Cannabis, The Multibillion Dollar Plant That No Genebank Wanted

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Cannabis, The Multibillion Dollar Plant That No Genebank Wanted

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1 **Abstract**

2 Although cannabis is legalized and accepted as an agricultural commodity in many places around
3 the world, a significant lack of public germplasm repositories remains an unresolved problem in
4 the cannabis industry. The acquisition, preservation and evaluation of germplasm including
5 landraces and ancestral populations is key to unleash the full potential of cannabis in the global
6 marketplace. We argue here that accessible germplasm resources are crucial for long-term
7 economic viability, preserving genetic diversity, breeding, innovation, and the long-term
8 sustainability of the crop. We believe that cannabis restrictions require a second look to allow
9 genebanks to play a fuller and more effective role in conservation, sustainable use, and exchange
10 of cannabis genetic resources.

11 **Key words:** Plant genetic resources, cannabis, breeding, genetic diversity.

Figure 1. Extensive phenotypic variation among cannabis accessions. Image credit: Dutch Passion

Cannabis: an increasingly popular crop

Cannabis sativa L. has a long history of human use for fibre, food, medicine, and its psychoactive properties (Russo, 2007; Salami et al., 2020). The species can be categorized based on taxonomic relationships or chemotype but is often divided and regulated based on the level of psychoactive cannabinoids that are produced. In most countries (e.g., Canada, US, EU), plants that produce below 0.3% Δ^9 -tetrahydrocannabinol (THC) are regulated as hemp and plants with 0.3% or greater THC are classified as drug-type. While hemp has been legal for commercial cultivation in Canada since 1998, drug-type cannabis was only legalized for commercial production for medicinal use in 2014 and for recreational use in 2018. During the last decade, industrial properties of cannabis for applications in textiles, paper, building materials, cosmetics, foods, and pharmacological properties have been broadly studied and supported (Schilling et al., 2020; Schultz et al., 2020). With legalization, isolated cannabinoids are now legal for development as medicinal and edible products. To date, >115 unique cannabinoids (e.g., cannabidiol (CBD), cannabichromene (CBC), and cannabigerol (CBG)) with potential medicinal applications (Martínez et al., 2020) and >560

secondary metabolites have been identified in cannabis (Zager et al., 2019; Hesami et al., 2020; Cai et al., 2021; Balant et al., 2021). The cannabis market is exponentially growing. The U.S. industrial hemp-derived CBD market alone is expected to reach \$23.7 billion by 2023, up from the current value of \$5 billion, and U.S. farmers are seeing revenues of up to \$45,000 per acre (www.brightfieldgroup.com).

So far, the focus of growers has been on major cannabinoids (e.g., THC and CBD). Recently, however, more rare cannabinoids (e.g., cannabigerol (CBG), tetrahydrocannabivarin (THCV)) are gaining interest to the pharmaceutical industry (Abioye et al., 2020). It is noteworthy that cannabis cultivars with high levels of some rare cannabinoids (i.e., THCV) tend to share a genetic background with landraces known for their invigorating highs (CGRC, www.medcanabase.org; CANNUSE, <http://cannusedb.csic.es/>; Balant et al., 2021). This new interest represents great potential for evaluating and breeding with a diverse collection of cannabis cultivars as new sources of rare cannabinoids, but researchers' access to germplasm is fraught with challenges. Conventionally, plant breeders and researchers depend on genebanks around the world as a source of new traits to develop improved cultivars (i.e., commercial cultivars, landraces, wild crop relatives, etc.). While there are some public hemp collections (Welling et al., 2016), there are currently no public seed or clonal genebanks for drug-type cannabis. From a biological standpoint, the distinction between hemp and drug-type cannabis is very minor and this discrepancy significantly limits the genetic diversity that is currently preserved in the public domain. With an ever-increasing demand for cannabis products, there is a pressing need to identify suitable genetics that can be used for production and as source of diversity (Figure 1) for further breeding and development.

