis sativa* L.; hemp; agronomy; environmental factors; abiotic stress; cannabinoids; photoperiod effect; latitude of adaption; future research

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1. Introduction

There is uncertainty and debate regarding the origin of cannabis (the genus *Cannabis*). Humans have been in constant contact with hemp (*Cannabis sativa* L. ssp. *sativa*) as a multifaceted agricultural crop for centuries [1,2]. Most studies have proposed various theories that the origin of hemp was in Central, East, and South Asia [3,4].

Hemp is a dioecious, herbaceous, and anemophilous (wind-pollinated) annual crop that grows to 1 to 5 meters in height. However, monoecious varieties have been developed through breeding and selection [5]. In the past, hemp production has been reduced due to several reasons, particularly the decline in the demand for end-commercial products and competition with other crops [2,6,7]. Importantly, the biotypic connection of hemp to marijuana (*Cannabis sativa* L. ssp. *indica*), a related species with a high psychoactive delta-9-tetrahydrocannabinol (THC) (up to 20% dry weight), led to the banning of hemp in several countries, including the USA, which enacted the Marihuana Tax Act in 1937 [7,8]. Per the law in each country, THC in hemp should not exceed the threshold limit permitted by government regulations. For instance, the internationally approved THC threshold limit in hemp is 0.3%; however, the national limits are 0.2% in Europe and 1.0% in Australia [9–11]. Regardless of the THC content, industrial hemp is any hemp or hemp product that is below the national standard minimum allowable percent THC. Meanwhile, a higher nontoxic cannabidiol (CBD) and lower THC content are two of the advantages of hemp over marijuana for agricultural production. There are 80 to 144 identified cannabinoids, including

THC, and approximately 300 non-cannabinoids produced by *Cannabis* plants. Among the cannabinoids, CBD may have multiple medicinal properties [1,10,12].

However, increasing demand for organic, eco-friendly, and environmentally sustainable products opens the doors for hemp products in the global market. About 25,000 potential hemp products are currently available in markets [13,14]. Recently, many countries started legalizing hemp. The USA was the biggest importer of hemp, and in 2018, the USA legalized the production of hemp federally as an agricultural commodity, which was eventually accepted in 47 states [15,16]. Hemp has regained its potential as an important agricultural crop due to its versatile contributions as a source of CBD, fiber, oil, and grain. Its weed suppression potential is well suited to crop rotation. Hemp oil and crop residues can be used in organic farming as eco-friendly organic insecticides and pesticides [17,18]. Amaducci et al. [19] found that due to the variation in root morphology under different growth conditions, hemp could play an important role in sustainable cropping systems.

In 2018, hemp was cultivated in 30 nations [13]. In 2020, global hemp oil seed production was 5449 tons, with Russia being the first with 3128 tons of hemp seed produced per year, followed by Chile and Ukraine (Figure 1) [20]. In 2021, the global CBD market was valued at $4.2 billion [21].

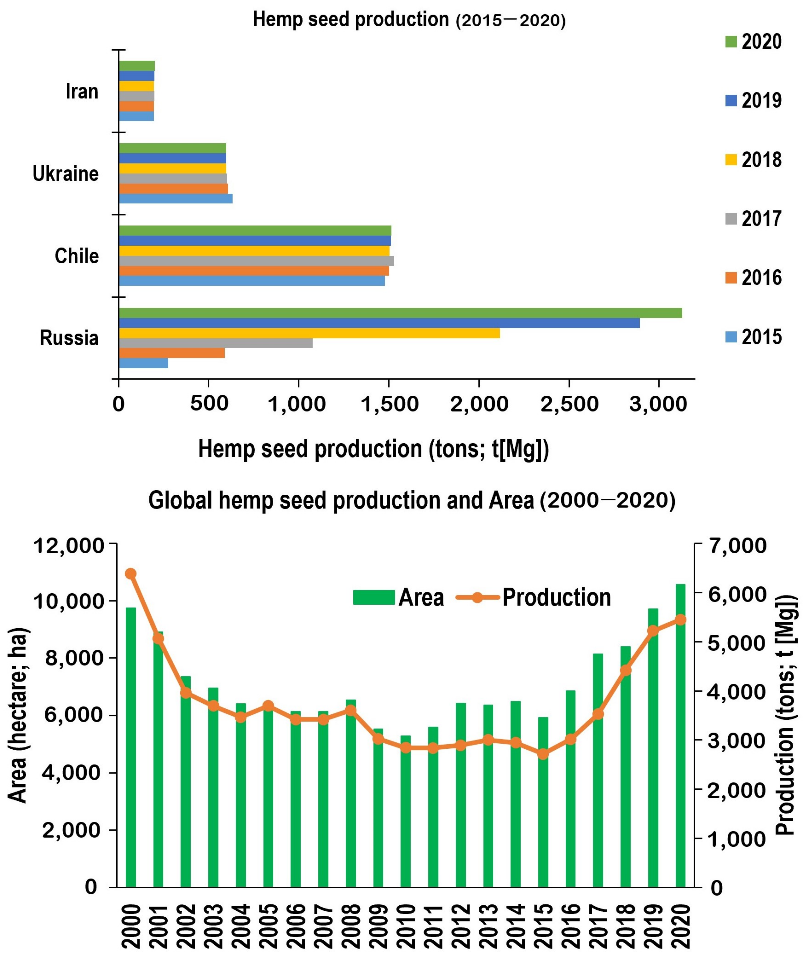

Figure 1. Trend in global hemp seed production (2015–2020) and area (2000–2020), based on data from [20].

At the same time, in 2021, the total value of all industrial hemp grown indoors (in a greenhouse, for example) and outdoors in the USA was $824 million. The outdoor industrial hemp production alone was valued at $712 million. Floral, grain, fiber, and seed hemp production were valued at $623, $6.0, $41.4, and $41.5 million, respectively. In the

USA, the total area of industrial hemp planted in 2021 was 21,915 ha, and that harvested was 13,549 ha. This is in contrast to >160,000 ha hemp for all purposes planted in the USA in 2019, primarily for CBD. But overproduction and reduced prices by as much as 90% have greatly reduced planting. The 2021 total outdoor area harvested for floral, grain, and fiber hemp was 6467, 3341, and 5136 ha, respectively. The total production of floral, grain, and fiber hemp were 8952, 1983, and 15,082 tons (t; Mg), respectively (Figure 2) [22]. (In Figure 2; data are incomplete due to nondisclosure of individual operations in some states).

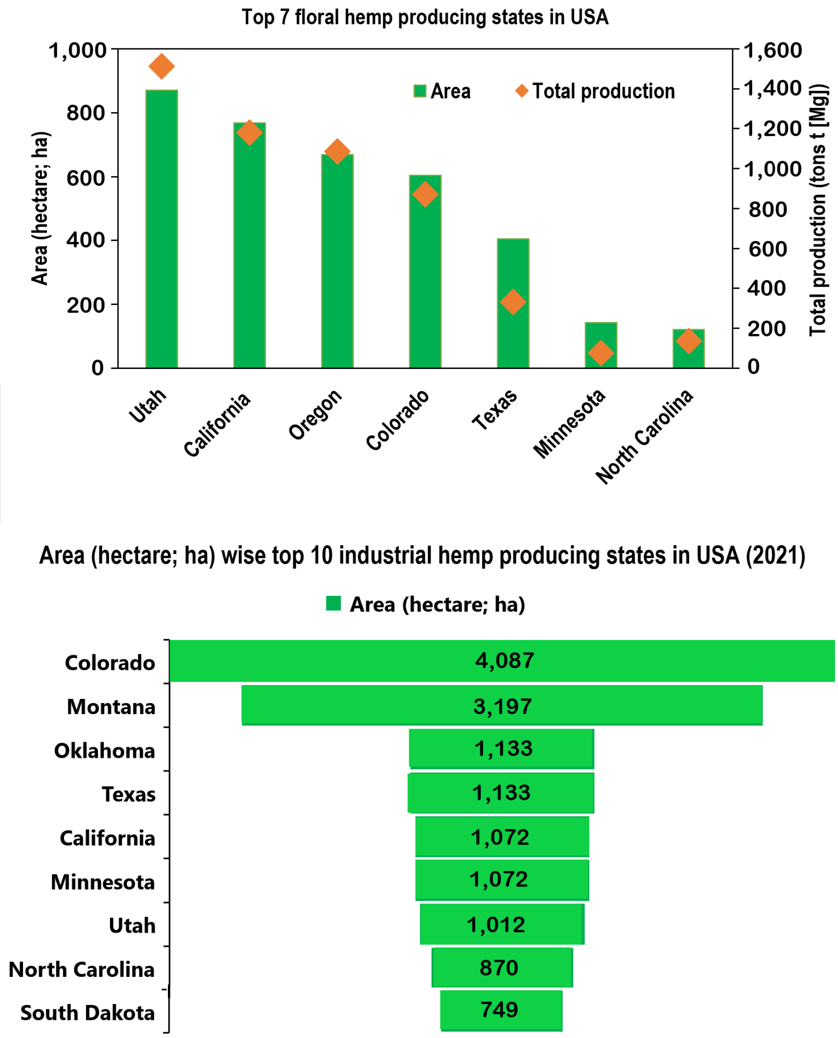

Figure 2. Area and production of the top 10 industrial and floral hemp producing states in the USA in 2021, based on data from [22].

