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Review Article

High Times and Headaches for Hemp as it Seeks to Re-Establish Itself as a Viable Industry

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Abstract

The US hemp industry is poised for a renaissance after prohibitions on hemp production were recently lifted. While this newly opened market is an opportunity for growers, processors, and manufacturers there are a lot of factors to consider. The lack of crop improvement research done on hemp leaves hemp far behind other crops that have benefitted from nearly a century of improvement. This review provides a basic summary of hemp and research needs that are high priorities to address as hemp seeks to re-establish itself as a productive part of the US agricultural system. While some headaches will be experienced along the way, prudent investment in research can help hemp producers capitalize on the high potential of this re-emerging crop.

Keywords: Hemp; Cannabis; Cannabis sativa; THC; CBD; CBC

Abbreviations: THC - Tetrahydrocannabinol; CBD - Cannabidiol; CBC - Cannabichromene; CBG - Cannabigerol

Introduction

Hemp, grown primarily for fiber, was a thriving industry in the US that until passage of the 1937 Marijuana tax act. This bill essentially terminated hemp production in the US with a few exceptions including a short spurt in hemp production to replace lost fiber imports during World War II. Eighty-two plus years later the US hemp industry is seeking to re-establish itself after passage of the 2018 US farm bill which removed federal prohibitions on hemp production. This has many producers eager to cash in on the opportunities in this re-emerging industry. Successful re-establishment of this industry will require some effort to catch up on eight plus decades where little to no formal research was done on hemp as well as some careful planning for how to adapt to changes that occurred in the hemp product ecosystem.

Many challenges are related to the lack of research activity during a period where other crops benefited from advances in crop production research that span a timer period beginning with broad adoption of synthetic fertilizers and pesticides and continued through decades of advances in genetics and breeding including the recent application of biotechnology and genetic engineering. Nearly all of the crops we rely on today benefitted from advances in all of these areas while hemp laid dormant through all of these advances.

While this review will focus on areas of research for hemp to catch up in, it is also worth noting that hemp is waking up to a different world than it left. While hemp was produced mostly for fiber a century ago the US now relies heavily on cotton and synthetic fibers and currently lacks the facilities for hemp fiber processing at significant levels, although news of planning and construction of new hemp fiber processing plants appears in the national news media frequently. And while there were no retail outlets for CBD a century ago, this is a major focus of current hemp production. Thus, the product side of the hemp industry will likely be in turmoil as processors seek to increase capacity for fiber production while work on developing other terminal products like animal feeds, fuels, and secondary metabolites with medicinal and / or recreational value, all while trying to keep supply in line with demand for a product stream that is much more diverse than it was when hemp production was banned. While hemp has a lot of promise as a green source for fiber and many other products, growing pains are likely until processing capacity is increased and equilibrium between supply and demand is achieved for all of the product end points.

Discussion

On the research side there are many important areas to catch up in. One is simply defining what “hemp” is exactly. “Hemp” and “cannabis” are broad colloquial terms that generally describe the character of different lines within the species *Cannabis sativa*, with hemp type lines being those that accumulate low levels of the psychoactive compound THC. The THC cutoff levels are arbitrarily determined and subject to change. There is tremendous diversity in *C. sativa*, similar to the familiar diversity in *Canis familiaris*, a species that includes all dog breeds from Teacup Poodles to Great Danes and everything in between. Because much of the breeding that occurred over the past century or so was done by clandestine growers seeking to produce higher THC lines for the illicit cannabis trade few formal records were kept. Therefore, the phylogeny of C. sativa in general and the pedigrees of individual hemp and cannabis lines are poorly understood [1]. Thus, clarifying the systematics of *C. sativa* will be an important endeavor that will provide a solid foundation for improvement of many traits through conventional breeding approaches. And while there is a lot of ground to be made up here, application of genomics-based approaches for systematics should allow for rapid progress in this area [2].

Because all lines of *C. sativa* contain complete metabolic pathways for synthesis of cannabinoids, including psychoactive THC, hemp must be tested for THC before harvest with mandatory destruction of crops that exceed the defined threshold. Because environmental conditions can influence THC levels it is not uncommon for very low THC producing lines to “go hot” with requisite destruction of these fields. In 2019 the state of New Mexico issued 33 destruction orders from 500 inspections and 41% of hemp fields in Arizona were ordered destroyed for exceeding THC thresholds [3,4]. Thus, creating of a true THC free hemp lines via stable genetic alteration is an important goal. Freeing growers of the risk for losing and entire crop due to high THC levels might be the highest priority current need for growers.

