Green Reports

Ariviyal Publishing

Review Article

DOI: 10.36686/Ariviyal.GR.2023.04.10.054

Green Rep., 2023, 4(10), 13-22.

Hemp as Agricultural Crop

Muhammad Arshad Ullah*[a] and Ali Hassan[b]

[a]*Pakistan Agricultural Research Council, Islamabad, Pakistan.*
[b]*PMAS- University of Arid Agriculture, Rawalpindi, Pakistan.*

***Corresponding author E-mail address**: arshadullah1965@gmail.com (Muhammad Arshad Ullah)

ISSN: 2582-6239

Crossref

Publication details
Received: 11th October 2022
Revised: 31st December 2022
Accepted: 31st December 2022
Published: 27th April 2023

Abstract: Agriculturally, hemp is a relatively high-yielding crop, with low or no pesticide requirement, and modest demands for fertilizer. Due to these features, its introduction into the intensive farming systems could be constitute a long-term strategy in maintaining farming systems and practices that are particularly favorable to environmental and climate policy goals.

Hemp (*Cannabis sativa* L.) belongs to the oldest and most known versatile plants. It was cultivated all over the world, due to its fast growth and low-demand in resources. However, demand for renewable raw materials has recently increased and hemp cultivation has returned as a sustainable and high yielding crop that can be grown for a multitude of products and industrial applications. Hemp has also participated in many agro-industrial fields such as agriculture, textiles, bio-composite, paper-making, automotive, construction, bio-fuel, functional food, oil, cosmetics, personal care and pharmaceutical industry, because of the high-quality cellulose in its stems, the high-quality oil in seeds and valuable resins in the inflorescence. In addition, industrial hemp varieties (cultivated for stem fibres and seeds) registered in the European Catalogue has to contain less than 0.2% D9-tetrahydrocannabinol (THC) according to EC regulation 809/2014.

Hemp is cultivated mainly for its fibrous stem but the most profitable practice seems to be the combination of utilizing both fibre and seed in multiple uses and available varieties may present noticeably divergent characteristics, making them more suitable for different end products.

Cultivation of industrial hemp to produce insecticides displays the following strengths: (i) lack of similar products (i.e. hemp-based insecticides); (ii) low costs of raw material and availability of agricultural lands for its cultivation; (iii) increasing demand for eco-friendly and safe products; (iv) possibility to split the end products in other fields (e.g., cosmetics and pharmaceutics). Supporting literature comes from the recent investigations, who found that the hemp essential oil is effective against larvae of mosquito vectors and moth pests, as well as against flies and snails.

Furthermore, we explored the insecticidal effects of industrial hemp cultivated in central Italy on a panel of economically important target insects, including two vectors of public health importance, i.e., the mosquito *Culex quinquefasciatus* Say (Diptera: Culicidae), and the house fly *Musca domestica* L. (Diptera: Muscidae) and two insect pests attacking crops of high economic interest, i.e., the aphid Myzus persicae (Sulzer) (Rhyncota: Aphididae), and the tobacco cutworm *Spodoptera littoralis* (Boisduval) (Lepidoptera: Noctuidae). In particular, *C. quinquefasciatus* is recognized as a vector of lymphatic filariasis, West Nile and Zika virus, while *M. persicae* and *S. littoralis* are able to feed on more than 400 and 80 plant species, respectively, with severe economic damages for farmers.

Keywords: *Cannabis sativa*; hemp; Marijuana; Cannabidiol (CBD) oil; crop; agriculture

1. Introduction

There are many different varieties of cannabis plants. Marijuana and hemp come from the same species of plant, *Cannabis sativa*, but from different varieties or cultivars. However, hemp is genetically different and is distinguished by its use and chemical makeup, as well as by differing cultivation practices in its production. Hemp, also called "industrial hemp", refers to cannabis varieties that are primarily grown as an agricultural crop (such as seeds and fiber, and by-products such as oil, seed cake, hurds) and is characterized by plants that are low in THC (delta-9 tetrahydrocannabinol, marijuana's primary psychoactive chemical). THC levels for hemp are generally less than 1% (Datwyler and G. D. Weiblen, 2006).[1]

Marijuana refers to the flowering tops and leaves of psychoactive cannabis varieties, which are grown for their high content of THC. Marijuana's high THC content is primarily in the flowering tops and to a lesser extent in the leaves. THC

levels for marijuana are much higher than for hemp, and are reported to average about 10%; some sample tests indicate THC levels reaching 20%-30%, or greater (National Institute of Drug Abuse, 2008).[2]

A level of about 1% THC is considered the threshold for cannabis to have a psychotropic effect or an intoxicating potential (Small and Marcus, 2008).

Current laws regulating hemp cultivation in the European Union (EU) and Canada use 0.3% THC as the dividing line between industrial and potentially drug-producing cannabis. Cultivars having less than 0.3% THC can be cultivated under license, while cultivars having more than that amount are considered to have too high a drug potential (Small and Marcus, 2003).[3]

Some also claim that industrial hemp has higher levels of cannabidiol (CBD), the non-psychoactive part of marijuana, which might mitigate some of the effects of THC (Hillig and Mahlberg, 2004).[4]

A high ratio of CBD to THC might also classify hemp as a fiber-type plant rather than a drug-type plant. Opinions remain mixed about how CBD levels might influence the psychoactive effects of THC (Zuardi et al., 2006).[5]

Production differences depend on whether the cannabis plant is grown for fiber/oilseed or for medicinal/recreational uses. These differences involve the varieties being grown, the methods used to grow them, and the timing of their harvest (see discussion in "Hemp" and "Marijuana", below). Concerns about cross-pollination among the different varieties are critical. All cannabis plants are open, wind and/or insect pollinated, and thus cross-pollination is possible.

Because of the compositional differences between the drug and fiber varieties of cannabis, farmers growing either crop would necessarily want to separate production of the different varieties or cultivars. This is particularly true for growers of medicinal or recreational marijuana in an effort to avoid cross-pollination with industrial hemp, which would significantly lower the

THC content and thus degrade the value of the marijuana crop. Likewise, growers of industrial hemp would seek to avoid cross-pollination with marijuana plants, especially given the illegal status of marijuana. Plants grown of oilseed are also marketed according to the purity of the product, and the mixing of off-type genotypes would degrade the value of the crop (Anndrea, 2009).[6]

Hemp (*Cannabis sativa* L.) belongs to the oldest and most known versatile plants. It was cultivated all over the world, due to its fast growth and low-demand in resources, until its ban in the 1930s (Struik et al., 2000).[7] However, demand for renewable raw materials has recently increased and hemp cultivation has returned as a sustainable and high yielding crop that can be grown for a multitude of products and industrial applications (Carus and Sarmento, 2016; Baldini et al., 2020).[8,9] Hemp has also participated in many agro-industrial fields such as agriculture, textiles, bio-composite, paper-making, automotive, construction, bio-fuel, functional food, oil, cosmetics, personal care and pharmaceutical industry (Salentijn et al., 2015),[10] because of the high-quality cellulose in its stems, the high-quality oil in seeds and valuable resins in the inflorescence. In addition, industrial hemp varieties (cultivated for stem fibres and seeds) registered in the European Catalogue have to contain less than 0.2% D9-tetrahydrocannabinol (THC) according to EC regulation 809/2014 (European Commission, 2014).[11]

Although weather conditions in southern Europe are favourable for hemp growth there is little background knowledge regarding the productivity of the recently registered varieties due to the interruption of hemp production in the second half of the last century (Baldini et al., 2020).[9]

Nevertheless, many farmers are interested in the reintroduction of hemp cultivation in Southern Europe and, according to the European Industrial Hemp Association (EIHA), in 2018 the hemp cultivation area in Europe was 50,081ha (European Industrial Hemp Association, 2018).[12] The main problems faced by the renewal of industrial hemp cultivation in Europe include

i. The selection of the most appropriate variety to European conditions,
ii. The lack regarding the agronomic data to incorporate into Mediterranean farming systems and practices (Campiglia et al., 2017),[13]
iii. The end use of the final product and
iv. The negative attitude towards hemp cultivation due to the THC content.