In addition to popular pharmaceutical applications, of which some were lost in time (i.e., China [23], India [24], and Greece [25], hemp production has been promoted due to its potential use in phytoremediation and bioenergy production [26], and its moderate need for biocides, fertilizer, and water [18,27]). Advances in modern technology have expanded the use of hemp in the production of nanosheets [28], biodegradable plastics [29], and construction concrete, known as hempcrete [30]. There have been a few reviews published on hemp (i.e., [1,3,31,32]). However, due to the rapid growth of hemp literature in recent years, a more comprehensive and updated survey about this multifaceted agronomy crop is needed. This will help to address the following knowledge gaps and questions: Given the rapidly increasing interest of growing hemp in different regions, we do not know if the basic agronomic knowledge of hemp cultivation in a new region is readily available from the literature. This includes but is not limited to hemp's water, nutrient (especially

N, P, K), temperature and photoperiod requirements in both high latitude (37–52° N or S) regions where hemp has traditionally been grown, and low-latitude regions (<35° N or S) where it has just started as a new crop, as well as the extent to which the above agronomic requirements vary under different weather and management conditions. Specifically, this review highlights the main factors influencing hemp cultivation and summarizes the recent advances, challenges, and knowledge gaps in diverse areas of hemp research. We also pose questions for future research to improve hemp cultivation and enhance the quality of new hemp products and value-added products. Finally, through this literature review, we identify new opportunities by which the agronomic knowledge of hemp as a multipurpose and multifaceted crop can be accelerated by promoting a paradigm where experimentation and modeling approaches are integrated to foster the generation and testing of competing hypotheses [33]. We also encourage agronomists to expand their research toolboxes to include some of the economic optimization methods [34], so that variables such as THC can be directly considered along with other agronomic variables in the decision-making process in farm-level hemp production. Details of genotypes used in different studies in this review are available in Supplementary Table S1.

2. Factors Influencing Growth, Development, and Yield of Hemp

The amount of light, nutrients, and water received, groundwater availability, photoperiod, and day/night temperatures are crucial factors that influence the growth, development, and yield of different hemp genotypes. Studies have revealed that variation in environmental factors can affect the flowering time and sex characteristics, resulting in changes in the cannabinoids and seed oil content, and composition, yield, biomass, and fiber quality [8,35,36].

Flowering time influences biomass and seed yield. Moreover, flowering is considered as a reference growth stage for harvesting floral and fiber hemp [37]. In North Carolina, USA, researchers observed that bast fiber harvest should occur no later than the initial appearance of male reproductive growth. For hurd oriented fiber, it is an arbitrary decision, but if a variety is prone to developing THC, then it may be harvested by initial female reproductive growth (Personal communication with farmers and scientists).

Hemp is a short-day plant sensitive to photoperiods. Studies report that hemp requires a photoperiod of 12–14 daylight hours. For most hemp genotypes, a more extended photoperiod (longer days and shorter nights or longer exposure to light) increases plant height, delays flowering, and prolongs the vegetative stage, which is suitable for fiber and biomass production. Meanwhile, a longer dark period causes early flowering and restricted yield [32,38–40]. Sengloung et al. [41] reported that 11–12 hours of photoperiod is required to induce flowering in Thai hemp. Zhang et al. [8] revealed that even a minor change of 15 mins in the photoperiod can affect floral initiation in some cultivars. In contrast, some genotypes among tested hemp cultivars (15 cannabinoid and 12 fiber/grain) are less affected by photoperiodicity [8].

An aeroponic study by Islam et al. [42] with 25-day-old seedlings exposed to ten different LED light spectra and a photoperiod of 16-hours indicated that the light spectrum of red, blue, and green in the ratio of 7:2:1 increased all the tested cannabinoids (CBD, delta 9-tetrahydrocannabinolic acid [THCA] and cannabidiolic acid [CBDA]). The magnitude of changes in cannabinoids varied with different spectra and light treatments. Contrasting findings about photoperiod sensitivity, insensitivity, and diverse responses to varied light spectrums in different genotypes require further research.

The temperature for the optimum development of hemp varies with genotypes and their origin. For instance, 30 °C is the maximum cardinal temperature (T Max) for six hemp varieties with different origins such as Poland, Netherlands, Italy, France, and Ukraine [43]. Anwar et al. [44] noted that wild hemp from three agroclimatic regions of Pakistan grew suitably in a mild, humid climate at 16–27 °C. Seasonal changes in daily mean temperature can affect seed production and quality, biomass accumulation, and seed oil [43,44]. Identifying cultivars with local adaptation is an important strategy to improve hemp's vegetative and flowering performance [8]. Hemp cultivation is challenging in tropical and subtropical regions compared to those in high latitudes due to high temperature, humidity, and greater pest pressure. Moreover, longer dark periods in these areas cause early season transition from vegetative to the flowering stage, limiting stem elongation and biomass accumulation and adversely affecting the successful commercial cultivation of hemp [39,40,45].

Hemp is commonly reported as a low-water use crop [46]. This claim needs further evaluation in warmer regions relative to the more northerly latitudes where hemp is grown. Yet, even in the high latitude region, water deficit stress is considered a main factor limiting hemp biomass yield [47]. A common reference crop for hemp water requirements is cotton (*Gossypium hirsutum* L.). In the southern U.S. (latitudes south of 37° N) hemp does best where annual rainfall (plus irrigation) is 750 mm or more. Early claims of drought tolerance and low water requirement for all hemp types (cannabinoid, grain, and especially fiber) in Texas, USA appear unfounded. Some Texas production regions and the U.S. Southwest where precipitation is <500 mm annually and evaporative demand is higher require substantial irrigation to achieve good yields. Cotton farmers in this region who grow fiber hemp report that hemp requires about 20% more irrigation than cotton for optimal economic yield. Little to no hemp is grown in the U.S. Southwest and much of the lower western U.S. without supplemental irrigation (Personal communication with farmers).

Hemp requires high soil water during the initial stage of root establishment. After that, a well-developed root system may allow hemp to withstand moderately drier conditions [27,48]. Several studies have been conducted to understand the water requirements of hemp in different agroclimatic zones. For instance, studies conducted in Europe revealed that hemp needs 500–700 mm of water for growth and development. Meanwhile, in the vegetative stage, a minimum of 250–300 mm of water is needed for optimum growth [49,50]. Cosentino et al. [51] reported that 250 mm of water was required for monoecious early fiber genotypes and 450 mm for dioecious late genotypes grown in a semi-arid Mediterranean environment (southern Italy). Another study conducted in southern Italy over two years with diverse genotypes showed that the replenishment of 66% of the water lost through evapotranspiration is required for excellent hemp production. Furthermore, the water requirement of hemp (435 mm) is higher than soybean and sunflower, but lower than sorghum [52]. But these studies were conducted at northerly latitudes at mild temperatures where evapotranspiration is lower than southern latitudes. However, the amount of water required for hemp cultivation depends on the agro-climatic region, genotype, soil characteristics, weather conditions, and evapotranspiration. Hemp is susceptible to waterlogging. Thus, well-drained loam soils rich in organic matter are best suited for hemp cultivation [53]. Sandy loam soil, followed by clay loam soil, was reported to be suitable for hemp cultivation. Heavy clay soil and sandy soil are not well suited. The optimal soil pH for hemp cultivation is 6.0–7.5. Preferably, the optimal soil for hemp should have good drainage and adequate water holding capacity, good aeration, and residual nutrients. These conditions are best met in sandy loam soil [54].

There is a strong and crucial interaction between the environment, genotypes, and nutrients, and a strong relationship between cannabinoids and nutrients [55]. Cockson et al. [56] studied the early-stage visual diagnosis of macro- and micronutrient deficiency and toxicity in hemp. This is useful for farmers for implementing corrective measures to maintain or optimize yield. The study revealed significant mineral deficiencies impacting hemp only occurred for nitrogen (N), potassium (K), boron (B), and copper (Cu). Nitrogen is most important for hemp growth, development, and production and essential for secondary metabolites [57–59]. Increasing the application of N (0 to 60 kg N ha^{-1}) results in higher chlorophyll content, better performance of photosystem II (PSII), increased photosynthesis, plant height, stem diameter, and total biomass accumulation. At the same time, N deficiency (0.30 mmol L^{-1}) results in cell membrane damage (cell membrane lipid peroxidation; high MDA [malondialdehyde] content), an increase in superoxide dismutase (SOD) activity, and a reduction in biomass due to decreased leaf area index (LAI) [60,61]. Anderson et al. [62] reported that compared to the optimal rate of N (50 ppm) through fertilization, a higher rate of N (>300 ppm) significantly reduced hemp plant growth, biomass accumulation, and cannabinoids, and an excess application of N can result in ammonia toxicity. In another study, Yang et al. [63] indicated that although N supply improved plant growth, it should not exceed 6.0 mmol/L. Such circumstances draw attention to the need for matching agroclimatic regions with genotype-specific N requirements to optimize N application in the field.