Cannabis and genebanks: a controversial relationship

Genebanks have the long-term mission of preserving plant genetic resources (PGRs) with the aim that they might be used in the future, either directly or as material in breeding programs to address changing environmental conditions, new biotic pressures, or societal needs (Halewood et al., 2018; Belzile et al., 2020). Today, large collections of genetic resources (>10 000 accessions) are maintained for every major crop (e.g., wheat, rice, barley, soybean, etc.) by national entities such as the USDA's National Plant Germplasm System (NPGS) or the Plant Gene Resources of Canada (PGRC), as well as international research centers that are part of the Consultative Group for

1 International Agricultural Research (CGIAR). These sizable resources contain a wealth of genetic
2 diversity and hence phenotypic variation that can be used to develop new improved varieties with
3 key traits. Bretting (2018) provided striking examples of traits of interest that were sourced in
4 genebanks and that individually bring yearly benefits exceeding \$100 million (Bretting 2018).
5 Consequently, in the last few decades, a legally binding international agreement (the International
6 Treaty on Plant Genetic Resources for Food and Agriculture (ITPGRFA)) has been developed to
7 govern access and benefit-sharing of PGRs (Moore and Witold 2003). Accordingly, to collect and
8 ensure the accessibility of phenotypic and genotypic information of PGRs, several international
9 initiatives (e.g., DivSeek, the Global Open Data for Agriculture and Nutrition (GODAN), the
10 Research Data Alliance (RDA) and the Breeding API (BrAPI)) have been established (Meyer et
11 al., 2015; Halewood et al., 2018). An important aspect of the existing genetics and proposed
12 frameworks is that the collections are in the public domain to ensure equitable access, which is not
13 the case with private collections.

14 Despite its economic, medicinal, and societal importance, drug-type cannabis is missing from the
15 list of available species in public genebanks and only exist as private collections. In the context of
16 the rapidly changing cannabis market in Canada, the USA, and other regions around the world, it
17 is certain that genebanks could play an important role in helping to not only preserve genetic
18 diversity but also to adapt and improve varieties. The reason cannabis is absent from genebanks
19 can mostly be attributed to governmental regulations surrounding the plant. In most countries
20 cannabis is illegal, but even in Canada, where cannabis was legalized in 2018, regulatory barriers
21 persist and include stringent restrictions both on partnerships between the cannabis industry and
22 researchers and researchers access to cannabis germplasm. In addition to current stringent
23 restrictions (i.e. access to new genetics, strict inventory requirements, etc.) and security
24 requirements (e.g., full-time surveillance, storage in safes, etc.), there is a general lack of support
25 for public genebanks (e.g., PGRC) to preserve cannabis seeds or clonal accessions. Preserving
26 public health and public safety while also promoting social justice and economic development
27 requires strong partnerships among governments, universities and industry. Thus, we think these
28 restrictions require a second look to ease cannabis seeds import, export, and transfer. In addition,
29 a rigorous workflow is needed to control viability, uniformity, and labeling of cannabis seeds.

30 **Cultivar extinction: loss of cannabis crops' genetic diversity**

1 The oldest known written record on cannabis use comes from the Chinese Emperor Shen Nung in
2 2727 B.C. Ancient Greeks and Romans were also familiar with cannabis, while in the Middle East,
3 use spread throughout the 7th to 14th century C.E. to North Africa. In 16th century cannabis spread
4 to the western hemisphere mainly for its use as fiber (Bennett 2010; Long et al., 2016). In the U.S.,
5 prior to first Federal restriction of cannabis in 1937 (i.e., Marihuana Tax Act.), cannabis was
6 widely used as a patent medicine during the 19th and early 20th centuries (Bridgeman & Abazia,
7 2017).

8 In the early years (1980s) of the clandestine cannabis industry, nearly all of the genetics were
9 imported from places like South America and the Middle East. Many valuable seeds
10 (landraces/cultivars) brought in from these regions were bred and further developed in tropical
11 countries (e.g., Jamaica and Panama) (Campos 2018). The products derived from these seeds came
12 to be known as “homegrown”. After a few years of trial and error, growers learned how to breed
13 desirable traits and ultimately created the foundational gene pool that produced the hybrids and
14 modern cultivars grown today (Dufton 2017). During the 1980s and 1990s many genetic
15 combinations were developed in North America that were then exported and created the foundation
16 of Dutch companies (Bennett 2010). From the 1990s, fads and trends driven by the desire to get
17 new choices began to change the shape of the cannabis industry, which resulted in a massive global
18 cultivar extinction. This reality has also impacted the countries of origin (e.g., Pakistan,
19 Afghanistan, Iran, Tajikistan, Northern India, and Morocco (Soorni et al., 2017)) where they have
20 started to replace landraces with the more potent hybrid genetics of today, which yield a higher
21 percentage of active ingredients.