The germplasm used is crucial for the success of the cultivation, because of its environmental adaptability and production potential, as well as in terms of final quality and end-use (Angelini et al., 2016),[14] Hemp is cultivated mainly for its fibrous stem but the most profitable practice seems to be the combination of utilizing both fibre and seed in multiple uses (Faux et al., 2013; Tang et al., 2016)[15,16] and available varieties may present noticeably divergent characteristics, making them more suitable for different end products.

The planting season of industrial hemp in the Northern hemisphere is in spring, from the second half of April to mid-May (Cosentino et al., 2013).[17] These sowing times allow the period of vegetative growth to coincide with the optimal growing temperatures and longest days necessary to delay flowering and maximize stem growth (Hall et al., 2013).[18] Earlier or later plantings in the Northern hemisphere limit crop growth and yield, mainly in response to low temperatures, inadequate solar radiation, and short-day lengths. The crop response in the field is the result of an interaction between genotype, environment, and management, with plant density, mineral nutrition, and irrigation regime being the main factors involved in the final yield and its quality (Sikora et al., 2011).[19] Cannabis plants grow well under temperate conditions. Rapid growth is achieved on well-drained, fertile, medium-heavy soils and the crop should be established in a well worked seedbed free of compaction. Early flowering can be related to a reduction in final yield because, once flowering occurs, the plant responds by suppressing its vegetative development, thereby ending plant (stem) elongation (Cosentino et al., 2013).[17] Agriculturally, hemp is a relatively high-yielding crop, with low or no pesticide requirement, and modest demands for fertilizer. Due to these features, its introduction into the intensive Mediterranean farming systems could be constitute a long-term strategy in maintaining farming systems and practices that are particularly favorable to environmental and climate policy goals. When hemp crops are healthy and under no limiting factors (water or nutrients), biomass production is directly related to the amount of light received by the crop (García-Tejero et al., 2014).[20]

In the last years, the market of conventional agrochemical products to combat insects and agricultural pests has experienced a significant decrement due to the development of botanical pesticides that have conquered the trust of farmers and have been increasingly employed in Integrated Pest Management (IPM) programmes (Isman and Machial, 2006; Thakore, 2006; Benelli et al., 2017a, 2018a,b).[21-25] In this regard, botanical insecticides are favorably accepted by consumers due to their recognized efficacy, eco-friendly impact, low toxicity on mammals and beneficial organisms (Desneux et al., 2007; Benelli et al., 2016; Pavela and Benelli, 2016; Stevenson et al., 2017),[26-29] and limited possibility to cause resistance in arthropod pests. Thus, this trend is expected to still go up in the next years because of marketing of new products (Isman, 2015; Pavela, 2016)[30,31] and of the streamlining regulation operated by authorities.

Among various crops having the potential to be employed in IPM programmes, here we focused on industrial hemp (*Cannabis sativa* L.). Indeed, a hallmark of hemp (in both var. indica and sativa) is the presence of glandular hairs concentrated on leaves and, to a major extent, on inflorescences, which secrete a sort of oleoresin functioning as a barrier entrapping and killing plant enemies (Potter, 2009).[32] These parts are normally discharged during the conventional hemp processing, thus representing an underutilized biomass for further application.

In particular, they are a rich source of essential oil containing mainly monoterpene and sesquiterpene hydrocarbons (Bertoli et al., 2010).[33]

The exploitation of hemp by-products as a source of botanical insecticides is a matter of interest for farmers, allowing them to maximize the commercial value of hemp cultivation. Our idea is to obtain bioactive essential oils from the inflorescences of industrial hemp that usually remain underutilized, to manufacture natural insecticides to be employed in organic agriculture and IPM programmes. Indeed, research on this issue is still poor. Cultivation of industrial hemp to produce insecticides displays the following strengths:

a) lack of similar products (i.e. hemp-based insecticides);
b) low costs of raw material and availability of agricultural lands for its cultivation;
c) increasing demand for eco-friendly and safe products;
d) Possibility to split the end products in other fields (e.g., cosmetics and pharmaceutics). Supporting literature comes from the recent investigations by Benelli et al. (2018a)[34,35] and Bedini et al. (2016),[36] who found that the hemp essential oil is effective against larvae of mosquito vectors and moth pests, as well as against flies and snails.

In the present work, we used GC–MS analysis to investigate the chemical composition of the essential oil from the inflorescences of industrial hemp cv. Felina 32 cultivated in central Italy. The quantification of the marker compounds α-pinene, myrcene, terpinolene, (E)-caryophyllene and cannabidiol in the essential oil was performed by GC-FID. Furthermore, we explored the insecticidal effects of industrial hemp cultivated in central Italy on a panel of economically important target insects, including two vectors of public health importance, i.e., the mosquito Culex quinquefasciatus Say (Diptera: Culicidae), and the house fly Musca domestica L. (Diptera: Muscidae) Benelli and Mehlhorn, 2016; Davies et al., 2016),[37,38] and two insect pests attacking crops of high economic interest, i.e., the aphid Myzus persicae (Sulzer) (Rhyncota: Aphididae), and the tobacco cutworm Spodoptera littoralis (Boisduval) (Lepidoptera: Noctuidae). In particular, C. quinquefasciatus is recognized as a vector of lymphatic filariasis, West Nile and Zika virus (Benelli and Romano, 2017; Vadivalagan et al., 2017),[39,40] while M. persicae and S. littoralis are able to feed on more than 400 and 80 plant species, respectively (Bass et al., 2014; OEPP/EPPO, 2015),[41,42] with severe economic damages for farmers.

Hemp (*Cannabis sativa*) is an annual plant and the only species in family Cannabinaceae (Chabbert, 2013).[43] The term 'hemp' is given to *Cannabis sativa* varieties and biotypes containing less than 0.3% delta-9 tetrahydrocannabinol (THC) (a psychoactive compound) as defined by the 2014 US Farm Bill provision (H.R. 2642 sec. 7606 (2)).[44] The distinction is a legal definition rather than a physiological one, as both hemp and 'marijuana' (i.e. by the legal definition, any *Cannabis sativa* with THC content above the 0.3% threshold) represent intraspecific variations within the *Cannabis sativa* species and readily cross with each other. For the remainder of this thesis, 'hemp' will refer to *Cannabis sativa* below the 0.3% limit required for agricultural production and research in the United States and 'marijuana' will refer to *Cannabis sativa* above this limit. 'Cannabis' will collectively refer to both types when a distinction between the two is not relevant.