In contrast to Cockson et al. [56], Aubin et al. [64] reported that supplementary P and K are less important in hemp cultivation compared to N. Meanwhile, K deficiency and toxicity are less studied in hemp. However, Cockson et al. [56] showed a reduction in the dry weight of hemp grown in K deficient soil, while the plant response was nonsignificant in phosphorus (P) deficient soil. Contradicting the findings of Cockson et al. [56], Finnan and Burke [65] reported that K does not influence hemp biomass accumulation. But P is important for the central biosynthesis pathways, cell division, seed, and root growth, and foliar gas exchange [2,55,66]. Recently, Shiponi and Bernstein [55] confirmed moderately high P application supported optimum plant growth and development and increased total cannabinoids (more details are in Section 3).

Interaction of hemp cultivars with the environment in response or adaptation to abiotic stress factors may be more important than cultivar traits associated with high yield [67]. Changes in environmental factors can adversely affect yields. Several abiotic stress factors affect hemp cultivation, particularly, high temperatures, drought, salinity, flood, or excess soil moisture. However, limited studies have been conducted to understand the effect of abiotic stress factors on hemp and its cultivation.

2.1. Water Deficit Stress

A field investigation to understand the interaction of hemp genotype and the environment was carried out at Fort Collins and Yellow Jacket, Colorado, USA in 2016 [67]. Thirteen cultivars from a diverse set of germplasm from breeding programs (European project MultiHemp) across Europe and Asia were used to study the environmental effects, and genotype and environment interactions (GEI). Two irrigation treatments were applied in Fort Collins (limited irrigation [147 mm] and fully irrigated [398 mm]) and a single sprinkler irrigation treatment (fully irrigated; 203 mm) was applied in Yellow Jacket. The yield in Fort Collins was 1123 kg ha^{-1} under full irrigation, but lower under limited irrigation (404 kg ha^{-1}). Total plant biomass (2482 kg ha^{-1}), plant height (135 cm), basal stem diameter (5.77 mm), and stand establishment (14%) were reduced under limited irrigation. A lower CBD content (1.43%) and a slightly higher cannabichromene (CBC) content (0.0052%) were detected in plants under limited irrigation. Notably, genotypic differences were found between treatments in both locations. Overall results imply the strong interaction between genotype and environment. At the same time, a study performed in southern Italy using high throughput techniques (Ground Penetrating Radar [GPR] and Sentinel-2 multispectral satellite [S2-MSI]) reported that hemp can draw soil moisture in the absence of precipitation and/or irrigation. The results show that the water deficit stress resistance of hemp, however, depends on crop vigor [68].

Sheldon et al. [69] compared controlled environment versus in-field screening to identify the traits responsible for drought-tolerance in hemp. Twelve diverse genotypes were grown in a growth chamber. The magnitude of water deficit stress was calculated by measuring net transpiration rate (NTR) and the fraction of transpirable soil water (FTSW). Three experiments were conducted with different objectives such as (1) understanding the transpiration rate (TR) response to soil drying, (2) the sensitivity of TR to high vapor pressure deficit (VPD), and (3) field evaluation of the expression of traits related to CBD. The range of threshold of FTSW across genotypes was 0.16 to 0.81. Five cultivars closed stomata when the FTSW threshold was reduced to 0.55 and four cultivars reduced transpiration only when VPD increased (>2.5 kPa). However, other genotypes showed transpiration-limiting traits when VPD increased to a range of 1.5–2.5 kPa. Cultivar Ha3ze showed a quick response to drought by reducing TR and showed a higher CBD as well.

Meanwhile, Caplan et al. [70] reported that controlled exposure to drought can increase cannabinoids in hemp. In this study, drought was calculated by measuring plant water potential (range between −1.4 to −1.5 MPa was considered moderate drought). Controlled exposure to drought increased the yield per unit growing area of THCA (43%), CBDA (47%), THC (50%), and CBD (67%) and reduced photosynthesis (42%) and plant water potential (50%) as compared with the control. Researchers also recommended that controlled drought can be used to increase inflorescence dry weight and cannabinoid yield and indicated the possibility of genotypic variation in response. On the other hand, Park et al. [71] reported that 7 days of exposure to drought (with 20% relative water content in the soil considered as drought) increased CBG content (622 μg g^{-1}) while CBD and THC content decreased. In both studies [70,71], however, yield per unit area of production was not shown.

In Tehran, Iran, field screening for drought tolerance was performed on 47 hemp ecotypes grown with irrigated conditions based on evapotranspiration [72]. Five hemp ecotypes had higher water use efficiency and yield under drought treatment. In Italy, three laboratory-based screenings were conducted to identify the osmotic stress tolerance and transpiration efficiency of 26 European hemp cultivars [73]. The first screening monitored seed germination of selected cultivars under osmotic stress. The second was conducted to understand the physio-biochemical traits, and the third was to understand the transpiration efficiency. A high level of genotypic variation was found in response to osmotic stress, which divided tested genotypes into tolerant and susceptible groups.

Recent studies applied chemical treatments to hemp in order to mitigate the effect of drought stress. Jiang et al. [10] used the plant growth retardant uniconazole (S-(+)-uniconazole). A hemp cultivar was exposed to 8 days of drought after spraying uniconazole, which resulted in higher chlorophyll content, photosynthesis, activities of carbon and nitrogen metabolism-related enzymes, and changes in phytohormone levels. But the study did not report yield or other traits of economic value. In Iran, Bahador and Tadayon [74] applied zeolite (aluminosilicate mineral) to hemp and monitored water use efficiency, oil yield, and phenology. The application of zeolite stopped the reduction of oil yield under water deficit conditions and increased the water consumption per unit of yield as compared to the control.

2.2. Heat Stress

Abiotic stress triggered by changes in day and night temperatures is equally crucial versus the effect of drought on hemp production. In north-east Italy, Baldini et al. [43] performed a two-year field suitability assessment of six hemp varieties with different origins, sexual types, and maturity to monitor the dual-purpose production (seed and stem) capabilities. During the grain-filling stage, a daily maximum temperature above 30 °C reduced seed quality (seed weight, oil content, protein content, crude fiber, and ash). Park et al. [71] conducted four experiments in the USA to understand the effect of mechanical wounding, herbivory (by tobacco hornworm *Manduca sexta* caterpillar larvae), high temperature (45–50 °C), and drought on different cannabinoids using a local hemp variety. Exposure of plants to high temperature for 7 days significantly reduced CBGA and CBG, however, CBDA, THCA, CBD, and THC did not change. Again, in this study, yield per unit area of production is not shown. Herppich et al. [50] performed a field experiment in Potsdam, Germany using two multipurpose industrial cultivars during drought-prone and high-temperature seasons (early May to end of October). During the experimental period, the maximum solar radiation was 1200 J m^{-2} s^{-1}, the temperature was 35 °C, and the precipitation was 16 mm (56 mm was the total precipitation during the entire growth period). Both cultivars adjusted to the harsh temperature and dry conditions, but the response magnitude differed between them. In both cultivars, leaf area, plant density, leaf area index, and photosynthesis were reduced with the early onset of senescence as the season progressed.

2.3. Salinity Stress

Limited information is available on the impact of flooding and salinity on hemp. Toth et al. [11] studied the effect of five stress factors on cannabinoids of three chemotype III hemp cultivars (CBD dominant with less than 0.3% THC). The flooding was induced by increasing the soil volumetric water content to field capacity (0.35–0.4 m^3 m^{-3}) using trickle irrigation. This was repeated two to three times per week throughout the sampling period (a total of four samplings with one week interval, September to October 2019) to maintain a soil volumetric water content >0.32 m^3 m^{-3}. There were no significant changes in cannabinoids and CBD:THC ratio after exposure to flooding. These researchers explained that flooding was induced by increasing the soil volumetric water content to field capacity. However, achieving field capacity cannot be considered as flooding and moreover, this study was conducted in well-drained Ontario soil. As discussed, in Section 2 of this review, well-drained soils are best for hemp cultivation. These factors may be the reason for the nonsignificant effect on cannabinoids and CBD:THC ratio in this study.

Studies on the effect of salinity on seed germination and seedling growth/physiology were conducted in China using seeds of two fiber hemp cultivars [75,76]. Neutral salt (NaCl, Na_2SO_4) and alkaline salt (Na_2CO_3, $NaHCO_3$) produced several salinity levels up to 300 mM. Germination rate decreased linearly with increasing salt concentration. Higher Na_2CO_3 had a more adverse effect on germination. Seed germination and length of radicles and hypocotyls increased at a low concentration of neutral salt. Hemp seedling was more sensitive to Na_2CO_3 than to NaCl stress. Dixit [77] used four genotypes to study the effect of salinity up to 200 mM on seed germination and root morphology (root length and fresh weight). Additionally studied were the oxidative stress indices (hydrogen peroxide (H_2O_2) and lipid peroxidation) and the enzymatic antioxidant quenching system (activities of superoxide dismutase [SOD], catalase [CAT], guaiacol peroxidase [GPOD], ascorbate peroxidase [APOD] and glutathione reductase [GR]). Seed germination percentage, root length, and fresh weight decreased linearly with increasing salinity levels. At the same time, oxidative stress indices and antioxidant enzymes activity increased in roots with distinct genotypic variation.