22 While the specific history of cannabis cultivation and breeding are somewhat unique, the loss of
23 genetic diversity is well known from many crops around the world. As new, higher yielding,
24 disease resistant cultivars are released, they often displace the diversity that was previously grown
25 along with all of the potentially useful traits that they contained. For example, in 1959, over 2000
26 varieties of rice could be found under cultivation in Sri Lanka but only 100 were recorded by 1992,
27 of which 75% came from common genetic stock (Thrupp, 2000). Likewise, in the USA just 4
28 cultivars of potato represent 75% of total production, 6 cultivars of soybeans are responsible for
29 50% of production, and 9 cultivars of wheat encompass 50% of production (Thrupp, 2000). As a
30 whole, the Food and Agriculture Organization of the United Nations (FAO) estimates that a

1 staggering 75% of agrobiodiversity was lost during the 20th century (Commission on Genetic
2 Resources for Food and Agriculture, 2010). While these losses are tragic and could lead to long
3 term consequences for producers, the impact is partially abated due to the extensive germplasm
4 collections around the world that have collected, catalogued, and conserved a wide range of this
5 diversity.

6 In the case of cannabis, the landrace genetics that are the results of thousands of years of selective
7 breeding are in danger due to the cannabis trend-driven market and displacement by newer, higher
8 yielding, more potent, or more disease resistant cultivars. As cannabis regulations liberalize, it is
9 expected that modern breeding will increase the speed with which new cultivars are developed and
10 only further displace valuable germplasm around the world. Landraces represent the major gene
11 pool not only to preserving genetic diversity but also as a reservoir for rare cannabinoids and
12 terpenes with a high medicinal impact (McPartland & Small, 2020). The last thing the cannabis
13 community needs is a smaller gene pool, as history shows the dire consequences of a narrowing
14 genetics selection (e.g., Potato famine (Goss et al., 2014), southern corn leaf blight (Tatum, 1971)).
15 There is no doubt that diversity must be maintained in both genetic and cytoplasmic constitution
16 of every important crop, which includes all cannabis cultivars, old and new. It is fundamental to
17 balance the market needs while not losing sight of the long-term value of preserving genetics that
18 might hold the key to disease or pest immunity. Therefore, it is essential that genebanks and
19 researchers collect, protect and preserve all available cannabis genetics of today before they are
20 permanently lost.

21 **Cannabis breeding: a multilayer challenge**

22 Cannabis is facing a multitude of methodological challenges and regulatory, financial, and access
23 barriers to conduct comprehensive basic and applied research (National Academies of Sciences,
24 Engineering, and Medicine, 2017). Most importantly, the cannabis research community suffers
25 from a lack of sufficient understanding of plant's genetics and how the key traits are expressed.
26 While agriculture has catapulted into the modern era with the application of modern breeding
27 techniques and genomic tools, cannabis remains years behind other crops due to the long legacy
28 of prohibition and stigmatization. Until very recently (i.e., legalization), breeding cannabis
29 happened in clandestine operations with undocumented methods and a lack of modern
30 technologies. In order to promote targeted breeding of cannabis, the following biological

challenges should be considered; (i) better classification of cannabis taxonomic groups (e.g., indica and sativa); (ii) dioecy behavior of the cannabis plants; (iii) molecular mechanisms underlying flower development; (iv) stabilization of cultivars for uniformity; and (v) developing cultivars with unique cannabinoid profiles targeting minor cannabinoid production (Barcaccia et al., 2020; Kovalchuk et al., 2020). In addition, the composition and content of cannabis secondary metabolites can be affected by the age of plants, sex, developmental phase, growth and environmental conditions, harvesting time, storage conditions, and methods of cultivation, so a better understanding of these interactions is needed (Aliferis and Bernard-Perron, 2020; Schultz et al., 2020).

Conventionally, a foundational germplasm (i.e., the seeds, plants, or plant parts) that includes landraces, crop wild relatives, and developed varieties, forms the basis on which modern plant improvement rests (National Research Council (US) Committee on Managing Global Genetic Resources, 1991). Hence, the germplasm accessions are the building blocks in breeding new cultivars. Similar to other crops, access to germplasm collections is an essential for research and breeding in cannabis and to ensure that genetic diversity is maintained for future use.

Concluding remarks

Although we are convinced that the dawn of a new era has arrived for cannabis, we recognize that it will take time for cannabis research and breeding to take off due to the lack of public germplasm repositories. Nonetheless, these are exciting times for, more than ever, public genebanks to adopt cannabis and preserve its diversity. In the context of our rapidly changing cannabis market it is certain that we can expect genebanks to play a major role enabling researchers to develop new cultivars.

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