Both hemp and kenaf (Hibiscus cannabinus) have been cultivated as fiber crops worldwide for centuries. The tough bast fibers, produced from the outer bark, are ideal for cordage, cloth, and paper (Alligret, 2013).[45] While the exact origins of cannabis are unclear, current evidence suggests a point of domestication in Asia. This is reinforced by a long history of production in China where it has been cultivated since 8000 BC (Alligret, 2013; Small and Marcus 2002).[45,46] After arriving in Europe around 2000 BC, hemp remained an important crop throughout Roman, Medieval, and Renaissance times for sail cloth. Only after the arrival of the cotton gin and the steam engine did European hemp cultivation begin to decline (Alligret, 2013).[45]

There is considerable debate over whether cannabis has been truly domesticated. Cannabis retains a number of qualities atypical of domesticated crops. Specifically, while monoecious lines exist, cannabis retains a dioecious reproductive system, seeds do not fill or ripen simultaneously, and once seeds ripen, they typically shatter rather than remaining on the plant (Small and Marcus, 2002).[46]

It has been reported that hemp could provide similar levels of nutrition and may be considered as "emergency forage", (i.e. a crop that is able to produce large quantities of biomass over a short period of time while still providing a suitable level of nutrition for livestock) (Rude et al., 2002).[47]

Little research has been conducted on hemp as forage, but there have been reports that hemp leaves removed from stalks are fed to swine and other livestock in rural China (Clarke, 1995). Much more extensive research has been conducted on the nutritional value of hemp grain as an animal feed, particularly in the European poultry industry (Small and Marcus, 2002).[46] Hens fed a diet consisting of 20% hempseed had statistically higher egg weights (60.5g) compared to the control (60.5g) (56.2g) while hen body weight, total egg production, and feed intake were unaffected (Gakhar et al., 2012).[48] Steers fed diets ranging from 0%, 9%, or 14% hemp seed meal showed no differences in average daily gain, while the proportions of desirable omega-3 fatty acids in the meat increased from 32% to 41% (Gibb, 2005).[49] Similarly, sheep fed various proportions of hemp meal (0%, 25%, 50%, 75% or 100%) also had no significant differences in dry matter intake. Calves fed hempseed cake as a protein source in their diet had higher fiber intake (NDF 1.68 kg) and lower starch intake (1.43 kg) compared to soybean meal (NDF 1.28 kg; 1.55 kg), and had no significant difference in weight gain (Hessle et al., 2008).[50] These studies suggest using grain type hemp for forage or inclusion of a portion of the grain could promote higher levels of crude protein, fiber, and omega-3 fatty acid content.

Research from the European hemp fiber industry has found that the amount of bast fiber in the stem has been finalized by the onset of flowering but the core or secondary fibers still have the potential to increase (Mediavilla et al., 2000; Amaducci et al., 2008).[51,52] Core fiber increased from 20% to 45% of total stem content after flowering in fiber hemp (Mediavilla et al., 2000).[51] Traditionally hemp has been harvested at the onset of flowering for optimal fiber yields (Amaducci et al., 2008).[52] However, most forage is harvested prior to flowering and increased lignification after flowering may decrease the potential of hemp as forage by lowering its nutritive value.

It is possible to produce silage from hemp. It has been reported that when processed into silage, harmful compounds present in the raw plant are reduced (Small and Marcus, 2002).[46] Felina 32 was found to produce silage with a pH of 7.4, crude fiber content of 45.5% DM, and total sugar 5.8% DM (Pecenka et al., 2007).[53] Chop size was evaluated at both 10 mm and 20 mm, with the 20 mm chop size producing 10% more fine pieces than the 10 mm (23% compared to 13%).

Industrial hemp (*Cannabis sativa* L., Cannabaceae) is a versatile herbaceous crop that has been used for fiber, food, and medicinal purposes (Andre et al., 2016; Vonapartis et al., 2015).[54,55]

The cultivation of industrial hemp is more efficient and less environmentally degrading than that of many other crops (Ranalli and Venturi, 2004).[56] Hemp can be grown under a variety of agro-ecological conditions and has a capacity to grow quickly, especially after the first 4–5 weeks after emergence, making it an excellent candidate for carbon sequestration (Struik et al., 2000;[7] Ranalli and Venturi, 2004;[56] Adesina et al., 2020).[57] Hemp grows best in sandy loam with good water retention and drainage at temperatures between 16–27°C, in nutrient balanced soil (especially nitrogen, phosphorus, potassium, magnesium, copper, and others). The planting density depends on the type of crop. Fiber hemp does well in high density to encourage stalk growth, but oilseed and CBD hemp should be planted farther apart to encourage greater branching and flower yields (Adesina et al., 2020).[57] Densely seeded fiber varieties may reach 5–6 m tall, while some recent grain varieties may only reach 1–1.2 m tall.

Many multiple-use or resin cultivars are intermediate in height. Industrial hemp is either harvested for the stalk or seeds, whereas the flowering buds are collected from the narcotic type cultivars (Datwyler and Weiblen, 2006;[1] Adesina et al., 2020;[57] Agriculture and Agri-Food Canada, 2020;[58] West, 1998).[59] Selection for a specific final product (fiber, seeds, or products from the inflorescences) is reflected in the plant architecture of available varieties and clones (Small, 2017).[60] However, architecture also strongly depends on plant density, day length, and nutrients and moisture available in the soil (Campiglia et al., 2017).[13]

As a fiber crop, hemp provides a high yield; it produces 250% more fiber than cotton and 600% more fiber than flax, from the same acreage (Ranalli and Venturi, 2004; Mass, 2009).[56,61] Due to the fast-growing, dense canopy, fiber hemp is a natural weed suppressor and could be grown without herbicides; it also suppresses levels of fungi and nematodes in the soil and can be grown without fungicides or pesticides (Ranalli and Venturi, 2004; Mass, 2009; Adesina et al., 2020; Agriculture and Agri-Food Canada, 2020). Hemp contributes to the maintenance of soil quality by its anchored roots, which prevent soil erosion and nutrient leaching, may extract nutrients from deeper soil layers, and are effective for phytoremediation by absorbing heavy metal contaminants from the soil and storing them within the plant. The continual shedding of leaves through the growing season adds moist organic matter to the soil (Andre et al., 2016; Struik et al., 2000; Mass, 2009). Because of the functions in improving the soil quality, hemp is a prime candidate to be used for crop rotation programs to improve the yield of the main crop (Adesina et al., 2020). Despite the historical functionality of this multi-purpose crop, global hemp production declined in the 19th century, and still only comprises about 0.5% of the total production of natural fibers (Shahzad, 2012).[62]

Illegal drug production and distribution are multi-billion-dollar global industries (UNODC 2014) with potential to transform ecosystems (Benessaiah and Sayles 2014, Mcsweeney et al., 2014).[63,64] Drug supply chains are generally thought to involve production in the Global South to satisfy demand in the Global North, but this assumption no longer holds true for cannabis (*Cannabis sativa* or C. indica) (Decorte et al. 2011).[65] The geography of cannabis agriculture is shifting, with import substitution now observed in almost every developed country in the world (Potter et al. 2011).[66]

In the United States, cannabis agriculture has been understudied and underestimated in scope and magnitude (Weisheit, 2011).[67] Research on cannabis agriculture systems is especially urgent in light of recent policy liberalization (Crick et al., 2013),[68] which is facilitating a transition in cannabis from an illegal drug to a licit agricultural crop. Cannabis is still federally illegal in the United States as a Schedule 1 drug according to the Drug Enforcement Agency, and this classification has stymied research on cannabis production methods and their environmental impacts (Eisenstein, 2015).[69] However, over the last 2 decades the majority of states have liberalized cannabis policy (Cole, 2013),[70] ranging from decriminalization to medical, permitting to the creation of retail markets for recreational use. The latest federal spending bill prohibits federal agents from interfering with the enactment of state laws allowing medical cannabis use. States are likewise left to address any collateral impacts of the burgeoning medical cannabis industry. State-level regulations have at times included explicit environmental protections, such as laws approved in late 2015 in California meant to hold cannabis agriculture to the same standards as other crops (State of California, 2015).[71] In general, policymakers are challenged to keep up with the rapid changes in cannabis agriculture on the ground.