Questions:

- How feasible is it to manipulate and standardize the light spectrum for the cultivation of region-specific diverse hemp under a controlled environment with an emphasis on precise production of cannabinoids for medicinal purposes?
- Are there any possibilities to develop a photoperiod-insensitive hybrid for the production of cannabinoids, seed and seed oil, and fiber?
- Is it feasible to cultivate hemp chemotype III (CBD dominant with less than 0.3% THC; genotypes for medicinal cannabinoid production) in tropical and subtropical regions with weather conditions not well suited for genotypes grown for seed and fiber yield?
- What is the role of hemp roots in confronting diverse abiotic stress factors, particularly, water deficit and high day and night temperatures?
- Irrespective of the types of hemp, what is the magnitude of tolerance of hemp genotypes to agroclimatic regions with high humidity such as the tropics?

3. Improving Hemp Production by Modifying Agronomic Practices

Much research is ongoing to improve sustainable hemp production of fiber, oil, seed, and cannabinoids by modifying agronomic practices. These include nutrient amount and timing, plant density, irrigation amount and timing, and sowing date. In addition, changing hemp genotypes, cropping systems, and growing seasons, and their combination are being investigated for optimal hemp production. This section summarizes important past and recent hemp agronomic research activities in various agroclimatic regions for sustainable hemp production, however, with a caution that each research activity and its outputs are dependent on the agroclimatic conditions. Though results are summarized below, recommended practices varied widely, likely because of the differences among agroclimatic regions. Hence, a systematic investigation is required to implement a similar agronomic practice emphasizing microclimatic conditions, soil type, and genotypes.

3.1. Nitrogen Amount and Timing

A one-year field-level evaluation in Indiana, USA to optimize the N application with three grain genotypes and two sowing dates with a difference of 13 days was carried out [78]. Nitrogen application of 224 kg N ha^{-1} increased foliar nitrogen, leaf mass per area (LMA), CBD, and THC as compared to a foliar N application of 168 kg ha^{-1}. Interestingly, THC was higher in plants with a later sowing date, while CBD was higher with an early planting date. The study also demonstrated that N application of 224 kg ha^{-1} increased fall armyworm (*Spodoptera frugiperda*) larval growth by 50% and leaf consumption by 16%, revealing the importance of pest management while implementing nutrient management practices.

A study in Florida, USA, under controlled environmental conditions, showed that higher N applications adversely affected plant growth and CBD yield [62]. In this study, five cannabinoid hemp cultivars grown in pots were treated with fertigation of nutrients with various N concentrations (0, 50, 150, 300, 450, and 600 ppm). Visual appearance showed variation in plant height, number of branches, and amount of healthy green foliage. Nutrient toxicity symptoms were the least in 50 ppm and 150 ppm N concentrations. Cannabinoids and total floral biomass were highest at 50 ppm N concentration. At the same time, N toxicity-induced leaf necrosis increased linearly from 300 to 600 ppm. Higher N applications (>150 to 600 ppm) stunted plant growth across cultivars and reduced CBD concentrations. THC content was higher with N fertilizer rates of 450 ppm and 600 ppm. At the same time, CBD was reduced with increasing N application (>50 ppm) and CBG was high in the N-deficient treatment.

Another study evaluated the environmental effect of N application and plant densities in grain hemp in the Mediterranean environment [79]. Seven hemp grain or grain/fiber cultivars, two levels of N applications (50 and 100 kg ha^{-1}), and three plant densities (40, 80, and 120 plants m^{-2}) were used to evaluate environmental impact. Using the life cycle assessment (LCA) method, the study demonstrated that a combination of lower level of N application (50 kg ha^{-1}) and lower plant density (40 plants m^{-2}) can limit plant growth, development, and production. In contrast, lower levels of N application can reduce the carbon footprint. The carbon footprint is the total amount of greenhouse gases released or generated by anthropogenic activities. Van der Werf et al. [80] pointed out the importance of plant density and N application due to higher self-thinning of plants at high (200 kg ha^{-1}) N applications compared to low (80 kg ha^{-1}), which can affect yield.

A multi-location European study of eight experiments recommended a systematic assessment of plant N status to optimize N application and plant density [60]. Although management combinations varied among sites, N application and plant density used in the study was in the range of 0 to 120 kg N ha^{-1} and 30 to 240 plants m^{-2}, respectively. In general, the study found that 60 kg N ha^{-1} is required for optimum hemp production (grain or grain and fiber) in all tested sites in Italy (Piacenza and Budrio), Latvia (Vilani), the Czech Republic (Sumperk), and France (La Trugalle). Recommended planting density was 90–150 plants m^{-2}. The study demonstrated that N application of 60 kg N ha^{-1} and plant density of 120 plant m^{-2} increased stem yield by 32% and 29%, respectively, as compared to the N deficient treatment and lower plant density. However, the increase in seed yield was statistically nonsignificant with increasing N application and plant density. An increase in plant density from 30 to 240 plants m^{-2} reduced plant height and stem diameter. At the same time, N application from 0 to 120 kg N ha^{-1} resulted in an opposite trend.

3.2. P and K Amount and Timing

A modeling study in Kunming, China revealed that fiber yield of hemp is primarily influenced by N application followed by plant density, K, and P applications. However, increasing the N, P, and K applications and plant densities can adversely affect fiber yield production [58]. The results recommended a planting density of 330,000 to 372,000 seeds ha^{-1}, N applied at 251–273 kg ha^{-1}, P at 85–95 kg ha^{-1}, and K at 212–238 kg ha^{-1} to achieve a fiber production above 2200 kg ha^{-1}. A similar study by Aubin et al. [64] on N, P, and K applications was performed in three sites in Quebec, Canada using two grain cultivars, but results contradicted those of Deng et al. [58]. Five different rates of fertilizer application (0, 50, 100, 150, and 200 kg N or K ha^{-1} and 0, 25, 50, 75, and 100 kg P ha^{-1}) were tested. The increase in biomass yield, seed yield, and seed crude protein concentration was linear with N applications, but the magnitude of response varied with different sites. However, P and K applications had a limited influence on plant growth and development. N application up to 200 kg N ha^{-1} was best for both hemp cultivars.

Though P is considered less critical for hemp biomass and yield, Shiponi and Bernstein [55] reported the positive effect of P application on total cannabinoids. In this study, different P concentrations (5, 15, 30, 60, and 90 mg L^{-1}) were applied to two cultivars (chemotype I [high THC and low CBD] and II [balanced THC and CBD]) grown in pots in a controlled environment. Application of P above 5 mg L^{-1} reduced up to 25% THCA and CBDA. The same study showed 30–90 mg L^{-1} P is optimal for plant development and function, but <15 mg L^{-1} can reduce foliar gas exchange and plant growth. A 2004 field study in Saskatchewan, Canada by Vera et al. [81] used two grain hemp cultivars and applied P at the time of sowing as monoammonium phosphate (12-51-0) at two rates (0 and 20 kg P ha^{-1}). Nitrogen was also applied (0, 40, 80, and 120 kg N ha^{-1}) as ammonium nitrate (34-0-0), 25–30 days after sowing. Phosphorus application increased plant height, while reducing plant density, biomass, and seed yield. Plant height, biomass, seed yield, and seed protein content increased linearly with N application. Contrasting results on the effect of P were reported by the same research team in the same location reported in 2010 [82]. Meanwhile, the effect of the N application was consistent with their earlier findings.

3.3. Seeding Density and Plant Density

Several studies focused exclusively on hemp plant density. In the North-Baltic region, Barčauskaitė et al. [83] found that increasing sowing density from 15 to 35 kg/ha increased CBD content by 23%, while N fertilizer addition decreased CBC content in one locally adapted hemp variety. Amaducci et al. [84] at Cadriano, Italy used two fiber and grain cultivars (monecious and dioecious) at 120, 240, and 360 plants m^{-2}. Plants were harvested at two phenological stages: initial flowering and at full flowering. Stem height, stem yield, fiber content, and fiber yield were high in plants harvested on full flowering and the monecious cultivar showed higher fiber yield. A plant density of 120 plants m^{-2} gave maximum fiber yield. Garcia-Tejero et al. [85] reported that in southwest Spain, high density (9777 plants ha^{-1}) and low density (5866 plants ha^{-1}) were the best agronomic practice. Both plant densities showed higher biomass accumulation and cannabinoids (CBD, cannabichromene [CBC], THC, and cannabigerol [CBG]) in five new hemp varieties (three CBD chemotypes and two CBG chemotypes) as compared to intermediate plant density of 7333 plants ha^{-1}.