Production of THC free lines may simultaneously enhance other desireable traits such as accumulation of other secondary metabolites of interest. *C. sativa* produces 540 or more secondary metabolites with potential pharmacological value [2]. These include non-psychogenic cannabidiol (CBD) which was recently legalized in the US, and psychoactive THC, both of which are derived from the common precursor cannabigerolic acid (CBGA). The third product derived from CBGA is cannabichromic acid (CBCA), a non-psychoactive whose properties are less well known but is currently being investigated for pharmacological applications based on its demonstrated agonistic interactions with the mammalian TRPA1, TRPV3 and TRPV4 receptors that are involved in pain sensing and homeostasis [5]. All of these metabolites are produced as organic acids (THCA, CBDA, and CBCA) which are non-enzymatically decarboxylated by heat or in the human body to produce THC, CBD, and CBC.

The recent popularization CBD in the US has benefitted hemp growers by providing a “value added” component to traditional hemp products (primarily fiber and animal feed). Since THC, CBD, and CBC are the end points for the branch of the cannabinoid pathway that runs through CBGA, it is highly likely that knocking THC synthesis will increase accumulation of CBD and CBC, and perhaps other compounds in other arms of the cannabinoid pathway, which could prove lucrative for hemp producers in addition to freeing them from the risk of having to destroy crops that exceed THC thresholds. Genetic engineering and mutation breeding are two likely productive pathways to producing true THC free hemp lines, though each has associated complications.

Genetic engineering has proven highly useful for engineering many valuable traits like herbicide tolerance, insect resistance, and disease resistance into many crop species [6]. Recently, genetic engineering including CRISPR have been applied to create crops with gene knockouts or deletions including slow browning apples and mushrooms that were recently approved for sale in the US [7,8]. While transformation and regeneration systems for *C. sativa* are still inefficient, the use of well-established transient Agrobacterium based systems simplifies engineering of plant tissues in the absence of regenerating fully fertile transgenic plants [9,10]. Thus, this approach can be used for proof of concept experiments to confirm expected gene knockout phenotypes before investing significant resources into the difficult task of producing transgenic hemp lines. Continued efforts to improve C. sativa transformation and regeneration systems are likely to improve these systems in the near future. One remaining obstacle with genetic engineering is consumer acceptance. Negative consumer perception may make it difficult to establish genetically engineered hemp lines depending on consumer sentiment associated with various products.

Mutation breeding is a well-established technique that uses radiation or chemical mutagens to introduce mutations (often deletions) into plant genomes. Mutation breeding has been used for over half a century to create many familiar agricultural products including. While the *diecious* diploid nature of *C. sativa* complicates this approach mutation breeding has proven useful in similar system. In particular, mutation breeding has frequently been used to generate novel traits in vegetative propagated crops like potato and banana where traditional sexual breeding involving cross pollination is not possible [11,12]. In potatoes, a vegetatively propagated tetraploid plant, mutation breeding was used to successfully identify a disease resistant potato line [11]. Thus, a mutation breeding approach may be useful for developing hemp lines with THC synthase deletions that are free from the stigma that often accompanies genetic engineering. The random nature of mutation breeding is also likely to produce other potentially valuable traits that should be simple to identify while screening for TCH free plants like dwarfed, male sterile, and seedless varieties. Needless to say, development of haploid *C. sativa* lines would simplify mutation breeding approaches greatly as they would enable discovery of recessive traits.

Clarifying the systematics of C. sativa and freeing growers from the risk of exceeding THC thresholds are high priority needs for the hemp industry. Other additional priorities include characterization of pests and diseases affecting production and concomitant breeding for resistance and evaluation of pesticides and / or development of lines with natural resistance. Basic research on hemp physiology to optimize production practices and develop lines with improved nitrogen use efficiency, drought tolerance, salt tolerance, and other beneficial traits will also be important for the industry.

Improvement through conventional breeding also holds great promise for addressing all of the needs outlined above and more. And in this area, hemp has as much if not more catching up to do. It is clear that the genus C. sativa contains extensive diversity that is poorly understood at present. Unfortunately, most of the breeding over the past century has been done under poorly controlled conditions with few records kept as producers sought to increase THC levels to boost illicit sales. Thus, there is a lot of catching up to do in terms of understanding the taxonomy of C. sativa and pedigree of the many lines in use today. Though efforts in this area will undoubtedly yield substantial benefits in improving many traits related to crop physiology, pest and disease resistance, secondary metabolite production, and more.

Conclusion

Overall, hemp holds tremendous promise as a profitable crop for growers and processors, particularly as consumer interest in sustainable sources of fiber and fuel increase. And while there are headaches will certainly be encountered along the way, catching up on decades of missed research is likely to help the hemp industry experience high times again in the future.

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Conflict of Interest

The author has no conflicts of interest with any of the material presented in this review.

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