Legal United States markets for cannabis were estimated to be worth $2.7 billion in 2014 and projected to reach $11 billion by 2019 (Arcview Market Research, 2014).[72] This expanding market, coupled with new opportunities to grow cannabis free from threat of federal enforcement, suggest significant near-term shifts in production. Even with new regulatory protections for the environment and their embrace by many growers (McGreevy 2015),[73] a boom in cannabis agriculture promises serious environmental implications (Carah et al., 2015).[74]

Building on other scholars' (Carah et al., 2015, Eisenstein, 2015, Sides 2015)[69,74,75] recognition of cannabis production as a topic of growing environmental concern and their calls for more rigorous research, we present here a study on the expansion and intensification of land use for cannabis agriculture. Our study, as an example of what could be done anywhere cannabis agriculture takes place, illustrates the value of a systematic environmental research approach.

In the current era of policy liberalization, the seat of cannabis agriculture in the United States is a region known as the "Emerald Triangle" in northern California (Corva, 2014).[76] Consisting of Humboldt, Trinity, and Mendocino counties, the Emerald Triangle is arguably the birth place of modern cannabis production in the United States, and Humboldt County might be the top cannabis-producing region in the world (Corva, 2014).[76] The Emerald Triangle is also home to outstanding natural resources including large stands of old-growth California redwood (Sequoia sempervirens (D. Don) Endl.) and relatively uninterrupted runs of endangered and threatened anadromous fish, such as steelhead trout (Oncorhynchus mykiss) and Chinook salmon (Oncorhynchus tshawytscha). The potential conflict between the rapidly growing cannabis industry and the habitat needed by these protected species is thus a federal-level, as well as a local-level, environmental concern.

Popular media speculation about environmental impacts of cannabis agriculture in this region, especially impacts on water, is widespread (Bland, 2014, Harkinson, 2014, Ryzik, 2014),[77-79] but empirical research is limited (Carah et al., 2015).[69] The small body of scientific research points to profound negative consequences, including decreased stream flows (Bauer et al., 2015),[80] rodenticide poisoning of rare carnivores (Gabriel et al., 2012),[81] and high carbon emissions from greenhouses (Mills, 2012).[82]

2. Experimental Section

It is one of the fastest-growing plants. Moreover, its extensive root system and characteristic of reduced weed pressure can support to improve soil structure and subsequent crop yield (Amaducci et al., 2008a).[83] Being a rotation crop it can also enhance the economic sustainability of growers (Finnan and Styles, 2013).[84] China is the main ex-porter of hemp fiber and hemp textiles.

Hemp plant is unique due to its multiple products. A plethora of research reported its domestic and industrial applications in paper packaging, cigarette paper, wax paper, electrical insulation paper, textile, pulp, composite material, construction material, fuel, medical treatment, food, cosmetics, synthetic plastic, and fiberglass (Dutt et al., 2002; 2003; 2007; Harris et al., 2008; Sgriccia et al., 2008; Rice, 2008; Kolosov, 2009).[85-91]

Hemp has medicinal value also, specifically grown for cannabidiol (CBD) oil to cure various diseases such as cancer, diabetes, and epilepsy. Although, the extraction of CBD from hemp flowers and leaves was illegal in some parts of the world, but it can also be processed from stems and stalks.

Hemp flowers are also source of fiber, carbohydrates, vitamins, minerals (B, Cu, Zn, Mn, and Fe) and essential amino acids as well as poultry and livestock feed. Hemp seeds are used in paints, varnishes and lamp oil, biofuel (ethanol), skin moisturizer, and plastics. Seeds are also high in fiber, aiding an animal's digestive system. Currently hemp fed livestock is limited to certain species, while excluding others, including poultry. Hemp can also play an important role in environmental conservation due to its growth potential in heavy metal polluted soils. Hemp can enrich and stabilize unproductive lands by reducing weed pressure and soil erosion. However, hemp cultivation was neglected in some regions, due to its psychoactive secondary metabolite contents. In Europe, industrial hemp varieties published by EU (Regulation (EC) N° 1251/99 and subsequent amendments) are accepted for cultivation which are allowed for planting after verifying their THC $< 0.2\%$ w/w (Regulation EC N°. 1124/2008-12 November 2008) (Da Porto et al., 2014).[92] Few years ago a regulation (N°172/2017) was published on the regulation of hemp production, commerce and its therapeutic use in Italy.

Different genotypes were selected and registered along with their cultivation methods to avoid new hybrids birth (Ferrante et al., 2019).[93]

Hemp has a rich history of use in human civilization, which dates back to 8,000 BC. Hemp was originated in Central Asia (Frassinetti et al., 2018).[94]

Hemp is native to Central and South Asian countries evident for last 5000 years (Nissen et al., 2010)[95] such as China, India, Iran and Pakistan but is now distributed in temperate countries, nearly worldwide. It can grow vigorously between 13 and 22°C and can adapt different soil types, particularly heavy non-acid soils. It prefers deep and well-aerated soils of pH around 6, having sufficient moisture and nutrient holding capacity. However, it is sensitive to soil compaction and flooding. Heavy rain water can cause hemp lodging in poorly drained soils. Uniform and fast seed germination required a fine seedbed. However, conventional seedbed preparation and drilling are almost certainly ideal. Seed depth is an important factor for seedlings emergence for example; seed depth > 2 inches may affect the uniform emergence of hemp seedlings.

"No-till systems" can be used with high outcome, which is more susceptible to variable emergence depending on growing season. Sufficient amount of nutrients is required by the crop which will finally be removed from the soil at harvest.

Cultivation of industrial hemp traditionally targets the primary bast fiber production. However, plant density and self-thinning are the limiting factors for fiber yield and quality (van der Werf and Turunen, 2008),[96] while according to García-Tejero et al. (2014), irrigation and density are the two main factors affecting hemp fiber quality in the Mediterranean semi-arid environment. Low plant density, lodging, and fun-gal infection can reduce the fiber yield and quality. Stem elongation and diameter; significantly depend on plant density and weather conditions (Schafer and Honermeier, 2006).[97] Hemp can grow well in mild climate, humid atmosphere with 25–30 in. rainfall per year. Sufficient soil moisture is necessary for seed germination to well established young plants. During vegetative growth, hemp responds to high temperatures at day time, showing fast growth and increased water needs. After the third pair of leaves develops, it can survive daily low temperatures as low as -0.5°C for 4 to 5 days.

Hemp provides raw material to a large number of traditional and innovative industrial applications (Amaducci et al., 2015).[98] Industrial hemp is a well-known source of bast fiber for textile industry. It can grow under diverse conditions due its relatively easy management and fiber separation (Kolodziejczyk et al., 2012;[99] Shahzad, 2012).[62] Hemp is an important crop enabling the production of environmentally friendly, locally produced, high-quality textiles.