A detailed study was conducted to understand the effect of plant density on weed suppression, crop growth, physiological responses, and fiber yield in a subtropical site (Bundaberg) in Queensland, Australia [17]. This study used an improved subtropical fiber and grain hemp variety with low THC to identify the suitable plant density after thinning (100, 200, 300, and 400 plants m^{-2}) with two sowing dates, 1 and 15 October 2010. However, the selected variety was not suitable at that latitude (Bundaberg; 24.91° S 152.32° E) with short photoperiod (longer dark period), which caused early flowering and shorter stem length. This led to a recommendation to introduce new varieties or develop better crop management practices in regions with a longer dark period. The results showed that increasing plant density from 100 to 400 plants m^{-2} reduced weed weight from 23.2 to 1.5 g m^{-2}. Low plant density (100 plants m^{-2}) resulted in shorter and thicker plants. Stem thickness was inversely proportional to the increased plant density, and at the time of harvest, plant height was lower at higher densities. At the same time, variation in plant density did not significantly affect leaf chlorophyll content and root mass. Raw bast fiber dry weight yield (133.1 g dry weight m^{-2}) and total stem yield (30.61 g dry weight m^{-2}) were highest at 300 plants m^{-2} plant density. However, total yield of raw bast fiber (1.28 t ha^{-1}) was below the typical European yield (2–3 t ha^{-1}).

Tsaliki et al. [86] reported no relationship between plant density and seed yield (4.57 t ha^{-1} [highest yield from the top yielded variety]). At the same time, fiber yield (4.27 t ha^{-1} [highest yield from the top yielded variety]) was negatively correlated with plant density. This three-year study used six fiber and seed hemp varieties under a Mediterranean environment in Thessaloniki, northern Greece. In 2016 to 2018, rainfall recorded from May to July was 63 mm, 139 mm, and 252 mm, respectively. Mean monthly temperature was 17 °C to 27 °C. In Queensland, Australia, Hall et al. [39] tried to find the optimum sowing time for planting hemp, and they selected five months (September, October, November, and December 2011, and January 2012) for spring and summer sowing. Based on one year of sowing data, November was optimal for growth, evidenced from higher plant height (999 mm) and biomass accumulation (7.8 t ha^{-1}). The experiment was conducted in the Burnett/Wide Bay region, Queensland, Australia. In this region, mean maximum temperatures from spring (September) to summer (January) range from 25.4 °C to 30.1 °C, with an average annual precipitation of 1032 mm.

3.4. Photoperiod Effects on Hemp Growth

The influence of longer dark periods on four genotypes was reported by Cosentino et al. [45] in southern Italy with different sowing times. The optimal sowing time is from the end of April to the first three weeks of May. Furthermore, the longer dark periods in southern Italy resulted in premature floral initiation and reduced stem and fiber elongation, biomass accumulation, and stem yield. Hall et al. [40] conducted greenhouse and field trials in Bundaberg, Queensland, Australia. They arranged different light regimes to create four different photoperiods under controlled conditions. An extended photoperiod increased plant height, stem thickness, and root density. The morphological changes and yield results imply that the photoperiod needs to be longer than 13 h 40 min to attain optimal yield. At the same time, in a nearby field trial using five planting dates (September to January), November planting is best for obtaining higher dry matter yield.

Recently, Zhang et al. [8] performed controlled environment and field studies in Florida, USA using 15 chemotypes and 12 fiber and grain cultivars with diverse backgrounds of origin to understand the photoperiodic flowering response. They observed a significant genotypic variation in response to photoperiodic flowering. After subjecting plants to 11 different photoperiods ranging from 12 to 18 hours, the researchers found four cultivars flowered in response to a photoperiod of 18 hours and these cultivars did not remain in the vegetative stage as long as other tested cultivars. Furthermore, even a small change in the photoperiod of 15 minutes can influence the floral initiation in some cultivars, revealing the importance and need for screening for photoperiod requirements in cultivars before introducing them into any agroclimatic region. These researchers suggested some of the cultivars tested in their study are suitable for tropical and subtropical regions.

3.5. Harvest Timing

Like sowing time, time of harvest has an immense impact on the stem, fiber, and seed yield, and quality of hemp. Cherrett et al. [87] reported the importance of harvesting immediately after flowering to improve fiber quality. Calzolari et al. [88] noted increased CBD and CBD/THC ratios by postponing harvest after seed maturity, though at the risk of exceeding legal THC. This field study at two sites in northern Italy in 2014 was carried out using a CBD chemotype, a CBG chemotype, and a low cannabinoid variety. In northern Germany, another study was conducted to understand the effect of the early harvest to avoid rainfall risk for dry sheltering of straw [89]. Eleven monoecious and three dioecious hemp cultivars of different maturity groups from different origins were tested. The first early harvest was at intensive flowering (80–115 days after emergence) and the second early harvest was at the stage of initial seed maturity (100–134 days after emergence). Significant differences were found between the two harvesting times in stem length and dry matter, seed yield, oil, and γ-linolenic acid concentrations, and primary fiber filling rate. The reduction in key fatty acids reported in the second harvest is important information for hemp farmers. The quality of seed and seed oil is determined by the fatty acid profile, which increases farmers' commercial value and economic benefit. Essential fatty acids (linoleic acid, γ-linolenic acid, and α-linolenic) are well known for health benefits [90]. Two field studies were performed in Alborz, Gilan, and Golestan, Iran. Native and non-native genotypes were tested to understand the genotypic and regional effects on cannabinoids and fatty acid seed oil profile [91,92]. Results found that the harvesting time affected the synthesis of fatty acids and their profile. Additionally, genotypes and microclimatic conditions of specific regions, mainly temperature, light and moisture, and farming conditions play a crucial role in fatty acid metabolism.

3.6. Multiple Factors and Hemp Growth

An interesting two-year study in Spain tested plant densities, sowing times, irrigation doses, and cropping systems [27]. In 2012, CBG chemotype and CBD chemotype cultivars were planted in three plant densities (33,333, 16,667, and 11,111 plants ha^{-1}) and irrigated at two levels (100% of crop evapotranspiration [ETC], 299 mm irrigation until harvest; and 75% of ETC, 219 mm irrigation until harvest). In addition to 2012, two cropping systems (open field conditions and plastic macro-tunnels) and two sowing times (end of April and end of May) were compared in the study in 2013. In the second experiment, the same cultivars were grown in the open field and received 451 and 398 mm irrigation, respectively, under 100% ETC at the time of first sowing (April) and 311 and 350 mm under 75% ETC. The cultivars Carma and Ermes received 401 and 348 mm, respectively, under 100% ETC at the time of the second sowing (May) and 309 and 269 mm under 75% ETC. Biomass accumulation and cannabinoids (CBG, CBD, Δ9-THC, and CBC) were higher in plants grown in a plastic macro-tunnel cropping system recommended for hemp cultivation in the Mediterranean region. Different irrigation levels did not show a significant effect on biomass production. Cultivar performances were better under the earliest sowing time, 100% ETC, and the higher plant densities (33,333 and 16,667 plants ha^{-1}).

Questions:

- What is the feasibility of intercropping hemp with other crops such as cereal crops or legumes to increase the economic benefit of farmers and reduce nitrogen input?
- What are the relationships between plant density, harvesting time, soil nutrient and water availability, and cannabinoid and fatty acid profiles in low latitude regions?

4. Advances in Cannabinoid Detection and Quantification

Extraction and quantification methods of phytocannabinoids are also critical for the development of products in the cannabis industry. Various analytical approaches are used for the detection and quantification of cannabinoids. A standardized procedure for sample preparation, extraction, and quantification is essential for the consistent quality of the cannabinoid profile. Based on selectivity, sensitivity, analytical accuracy, and precision, several advanced analytical techniques have been developed to detect and quantify various compounds from cannabis extracts.

As per the recent review by Lazarjani et al. [12], gas chromatography (GC) and high-performance liquid chromatography (HPLC) are widely used as the standard quantification techniques. Gas chromatography in conjunction with mass spectrometry (MS) or flame ionization detection (FID) is often used for acidic/volatile cannabinoids and terpenes. HPLC with MS or ultraviolet (UV) detectors can quantify both acidic and neutral forms of cannabinoids. Several other techniques are also used by researchers such as two-dimensional gas chromatography, HPLC-UV/diode array detection (DAD)/MS, HPLC-MS/MS, liquid chromatography (LC)-MS/MS and APCI, HPLC-ESI-qTOF/MS (HPLC coupled to electrospray ionization and quadrupole time of flight mass spectrometry), ultra-high performance liquid chromatography-quadrupole time-of-flight-MS (UPLC-qTOF), matrix-assisted laser desorption ionization-time-of-flight-MS (MALDI-TOF-MS), thin layer chromatography (TLC), Fourier transform infrared spectroscopy (FTIR), and nuclear magnetic resonance spectrometry (NMR).

Lazarjani et al. [12] suggested that for cannabinoids, HPLC-MS/MS is the ideal quantification method as it can detect and differentiate both acidic and neutral cannabinoids. Additionally, Sanchez et al. [93] introduced Raman spectroscopy (RS) to determine THCA.

Along with detection and quantification methods, variation in sample preparation also plays a significant role in cannabis analysis. Smith [94] found inter-laboratory variation in THC readings generated from the same sample by five different California state-licensed, ISO-certified laboratories in USA (ISO is an internationally recognized standard of practice for testing and calibration laboratories). The sample preparation process can depend on several variables including sample drying method, moisture content, grinding technique, extraction solvent, amounts of sample, etc. As the legality of hemp is based on the presence of cannabinoids like the percentage of THC, farmers must rely on laboratories using a standard method with high consistency and precision.

Question:

- How can a universal standard cannabis extraction and assay protocol be developed based on different cannabis assay techniques?

5. Environmental Impact of Hemp

Phytoremediation, Carbon Sequestration and Bioenergy

Hemp is considered a hyperaccumulator, a plant capable of accumulating metals or metalloids in tissues hundreds or thousand times greater than other plants. With this characteristic, hemp may be used for phytoremediation [26,95]. The economic importance of hemp with its substantial above-ground biomass accumulation as compared to other hyperaccumulators is an additional benefit. Developing a strategy to use hemp plants engaged in the phytoremediation process for bioenergy production can increase the demand for hemp as a phytoremediator with economic benefits. Traditional non-biological methods such as physical excavation of contaminated soil, chemical stabilization of contaminants, and volatilization of contaminants are fast and effective, but costly and not as environmentally beneficial as compared to the biological methods (phytostabilization, phytodegradation, phytovolatilization, and phytoextraction) [26,96]. A major concern about phytoremediation is the time required. However, the major advantage is the conversion of contaminants into small and manageable amounts, which is effective for proper disposal [97,98].

Engaging hemp as a phytoremediator in the Chernobyl Exclusion Zone, Ukraine, due to the 1986 nuclear accident, is an excellent example of the efficiency of hemp in phytoextraction (results are not published in peer-reviewed literature; [99,100]). Additionally, several studies prove hemp can restore soil contaminated with diverse contaminants, particularly heavy metals. Husain et al. [101] assessed the capability of hemp varieties to remediate coal mine land soil in Pennsylvania, USA. Results showed that hemp can extract heavy metals arsenic (As), lead (Pb), nickel (Ni), mercury (Hg), and cadmium (Cd) from the soil. In China, the Pb uptake capacity of hemp from artificially contaminated soil was studied by Deng et al. [102]. The soil was contaminated with lead chloride. Results showed that roots accumulated higher levels of Pb compared to the other plant parts. Similar findings are reported in [103]. In contrast to the above study, Linger et al. [104] reported that Ni, Pb, and Cd accumulated more in leaves than other plant parts. Another study by Linger et al. [105] reported that roots accumulated more Cd than other parts of the plant.

In China, Shi and Cai [106] compared Cd accumulation and tolerance of eight energy crops, including hemp. All selected crops (rapeseed, sunflower, soybean, hemp, castor, safflower, flax, and peanut) were grown in soils with several concentrations of Cd. The accumulation of Cd was more in the roots of hemp than other crops due to the higher biomass. Another study by Shi et al. [107] further supported the findings of Shi and Cai [106]. In Italy Citterio et al. [100] studied seeds grown in pots with artificially contaminated soil with two levels of chromium (Cr), Ni, and Cd. No heavy metal effect was observed in seed germination. Further, they found that hemp is protected from cell damage by activating molecular activities and modulating metabolites. There was no effect of heavy metal contamination on THC content with a threshold limit of 0.2% total dry matter. The results also showed that heavy metals are mainly stored in the roots and are translocated in very small quantities into the above-ground biomass as compared to other hyperaccumulators such as *Thlaspi caerulescens* and *Alyssum murale*.

Campbell et al. [108] reported the capability of hemp to remediate soil contaminated with polycyclic aromatic hydrocarbons (PAHs; chrysene and benzo[a]pyrene). High weight and height growth rate indicated that hemp is able to tolerate high levels of chrysene and benzo[a]pyrene and acts as an efficient phytoremediator for PAHs contaminated soil. The capacity of hemp to remediate soil contaminated with a radioactive contaminant (cesium; ^{134}Cs) was tested along with another fiber crop (flax) [109]. Researchers concluded that both hemp and flax are phytoaccumulators of radioactive cesium, but, due to high transfer factors (TFs; transfer of accumulated contaminant from one part to another), sufficient care should be given to using hemp seed products. A recent report has been released regarding the cultivation of hemp, as a phytoremediator in a superfund site along the U.S.-Canada border in Maine, polluted with polyfluoroalkyl substance (PFAS), a potential carcinogen [110].

Serious concerns regarding increasing carbon emissions around the globe have compelled countries to make policies and efforts to prevent global warming. Fast growth and high biomass accumulation of hemp are evidence of hemp's efficiency in carbon sequestration via photosynthetic conversion of atmospheric carbon dioxide (CO_2). Stored carbon in the plant biomass is sequestrated in the soil through the root system, biochar, wood burial, and durable plant products [111–113]. Adesina et al. [48] noted in a review that one hectare of industrial hemp could absorb 22 tons of CO_2. Recent studies on hempcrete demonstrated the carbon sequestration potential of hemp. Hempcrete is referred to as carbon-negative hemp-lime concrete, a new building material made up of two major components, hemp shiv (the chopped wood core of hemp) and lime-based binders. Arehart et al. [114] developed a theoretical model to quantify the in situ carbon storage and sequestration based on cement hydration and carbonation chemistry of several hempcrete binders. Carbon sequestration mechanisms of hempcrete consist of two components, biogenic, and non-biogenic. Hemp shiv is the biogenic component that contains 45% carbon stored in the plant by the assimilation of atmospheric CO_2 through photosynthesis, during growth. The non-biogenic component consumes CO_2 by carbonation during the blinding and hardening of lime blinders along with hemp shives [115,116]. Jami et al. [117] reported that the total carbon sequestration by hempcrete is 307.26 kg of CO_2 per m^3. Still, the precise carbon sequestration capacity of hemp is not well understood.

Hemp has been identified as an energy crop due to its high biomass and capability to produce biodiesel, biogas, bioethanol, and solid fuels [118]. The chemical and technical properties of hemp are equivalent to or higher than other bioenergy crops. Prade et al. [119] studied the net energy yields and energy output-to-input ratio to produce heat, power, and vehicle fuel from industrial hemp and compared them with other bioenergy crops. Results showed that hemp has good net energy yields per hectare and energy output-to-input ratio, indicating hemp is an above-average energy crop. Any dried biomass is considered a solid biofuel and hemp is a good source of solid biofuel due to the higher biomass [119]. Higher lignin and cellulose content in biomass, as a result of the longer duration of maturity period (transition from the vegetative stage to the flowering stage), makes harvesting time specifically important for bioethanol production [118,119].

Kreuger et al. [120] monitored the gross methane energy per hectare from anaerobic digestion of hemp using a methane potential test. The average gross methane energy yield was found to be 136 ± 24 GJ per hectare and biogas is recommended as a substitute for existing renewable transportation fuels made from wheat, maize, and rapeseed. Adamovics et al. [121] reported that hemp leaves are the best fit for biogas production. Li et al. [122] and Rashid et al. [123] tested the physical and chemical properties of hemp biodiesel and the results matched with biodiesel specifications of American Society for Testing and Materials (ASTM) methods (ASTM D6751) and European standards (EN 14214).

Questions:

- Is it feasible to utilize hemp for the phytoremediation of petroleum-contaminated sites (petroleum hydrocarbons; PAHs) and utilize biomass for the production of bioenergy?
- What is the feasibility to engage hemp genotypes with higher root growth and biomass to remediate heavy metal polluted locations?
- Several studies report uptake of heavy metals by hemp roots. Can roots be harvested economically or is higher root uptake also matched by higher concentration in leaves?
- How do hemp roots take part in phytoremediation, and can hemp genotypes with efficient hydraulic control increase foliar transpiration for the faster removal of contaminants?
- What is the precise carbon sequestration capacity of hemp in open field conditions?
- What are the possible ways to increase the carbon sequestration capacity of hemp by developing value-added products from hemp?
- How to increase bioenergy production from hemp with low input and processing costs?

6. Hemp Breeding

6.1. Public Hemp Breeding in the United States

Hemp varies genetically for each classified group such as plant-use (for fiber, seed, drug, and ornamental cultivars), flowering time, sexual type, and population type (wild, naturalized populations, landraces, and cultivars) [124]. Hemp breeding is in its infancy stage in the USA. At Cornell University, hemp research started in late 2016. Such research includes variety evaluation, assessment of disease, insect and pest threats, and crop management for diseases and weeds. The research has been involved in breeding hemp varieties, building a hemp germplasm collection, and developing marker assisted selection for hemp since 2017 [125].