True hemp has a fine, light-colored, lustrous, and strong bast fiber of high specific strength, low density, economical production, non-abrasiveness and biodegradability (Dhakal and Zhang, 2015).[100] However, fiber quality is affected by a variety of factors, such as agro-technique, growing conditions, and harvesting (Amaducci et al., 2005; Amaducci et al., 2008b; Höppner and Menge-Hartmann, 2007).[101-103] Due to high strength of hemp fiber, it is used in manufacturing of ropes (Shahzad, 2012), carpets, and rugs, etc., but have limited use due to difficult bleaching.

Jarabo et al. (2012)[104] reported that ordinary material from hemp is its strong and durable fiber. Hemp bast fibers are among the earth‘s longest natural soft fibers. Outer long fibers from are useful for textiles while, inner short fiber are used in paper making or other industrial products, which were left in the field for 10–20 days to “ret”. Fiber hemp could be an alternative to wood as a raw material for pulp and paper production. Vonapartis et al. (2015)[55] also reported that hemp fiber is durable and can be used to make clothes, canvas, fishnets, constructional materials, and reinforcement in preparing composite parts such as in thermal and acoustic insulation.

Pharmaceutical hemp contained bioactive compounds of interest for human health (Zuardi, 2006).[5] According to Maiolo et al. (2018)[105] hemp seed oil has been used as medicine in China for at least 3000 years. It can reduce stress, anxiety, pain, and improves sleep quality and digestion. Likewise, it can be used against cancer and cardiovascular diseases and to normalize cholesterol level and blood pressure (Devi and Khanam 2019).[106] Industrial hemp by-products, including inflorescences, represent an exploitable material to produce niche products for the medicinal industry (Fiorini et al., 2019).[107]

Hemp gained importance with a global market for low THC valued at $100 to 2000 million per year (Montserrat-dela Paz et al. 2014).[108] In traditional Chinese medicine hemp has its own worth for the treatment of constipation, dermatological diseases, and the gastrointestinal diseases (Cheng et al., 2011; Rodriguez-Leyva and Pierce, 2010).[109,110]

Hemp seed oil can be a dietary source of natural antioxidants to support health and avoid diseases (Yu et al. 2005).[111] Hemp seed lipids contain essential fatty acids (almost 80%) used in cell membranes, consisting of linoleic, ω-6 and α-linolenic acid, ω-3(3:1), which is good for human nutrition and to prevent several pathological disorders (Kiralan et al., 2010).[112]

Hemp seed extracts have been found to demonstrate strong antioxidant and anti-aging effects (Cai et al., 2010; Gowran et al., 2011; Chen et al, 2012; Moldzio et al., 2012; Lin et al. 2016)[113-117] as well as improved impaired learning and memory induced by chemical drugs in mice (Luo et al.2003).[118] The seeds contain amino acid arginine which is considered good for heart-health. However, L-arginine is a precursor to nitric oxide. Hemp seed gamma-linolenic acid (GLA) produces prostaglandin E1 to reduce prolactin hormonal effects. Prolactin is thought to play a role in premenstrual syndrome. According to Saberivand et al. (2010)[119] hemp seeds GLA can reduce menopause.

Furthermore, the soluble and insoluble fiber of seeds can effect digestion. Soluble fibers slow down the digestion by dissolving into a gel-like texture. Whereas, insoluble fiber helps add bulk to stool as they do not dissolve at all.

Dietary hemp seed affects platelet aggregation, ischemic heart disease, and cardiovascular health (Rodriguez-Leyva and Pierce, 2010).[110] Rezapour-Firouzi et al., (2013)[120] reported that co-supplemented hemp seed and evening primrose oils with Hot-nature diet have beneficial effects in improving clinical score in Relapsing-Remitting Multiple Sclerosis (RRMS) patients which were confirmed by immunological findings.

CBD extracted from hemp can help to reduce chronic pain by impacting endocannabinoid receptor activity, reducing inflammation and interacting with neurotransmitters (Darkovska-Serafimovska et al., 2018).[121] CBD oil has shown promise as a treatment for both depression and anxiety.

CBD oil has even been used to safely treat insomnia and anxiety in children with post-traumatic stress disorder (Shannon and Opila 2016).[122] CBD showed antidepressant effects (Zanelati et al., 2010; Sales et al., 2018).[123,124] CBD induced cell death in human breast cancer cells during a test tube study; this showed anticancer activity of CBD (Shrivastava et al., 2011).[125] In another study on mice, CBD inhibited aggressive breast cancer cells (McAllister et al., 2007).[126] However, these were test-tube and animal based studies, further human based studies are needed before conclusions can be made. CBD can be helpful to cure acne: a skin disease due to sebaceous glands inflammation and high sebum production, affecting more than 9% of population. CBD may be an efficient and safe way to treat acne (Oláh et al., 2014; Tan and Bhate, 2015).[127,128] CBD is also effective against Parkinson‘s disease and Alzheimer‘s disease (Chagas et al., 2014; Watt and Karl, 2017).[129,130] CBD can reduce high blood pressure (Jadoon et al., 2017).[131] CBD exerts anti-inflammatory effects in different disease models and lessen pain and spasticity associated with multiple sclerosis in humans (Rajesh et al., 2010).[132] With the increasing interest of hemp CBD and hemp oils medicinal use, more research is required to better understand their potential efficacy and purported safety profile.

Nutritional value of hemp made it an asset for human food (Devi and Khanam, 2019). Nutritional properties of hemp seeds and their products are achieving a growing popularity as food for humans (Andre et al., 2016) and animals in Asia and Eastern Europe. Hemp seeds are good source of plant-based protein for example, 2–3 table spoons of hemp seeds gives nearly 11g of protein, containing methionine, lysine and cysteine. Hemp seeds contain 20–25% proteins of biological value equal to hen‘s egg white (Mikulec et al.

2019),[133] 25–35% of lipids, 20–30% carbohydrates, 10–15% insoluble fibers and minerals such as phosphorus, potassium, sodium, magnesium, sulfur, calcium, iron, and zinc (Callaway, 2004; Galasso et al., 2016).[134,135] The seeds contain non-medicinal levels (< 0.3%) of psychoactive compound known as δ-9-tetrahydrocannabinol (THC). Health benefits of hemp seed are related to the high level of polyunsaturated fatty acids (PUFAs) present in the seed (Kolodziejczyk et al., 2012). Hemp-seed oil does not exert psychotic effect; whereas, it exhibits health beneficial activity due to its optimum proportion ofω-6 linoleic acid andω-3 alpha-linolenic acid (3:1) as recommended in healthy diet (Siudem et al., 2019; Da Porto et al., 2015).[136,137] Vitamins D and E (fat-soluble vitamins) are other important constituents in hemp-seed oil. After extraction of hemp seed oil, the residue can be converted into various protein-rich food products. Key storage proteins in hemp seed are water-soluble albumin (~25%) and salt-soluble globulins or edestin (~75%).

Presence of high level of arginine and a sulfur-rich protein fraction, in the seed protein boost up nutritional significance of hemp (Aluko, 2017).[138] Thus, hemp seed proteins and hydro-lysates can be used to formulate functional foods. and oil are used in several certified foods of high nutritional values due to their content in minerals, vitamins (mostly A, C and E complexes), carbohydrates, proteins, and lipids (Ferrante et al., 2019). Hemp flour influenced protein content and antioxidant properties of bread (Mikulec et al., 2019). It is also used for gluten-free bread production (Korus et al., 2017).[139] Addition of hemp flour or hemp seed cake can reduce the volume of wheat bread (Švec and Hrušková, 2013; 2015).[140,141] Hemp seeds or sprouts exert favorable effects on yeast and human cells and should be investigated as functional food (Frassinetti et al., 2018). In a recent study, Kladar et al. (2021)[142] reported that hemp-based food should not be consumed by under aged as hemp seed oil may represent significant health risk in term of Δ9-THC.

4. Conclusions

Hemp belongs to the oldest and most known versatile plants and it is one of the high-yielding crops with low or no pesticide requirement, and modest demands for fertilizer. Due to these features, its introduction into the intensive farming systems could be constitute a long-term strategy in maintaining farming systems and practices that are particularly favourable to environmental and climate policy goals. In this review, we summarized recent developments on the agricultural crop, hemp.

Conflicts of Interest

The authors declare no conflict of interest.

References

1 Datwyler S.L.; Weiblen G.D. Genetic Variation in Hemp and Marijuana (*Cannabis sativa* L.) According to Amplified Fragment Length Polymorphisms. *J. Forensic Sci*., 2006, **51**, 371–375. [CrossRef]

2 National Institute of Drug Abuse, — Quarterly Report, Potency Monitoring project, Report 100, University of Mississippi, 2008. Based on sample tests of illegal cannabis seizures (December 16, 2007, through March 15, 2008).

3 Small E.; Marcus D. Tetrahydrocannabinol Levels in Hemp (*Cannabis sativa*) Germplasm Resources. *Econ. Bot.*, 2003, **57**, 545-558. [CrossRef]

4 Hillig K.W.; Mahlberg P.G. A Chemotaxonomic Analysis of Cannabinoid Variation in *Cannabis* (Cannabaceae). *Am. J. Bot.*, 2004, **91**, 966-975. [CrossRef]

5 Zuardi A.W.; Crippa J.A.S.; Hallak J.E.; Moreira F.A.; Guimarães F.S. Cannabidiol, A *Cannabis sativa* Constituent, as an Antipsychotic Drug. *Braz. J. Med. Biol. Res.*, 2006, **39**, 421-429. [CrossRef]

6 Anndrea H. CRS communication with Hemp Oil Canada Inc., December 2009. Pollen is present at a very early plant development stage.

7 Struik P.C.; Amaducci S.; Bullard M.J.; Stutterheim N.C.; Venturi G.; Cromack H.T.H. Agronomy of Fibre Hemp (*Cannabis sativa* L.) in Europe. *Ind. Crops Prod*., 2000, **11**, 107–118. [CrossRef]

8 Carus M.; Sarmento L. The European Hemp Industry: Cultivation, Processing and Applications for Fibres, Shives, Seeds and Flowers. European Industrial Hemp Association (EIHA). 2016. [Link]

9 Baldini M.; Ferfuia C.; Zuliani F.; Danuso F. Suitability Assessment of Different Hemp (*Cannabis sativa* L.) Varieties to the Cultivation Environment. *Ind. Crops Prod*., 2020, **143**, 111860. [CrossRef]

10 Salentijn E.M.J.; Zhang Q.; Amaducci S.; Yang M.; Trindade L.M. New Developments in Fiber Hemp (*Cannabis sativa* L.) Breeding. *Ind. Crops Prod*., 2015, **68**, 32–41. [CrossRef]

11 European Commission (EC). Commission Regulation No. 809/2014 of 17 July 2014 laying down rules for the application of Regulation (EU) No 1306/2013 of the European Parliament and of the Council with regard to the integrated administration and control system, rural development measures and cross compliance. Off. J. Eur. Union, 2014, 227, 69–124. [Link]

12 European Industrial Hemp Association (EIHA). Hemp cultivation & Production in Europe in 2018. Available online: (accessed on 7 November 2020). [Link]

13 Campiglia E.; Radicetti E.; Mancinelli R. Plant Density and Nitrogen Fertilization Affect Agronomic Performance of Industrial Hemp (*Cannabis sativa* L.) in Mediterranean Environment. *Ind. Crops Prod*., 2017, **100**, 246–254. [CrossRef]

14 Angelini L.G.; Tavarini S.; Candilo M.D. Performance of New and Traditional Fiber Hemp (*Cannabis sativa* L.) Cultivars for Novel Applications: Stem Bark, and Core Yield and Chemical Composition. *J. Nat. Fibers,* 2016, **13**, 238–252. [CrossRef]

15 Faux A.-M.; Draye X.; Lambert R.; d'Andrimont R.; Raulier P.; Bertin P. The Relationship of Stem and Seed Yield to Flowering Phenology and Sex Expression in Monoecious Hemp (*Cannabis sativa* L.). *Eur. J. Agron*., 2013, **47**, 11–22. [CrossRef]

16 Tang K.; Struik P.C.; Yin X.; Thouminot C.; Bjelkova M.; Stramkale V. Comparing Hemp (*Cannabis sativa* L.) Cultivars for Dual-purpose Production under Contrasting Environments. *Ind. Crops Prod*., 2016, **87**, 33–46. [CrossRef]

17 Cosentino S.L.; Riggi E.; Testa G.; Scordia D.; Copani V. Evaluation of European developed fibre hemp genotypes (*Cannabis sativa* L.) in semi-arid Mediterranean environment. *Ind. Crops Prod*., 2013, **50**, 312–324. [CrossRef]

18 Hall J.; Bhattarai S.P.; Midmore D.J. The Effects of Different Sowing Times on Maturity Rates, Biomass, and Plant Growth of Industrial Fiber Hemp. *J. Nat. Fibers,* 2013, **10**, 40–50. [CrossRef]

19 Sikora V.; Berenji J.; Latkovic D. Influence of Agroclimatic Conditions on Content of Main Cannabinoids in Industrial Hemp (*Cannabis sativa* L.). *Genetika-Belgrade*, 2011, **43**, 449–456. [CrossRef]

20 García-Tejero L.F.; Durán-Zuazo V.H.; Pérez-Álvarez R.; Hernández A.; Casano S.; Morón M.; Muriel-Fernández J.L. Impact of Plant Density and Irrigation on Yield of Hemp (*Cannabis sativa* L.) in a Mediterranean Semi-arid Environment. *J. Agric. Sci. Technol*., 2014, **16**, 887–895. [Link]

21 Isman M.B.; Machial C.M. Chapter 2 Pesticides Based on Plant Essential Oils: From Traditional Practice to Commercialization. *Advances in Phytomedicine*, 2006, **3**, 29-44. [CrossRef]

22 Thakore Y. The Biopesticide Market for Global Agricultural Use. *Ind. Biotechnol*., 2006, **2**, 194–208. [CrossRef]

23 Benelli G.; Pavela R.; Iannarelli R.; Petrelli R.; Cappellacci L.; Cianfaglione K.; Afshar F.H.; Nicoletti M.; Canale A. Synergized