At Texas A&M University, the breeding program led by Russell Jessup is governed by state law, according to which the delta-9 THC threshold allowed for harvesting hemp is $\leq$0.3%. Any varieties (high cannabinoid content, high fiber yielding) with frequent THC concentration > 0.3% are not allowed to be planted. This has raised interest in lowering the delta-9 THC level in hemp by the Texas A&M AgriLife Research team [126]. To date, no European varieties (for fiber or grain) meet the expectation for a reliable production in the southern U.S. (south of 37 °N) due to lack of photoperiod adaptation. Therefore, in a collaborative grant, Russell Jessup and Calvin Trostle are studying adaptations of southerly hemp fiber and grain lines planted at three research locations [127]. In 2020, the breeding program partnered with Growing Together Research Inc. to develop genetic transformation protocols in industrial hemp. The goal is to generate hemp lines producing zero delta-9 THC, which ultimately guarantees lower than 0.3% THC limits in these hemp lines when grown in any environmental conditions. One industrial hemp cultivar was reported as a successful stable transformant [126]. In addition, industrial hemp research is being conducted at Colorado State University, Oregon State University, University of Kentucky, University of Florida, North Carolina State University, and the USDA-ARS in North Carolina, Kentucky, and elsewhere.

6.2. Hemp Breeding in Other Countries

In Europe, from 1995 to now, the number of registered hemp cultivars has increased from 12 to up to 46 industrial hemp cultivars. The first monoecious cultivars were generated by the breeding work conducted by a German scientist Von Segenbuch. Also, a high fiber content cultivar as the first hybrids was obtained by the breeding work of Hungarian scientist I. Bocsa [124,128]. In China, cultivating hemp for fiber and seed started more than 6000 years ago. Large collections (about 350 accessions) of hemp germplasms have been collected by the Yunnan Academy of Agricultural Sciences. Research on hemp breeding in China was limited until the end of the 20th century. However, hemp breeding has expanded since 2007. In Canada, the main target for hemp breeding is for stable production in either seed, fiber, or for both in typical environments. Since 1998, the Canadian hemp market has grown as Canada is the main hemp seed and oil supplier for the United States [13]. Commercial cultivars generated from wild Canadian stocks and superior oilseed cultivars for seed and fiber yield have been developed in many Canadian breeding programs [124,129]. A highly desirable fatty acid trait essential in the Canadian food market is gamma linolenic acid. Three cultivars with high fatty acid content, Canda, Debby, and Joey, have been developed [124]. These cultivars are not adapted to lower latitudes.

6.3. Breeding Methods and Breeding Goals

Mass selection, cross-breeding, inbreeding, hybrid breeding, and marker assisted breeding are commonly used methods in hemp breeding [124]. The studies in finding molecular markers for specific traits to reduce labor-intensive and time-consuming screening methods have become essential goals in hemp breeding [130]. However, due to a high level of variability in cannabis within and among accessions, genetic maps, and molecular markers are limited in practical use [124].

Traits that have been studied in hemp breeding include high fiber yield, fiber quality, cannabinoid content and composition, flowering time, resistance to diseases and pests, tolerance to herbicides, and sex determination trait, etc. [124]. High fiber yield and quality with low THC content have become primary goals in many hemp breeding programs. Cannabinoid content and phenological development are traits expressing high plasticity [124]. Flowering time was confirmed as being controlled by a single major gene [125].

Questions:

- Is it possible to develop hemp cultivars with THC levels low enough to allow them to be grown without exceeding legal THC limits under a wide array of agronomic and environmental conditions?
- Can gene editing efforts be useful in this regard?
- Although it has been reported that MAS (marker-assisted selection) was of low utility previously, with more advanced genomic tools, can this be changed?
- How many regions in hemp genomes can be possibly identified by genomic tools to elucidate the separation between drug and fiber types?
- Is it possible to use breeding to produce hemp cultivars with high levels of specific CBDs?
- Aside from CBD and THC contents, can new cultivars be developed that have suitable combinations of fiber content, disease resistance, and drought tolerance to make large-scale production for the fiber market feasible on land that would be otherwise unsuitable for agricultural production (for example, no irrigation in semi-arid climates)?
- Can alternative uses for hemp (e.g., hempcrete) be further developed, and cultivars with suitable agronomic traits be developed, that would allow for expanded markets for the crop?
- As the number of breeding programs in the U.S. is limited and the programs are fairly new, how well adapted are hemp cultivars across regions?
- There are numerous marijuana varieties available. Have these been developed by crossing or simply selection from existing materials? Has a screen of existing germplasm for useful traits been conducted in a systematic manner for industrial hemp?

7. Discussion and Future Perspectives

A survey conducted in the USA by Ellison [131], based on stakeholder's opinions, shows the requirement for further research in various categories. Many stakeholders recommended research on policy issues, economics, and marketing of hemp and to realize the effect of hemp products on human and animal nutrition. The major concerns about the health and nutritional aspects of hemp products point to the presence of cannabinoids in hemp, particularly narcotic THC. Hence, the legal limit of THC percentage is the important factor determining the final output of hemp cultivation. Moreover, due to poor prices and oversupply of CBD biomass, CBD is being converted to delta-8-tetrahydrocannabinol, which has narcotic effects similar to delta-9-THC. It is legal in several states. This delta-8-THC is then legally (for now) infused in many consumer products. Conversion of CBD to THC in artificial gastric juice (in vitro experiment) and conversion of CBD to THC and gradually to cannabinol (CBN; less psychoactive as compared to THC) in the CBD products stored for a long time are matters of concern [132,133]. However, theoretically, THC is absent in hemp seeds, but during harvesting or seed processing there are potential chances for THC contamination from the part that contains THC [134]. Conversion of CBD to THC and CBN needs to be thoroughly examined and earlier research in this aspect has not provided clear conclusions [133].

Variations in atmospheric and soil conditions, agronomic practices, and the effect of different abiotic stress factors can change the total cannabinoid content, particularly altering the CBD:THC ratio and content of THC. Studies should be meticulously conducted to understand the dynamics between the above factors and cannabinoid biosynthesis (Figure 3). Research activities for improving the yield of fiber, oil, and seed by altering existing agronomic practices or by introducing new practices in a particular agroclimatic region should consider the variation of THC. Although fiber, oil, and seed yields may be higher, THC levels above the regulated threshold can negatively affect the financial stability of farmers and allied sectors. The performance of genotypes can vary in different agroclimatic regions, thus selection of genotypes to a specific area is equally important as agronomy and microclimatic conditions. Early research in the USA overlooked the need to investigate the photoperiod and adaptation to identify adapted cultivars for lower latitudes. This has held back needed research progress in agronomics, production, and quality hemp materials.

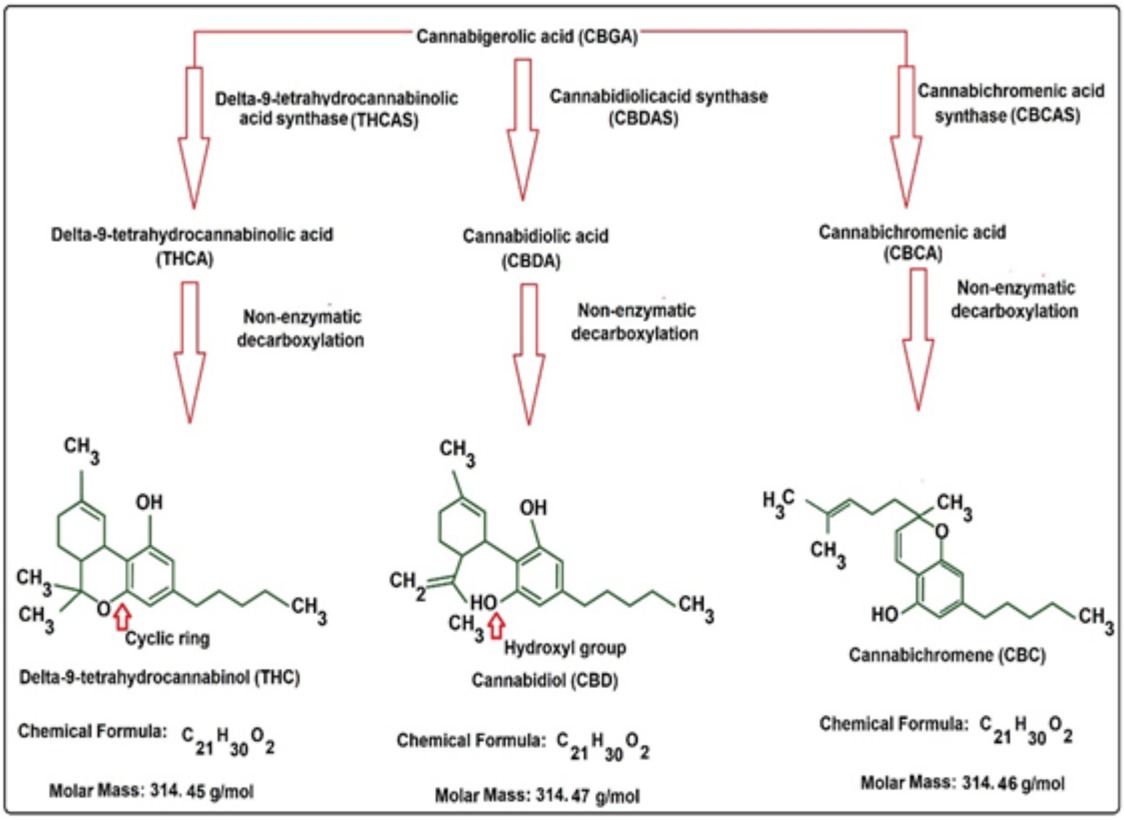

Figure 3. Summary of biosynthesis pathways of primary cannabinoids.