Mixtures of Apiaceae Essential Oils and Related Plant-Borne Compounds: Larvicidal Effectiveness on the Filariasis Vector *Culex quinquefasciatus* Say. *Ind. Crops Prod*., 2017a, **96**, 186–195. [CrossRef]
24 Benelli G.; Pavela R. Repellence of Essential Oils and Selected Compounds against Ticks – A Systematic Review. *Acta Trop*., 2018a, **179**, 47–54. [CrossRef]
25 Benelli G.; Pavela R. Beyond Mosquitoes − Essential Oil Toxicity and Repellency against Bloodsucking Insects. *Ind. Crops Prod*., 2018b, **117**, 382–392. [CrossRef]
26 Desneux N.; Decourtye A.; Delpuech J.M. The Sublethal Effects of Pesticides on Beneficial Arthropods. *Annu. Rev. Entomol*., 2007, **52**, 81–106. [CrossRef]
27 Benelli G.; Pavela R.; Canale A.; Mehlhorn H. Tick Repellents and Acaricides of Botanical Origin: A Green Roadmap to Control Tick-Borne Diseases? *Parasitol. Res*., 2016, **115**, 2545–2560. [CrossRef]
28 Pavela R.; Benelli G. Essential Oils as Eco-friendly Biopesticides? Challenges and Constraints. *Trends Plant Sci*., 2016, **21**, 1000–1007. [CrossRef]
29 Stevenson P.C.; Isman M.B.; Belmain S.R. Pesticidal Plants in Africa: A Global Vision of New Biological Control Products from Local Uses. *Ind. Crops Prod.*, 2017, **110**, 2-9. [CrossRef]
30 Isman M.B. A Renaissance for Botanical Insecticides. *Pest Manag. Sci*., 2015, **71**, 1587–1590. [CrossRef]
31 Pavela R. History, Presence and Perspective Of Using Plant Extracts as Commercia Botanical Insecticides and Farm Products for Protection Against Insects - A Review. *Plant Prot. Sci*., 2016, **52**, 229–241. [Link]
32 Potter D.J. The Propagation, Characterisation and Optimisation of *Cannabis sativa* L. as a Phytopharmaceutical. Pharmaceutical Sciences, 2009. King's College, London. [Link]
33 Bertoli A.; Tozzi S.; Pistelli L.; Angelini L.G. Fiber Hemp Inflorescences: From Crop-Residues to Essential Oil Production. *Ind. Crops Prod*., 2010, **32**, 329–337. [CrossRef]
34 Benelli G.; Pavela R.; Giordani C.; Casettari L.; Curzi G.; Cappellacci L.; Petrelli R.; Maggi F. Acute and Sub-Lethal Toxicity of Eight Essential Oils of Commercial Interest Against The Filariasis Mosquito *Culex Quinquefasciatus* and the Housefly *Musca domestica*. *Ind. Crops Prod*., 2018b, **112**, 668–680. [CrossRef]
35 Benelli G.; Pavela R.; Lupidi G.; Nabissi M.; Petrelli R; Kamte S.L.N.; Cappellacci L.; Fiorini D.; Sut S.; Dall'Acqua S.; Maggi F. The Crop-Residue of Fiber Hemp cv. Futura 75: From a Waste Product to a Source of Botanical Insecticides. *Environ. Sci. Poll. Res*., 2018a, **25**, 10515–10525. [CrossRef]
36 Bedini S.; Flamini G.; Cosci F.; Ascrizzi R.; Benelli G.; Conti B. *Cannabis sativa* and *Humulus lupulus* Essential Oils as Novel Control Tools against *the Invasive Mosquito Aedes albopictus and Fresh Water Snail Physella* acuta. *Ind. Crops Prod*., 2016, **85**, 318–323. [CrossRef]
37 Benelli G.; Mehlhorn H. Declining Malaria, Rising Dengue and Zika Virus: Insights for Mosquito Vector Control. *Parasitol. Res*., 2016, **115**, 1747–1754. [CrossRef]
38 Davies M.P.; Anderson M.; Hilton A.C. The Housefly *Musca domestica* as a Mechanical Vector of *Clostridium difficile*. *J. Hosp. Infect*., 2016, **94**, 263–267. [CrossRef]
39 Benelli G.; Romano D. Mosquito Vectors of Zika Virus. *Entomol. Generalis*, 2017, **36**, 309–318. [CrossRef]
40 Vadivalagan C.; Karthika P.; Murugan K.; Panneerselvam C.; Del Serrone P.; Benelli G. Exploring Genetic Variation in Haplotypes of the Filariasis Vector Culex Quinquefasciatus (Diptera: Culicidae) through DNA Barcoding. *Acta Trop*., 2017, **169**, 43–50. [CrossRef]
41 Bass C.; Puinean A.M.; Zimmer C.T.; Denholm I.; Field L.M.; Foster S.P.; Gutbrod O.; Nauen R.; Slater R.; Williamson M.S. The Evolution of Insecticide Resistance in the Peach Potato Aphid, *Myzus persicae*. *Insect Biochem. Mol. Biol.*, 2014, **51**, 41-51. [CrossRef]
42 PM E. 7/124 (1) *Spodoptera littoralis, Spodoptera litura, Spodoptera frugiperda, Spodoptera eridania*. *EPPO Bull*, 2015, **45**, 410-444. [CrossRef]
43 Chabbert B.; Kurek B.; Beherec O. Physiology and Botany of Industrial Hemp. In: P. Boulac S. Allegret L. Arnaud, editors, Hemp: Industrial Production and Uses. CABI, Boston, MA. 2013, 36-47. [CrossRef]
44 H.R. 2642, 113th Cong., (sec. 7606 (2)) 698-699 (2014) (enacted). [Link]
45 Alligret S. The History of Hemp. In: P. Boulac, S. Allegret, L. Arnaud, editors, Hemp: Industrial Production and Uses. CABI, Boston, MA. 2013, 4-26. [CrossRef]
46 Small E.; Marcus D. Hemp: A New Crop with New Uses for North America. In *Trends in New Crops and New Uses.* 2002, 284-326. ASHS Press. [Link]
47 Rude B.J; Baldwin B.S.; Hanson K.C. Performance of and Nutrient Utilization by Steers Consuming Kenaf, Pearl Millet, or Mixed Grass. *Prof. Anim. Sci*., 2002, **18**, 74-87. [CrossRef]
48 Gakhar N.; Goldberg E.; Jing M.; Gibson R.; House J.D. Effect of Feeding Hemp Seed and Hemp Seed Oil on Laying Hen Performance and Egg Yolk Fatty Acid Content: Evidence of their Safety and Efficacy for Laying Hen Diets. *Poult. Sci*., 2012, **91**, 701-711. [CrossRef]
49 Gibb D.J.; Shah M.A.; Mir P.S.; McAllister T.A. Effect of Full-fat Hemp Seed on Performance and Tissue Fatty Acids of Feedlot Cattle. *Can. J. Anim. Sci.*, 2005, **85**, 223-230. [CrossRef]
50 Hessle A.; Eriksson M.; Nadeau E.; Turner T.; Johansson B. Cold-pressed Hempseed Cake as a Protein Feed for Growing Cattle. *Acta Agric. Scand. Section A*., 2008, **58**, 136-145. [CrossRef]
51 Mediavilla V.; Leupin M.; Keller A. Influence of the Growth Stage of Industrial Hemp on the Yield Formation in Relation to Certain Fiber Quality Traits. *Ind. Crops Prod*., 2000, **13**, 49-56. [CrossRef]
52 Amaducci S.; Zatta A.; Pelatti F.; Venturi G. Influence of Agronomic Factors on Yield and Quality of Hemp (*Cannabis sativa* L.) Fibre and Implication for an Innovative Production System. *Field Crops Res.*, 2008, **107**, 161-169. [CrossRef]
53 Pecenka R.; Idler C.; Grundmann P. Tube Ensiling of Hemp- Initial Practical Experience. *Agric. Eng. Res.*, 2007, **13**, 15-26. [Link]
54 Andre C.M.; Hausman J.F.; Guerriero G. *Cannabis sativa*: The Plant of the thousand and One Molecules. *Front. Plant Sci*., 2016, **7**, 19. [CrossRef]
55 Vonapartis E.; Aubin M.P.; Seguin P.; Mustafa A.F.; Charron J.B. Seed Composition of Ten Industrial Hemp Cultivars Approved for Production in Canada. *J. Food Composit. Anal*., 2015, **39**, 8–12. [CrossRef]
56 Ranalli P.; Venturi G. Hemp as a Raw Material for Industrial Applications. *Euphytica*, 2004, **140**, 1–6. [CrossRef]
57 Adesina I.; Bhowmik A.; Sharma H.; Shahbazi A. A Review on the Current State of Knowledge of Growing Conditions, Agronomic Soil Health Practices and Utilities of Hemp in the United States. *Agriculture*, 2020, **10**, 129. [CrossRef]
58 Agriculture and Agri-Food Canada. Canada's Industrial Hemp Industry. 2016. [Link]
59 West D.P. Hemp and Marijuana: Myths & Realities. 1998. [Link]
60 Small E. Cannabis: A Complete Guide; CRC Press: Boca Raton, FL, USA, 2017. [Link]
61 Mass E. Hemp: The New, Old Fiber Makes a Comeback for Clothes, Fabrics, and Home Furnishings. *Nat. Life,* 2009, **127**, 36.
62 Shahzad A. Hemp Fiber and its Composites—A Review. *J. Comp. Mater*., 2012, **46**, 973–986. [CrossRef]
63 Benessaiah K.; Sayles J. Drug Trafficking's Effects on Coastal Ecosystems. *Science,* 2014, **343**, 1431. [CrossRef]
64 Mcsweeney K.; Nielsen E.A.; Taylor M.J.; Wrathall D.J.; Pearson Z.; Wang O.; Plumb S.T. Drug Policy as Conservation Policy: Narco-Deforestation. *Science*, 2014, **343**, 489–490. [CrossRef]
65 Decorte T.; Potter G.; Bouchard M. Worldwide Weed: Global Trends in Cannabis Cultivation and its Control. Farnham, UK: Ashgate Publishing, 2011. [Link]
66 Potter G.; Bouchard M.; Decorte T. The Globalization of Cannabis Cultivation. In: Decorte T.; Potter G.; Bouchard B., eds. Worldwide Weed. Global Trends Cannabis Cultivation its Control. Farnham, UK: Ashgate Publishing: 2011, 1–22. [Link]
67 Weisheit R. Cannabis cultivation in the United States. In: Decorte, T.; Potter, G.; Bouchard, M., eds. Worldwide weed. Global trends cannabis cultivation and its control. Farnham, UK: Ashgate Publishing: 2011, 145–162. [Link]
68 Crick E.H.; Haase J.; Bewley-Taylor D. Legally Regulated Cannabis Markets in the US: Implications and Possibilities. Policy Report 1. Wales, UK: Global Drug Policy Observatory. Swansea University, 2013. (11 January 2017). [Link]
69 Eisenstein M. Medical marijuana: Showdown at the Cannabis Corral. *Nature*, 2015, **525**, S15–S17. [CrossRef]
70 Cole J. Memorandum for all United States Attorneys. Guidance Regarding Marijuana Enforcement. U.S. Department of Justice. 2013. [Link]
71 State of California. 2015. Assembly Bill No. 243. [Link]