Despite the rapid expansion of hemp literature in recent decades, this review suggests that experimental data from the lower latitude regions remains limited [14]. There are several areas that need particular attention. One is the photoperiod sensitivity and its interaction with temperature [135] of different genotypes in the low latitude countries. Another consideration is related to water use, since evapotranspiration in the lower latitude and hot regions is higher than in cooler, high latitudes where hemp has traditionally been grown [136]. Limited field observations (Section 2) suggest the prior notion of hemp being a low water input crop may not hold in regions such as Texas, but more data are needed to determine hemp's water requirements in these regions. Due to complex interactions among various environmental and management factors, as well as the fact that hemp is frequently managed as a multipurpose crop, the recommended future research strategy should include the integration of experimental and modeling approaches to hasten new testable hypotheses about the influences of hemp production by various factors, especially under scenarios of climate change [43,47,137]. Additional future interest should include the use of new technologies for effective data acquisition, including Unmanned Arial Vehicle (UAV), provided funding is available [138].

Hemp has been considered as having a low nutrient requirement [137], but this notion has not received significant confirmation in this review considering the related literature in hemp nutrient requirements (see Section 3). It appears that the optimal nutrient requirement research for hemp production frequently is met by inconsistent and even conflicting findings [58,60,64]. This may be due to varied initial soil fertility levels and weather variables [139]. It may also be associated with researchers' unrealistic hope of obtaining a single optimal value out of the influence of many uncontrolled factors of multiple origin. Here again, the model-experiment integration [43] may help. Instead of targeting a single optimal nutrient requirement for a particular genotype, a better strategy for future research is to generate and evaluate the distribution of a range of potential optimal values for varied climate or management conditions [43], though studying a different topic. Thus, we can test specific hypotheses regarding any statistically significant differences between or among optimal N values corresponding to different soil/weather conditions. So, instead of waiting for the outcome of numerous experiments to gain confidence on the usefulness of the current hypotheses, it is more efficient to attempt to refute the hypotheses based on the outcomes of only a single, or very few, well-designed experiments, a strategy [140] that helped to propel the rapid growth of molecular biology in the 1960s [33,141].

Along with changes in agronomic practices, the identification, enrichment, and application of plant growth-promoting rhizobacteria (PGPR) [142] and arbuscular mycorrhizal fungi (AMF) [143] in the root zone of hemp genotypes can enhance the yield potential and reduce production from fertilizer. Scientific investigation in this area can provide fresh insight on hemp cultivation in low nutrient, stress-challenged, and contaminated regions. Further, the effect of PGPR and AMF on cannabinoids and their biosynthesis needs systematic evaluation.

The exact role of THC and other cannabinoids in plants is not yet fully understood. Their role as a repellent and defense against insect herbivory, pests, and microbes has been suggested [144–147]. These properties of hemp are supported by the practice of applying cannabis crude extract as a natural insecticide against nematodes and weevils in India [148], which needs further investigation. Advanced genome editing tools can be used to reduce the production of THC and to prevent the conversion of CBD to THC [149,150].

Efforts have been made by the scientific community to develop high-yielding and low THC hemp hybrids through conventional breeding. However, there are limitations to achieving the goals due to the lack of core and mutant germplasm collection and the higher chances of cross-pollination because of the anemophilous nature of hemp. These factors create difficulty in breeding programs [151–153]. Systematic and efficient methods need to be developed to release new hemp varieties for specific agroclimatic regions.

The effect of drought on hemp is extensively documented. Water deficit is a factor that severely affects the cannabinoid content and final yield. Proper understanding of the water requirement of genotypes and maintenance of optimum soil moisture is highly important for the optimum yield and legal limit of THC. At the same time, potential abiotic stresses such as elevated temperature, frost, and flooding or waterlogging are studied less. Along with drought, other abiotic stress factors need to be monitored to maintain the legal limit of THC and optimum yield. Studies on these factors are important because some cannabinoids may protect plants from cold, ultraviolet (UV) light, and desiccation [42,154–156]. Additionally, modulation of cannabinoid biosynthesis (Figure 3) and activities of phytohormones are significant under stress conditions. Thus, it is important to understand the interaction or cross-talk between phytohormones and cannabinoids biosynthesis and regulation of different cannabinoids, which are least studied [157].

The role of phytohormones in growth, development, sex determination, and most importantly the CBD:THC ratio in hemp needs to be investigated further to improve the yield and product quality. In addition to cannabinoids, hemp produces terpenes with multiple pharmaceutical properties [158–160]. However, pharmacological studies related to terpenes are rare. Likewise, studies on increasing the essential fatty acid (linoleic acid, γ-linolenic acid, and α-linolenic) content for improving the nutritional value of hemp seeds and oil are essential.

Maintaining THC content below the approved threshold and improving the carbon balance (photosynthesis [CO_2 assimilation] vs. night respiration [CO_2 release]) are important strategies to enhance the quality of hemp products and increase the biomass, yield, and carbon sequestration capacity, respectively. Improved carbon balance and higher rates of photosynthesis and growth respiration tend to increase biomass accumulation and yield [161–163].

Identified genotypes with high biomass accumulation can be deployed as phytoremediators and used for bioenergy production. The incorporation of phytoremediation and bioenergy production can help to overcome the economic limitations of phytoremediation projects. Roots are a crucial part, as the relationship between groundwater status and water use efficiency is vital for the growth, development, and yield of hemp [19]. Additionally, rooting depth and root development are key supporting factors for hemp to be an efficient phytoremediator [26,164]. Identifying genotypes with efficient root systems would be beneficial for drought-prone and high-temperature agroclimatic regions and contaminated sites. Research is needed to apply advanced non-invasive and novel techniques in hemp root phenotyping [165,166].

At the system level, the productivity and quality of hemp is simultaneously influenced by multiple factors of climate, weather, soil, and crop management. Methods of data synthesis using mechanistic models are frequently limited by the number of factors and biological processes considered [43,137,167,168]. Today there is no hemp model that can explicitly deal with both processes related to growth and development and THC production. Instead, economic optimization methods that measure the total production efficiency [169] offer a promising potential for untangling new opportunities to streamline the production of hemp as a multifaceted crop. Similar to the measurement of the efficiencies of individual firms [34], the production efficiencies of individual hemp fields, or of different topological positions of the same field, given the availability of fine-resolution data [170], can be calculated. Various inputs should be considered, such as inherent soil properties (texture or subsoil drainage), inherited soil properties (erosion, acidification, mining of nutrients, or compaction), recent agronomic management practices (irrigation, fertilizer and pesticide applications, capital/labor/technology investment), and various outputs that are either desirable (seed, fiber or CBD) or undesirable (THC). Research in this direction has gained momentum recently [171]. We anticipate further development in standardized hemp CBD profiling protocols, and regionally or nationally organized hemp agronomy-CBD testing programs covering a wide range of climate, weather, soil, and management practices. Aided with these coordinated research campaigns, the analysis of total production efficiencies can help to minimize the inconsistencies in yield performance and stress responses of hemp as observed in some prior studies that were conducted in individual locations looking only at limited factors influencing hemp growth and yield formation.

8. Conclusions

Despite the rapid growth of literature in hemp agronomy, consensus understanding of basic questions of hemp's water and nutrient requirements, and the performance of hemp genotypes under tropical and low-latitude conditions, is still limited. New experimental evidence is needed for all areas of hemp agronomy research. The application of new phenotyping and data acquisition tools will help. One important theme identified by this review is the strategy to combine experimental and modeling approaches to significantly expand the volume of information output that is otherwise difficult to obtain through synthesizing the individual experiments across different locations and/or years. The expanded information will accelerate new research hypotheses and guide new experimentation for future hemp research. New evidence reviewed in this paper further reinforced hemp's excellent value in improving phytoremediation, carbon sequestration, and bioenergy. Due to the urgent needs of hemp growers, breeding efforts to develop low or zero-THC hemp genotypes with a wide and stable adaptability are hot topics among hemp researchers, but are currently still in progress. Standard methods with high consistency and precision are still needed for cannabinoid detection and quantification. To explicitly consider THC along with numerous agronomic and economic factors pertaining to the farm-level hemp production, economic optimization methods, such as data envelopment analysis, may be used to guide streamlined management of hemp as a multifaceted, multipurpose crop with an adaptation to a wide range of climate and soil conditions.

Supplementary Materials: The following supporting information can be downloaded at: https://www.mdpi.com/article/10.3390/agronomy13020475/s1, Table S1: Details of genotypes used in different studies included in this review.

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