72 Arcview Market Research. The state of legal marijuana markets. 2014, 3rd ed. San Francisco: Arcview.
73 McGreevy P. California Sets New Rules for Medical Pot Industry. 2015. (11 January 2017). [Link]
74 Carah J.K.; Howard J.K.; Thompson S.E.; Short Gianotti A.G.; Bauer S.D.; Carlson S.M.; Dralle D.N.; Gabriel M.W.; Hulette L.L.; Johnson B.J.; Knight C.A.; Kupferberg S.J.; Martin S.L.; Naylor R.L.; Power M.E. High Time for Conservation: Adding the Environment to the Debate on Marijuana Liberalization. *Bioscience*, 2015, **65**, 822–829. [CrossRef]
75 Sides H. Science Seeks to Unlock Marijuana's Secrets. National Geographic Magazine. June, 2015. [Link]
76 Corva D. Requiem for a CAMP: The Life and Death of a Domestic US Drug War Institution. *International Journal of Drug Policy*, 2014, **25**, 71-80. [CrossRef]
77 Bland A. California's pot farms could leave salmon runs truly smoked. *National Public Radio,* 2014.
78 Harkinson J. The Landscape-Scarring, Energy-Sucking, Wildlife-Killing Reality of Pot Farming: This is your Wilderness on Drugs. *Mother Jones,* 2014.
79 Ryzik M. Dry California fights illegal use of water for cannabis. *New York Times,* 2014. [Link]
80 Bauer S.; Olson J.; Cockrill A.; van Hattem M.; Miller L.; Tauzer M.; Leppig G. Impacts of Surface Water Diversions for Marijuana Cultivation on Aquatic Habitat in Four Northwestern California Watersheds. *PLoS One*, 2015, **10**, e0120016. [CrossRef]
81 Gabriel M.W.; Woods L.W.; Poppenga R.; Sweitzer R.A.; Thompson C.; Matthews S.M.; Higley J.M.; Keller S.M.; Purcell K.; Barrett R.H.; Wengert G.M. Anticoagulant Rodenticides on our Public and Community Lands: Spatial Distribution of Exposure and Poisoning of a Rare Forest Carnivore. *PloS one*, 2012, **7**, e40163. [CrossRef]
82 Mills E. The Carbon Footprint of Indoor Cannabis Production. *Energy Policy*, 2012, **46**, 58–67. [CrossRef]
83 Amaducci S.; Zatta A.; Raffanini M.; Venturi G. Characterisation of Hemp (*Cannabis sativa* L.) Roots under Different Growing Conditions. *Plant Soil*, 2008, **313**, 227-235. [CrossRef]
84 Finnan J.; Styles D. Hemp: A More Sustainable Annual Energy Crop for Climate and Energy Policy. *Energy Policy*, 2013, **58**, 152-162. [CrossRef]
85 Dutt D.; Upadhyaya J.S.; Ray A.K.; Malik R.S.; Upadhyaya M.K. Development of Specialty Papers is an Art: Wax Match Tissue Paper from Indigenous Raw Materials—Part I. *J. Sci. Ind. Res.*, 2002, **61**, 1046–1050 [Link]
86 Dutt D.; Singh V.; Ray A.; Mukherjee S. Development of Specialty Papers is an Art: Electrical Insulation Paper from Indigenous Raw Materials-Part IX. *J. Sci. Ind. Res.*, 2003, **62**, 1145-1151. [Link]
87 Dutt D.; Tyagi C.H.; Malik R.S. Studies on Effect of Growth Factor on Morphological, Chemical and Pulp and Papermaking Characteristics and its Impact on Fluff Generation. *Ind. J. Chem. Technol*., 2007, **14**, 626–634 [Link]
88 Harris A.T.; Riddlestone S.; Bell Z.; Hartwell P.R. Towards Zero Emission Pulp and Paper Production: The BioRegional MiniMill. *J. Clean. Prod.*, 2008, **16**, 1971-1979. [CrossRef]
89 Sgriccia N.; Hawley M.C.; Misra M. Characterization of Natural Fiber Surfaces and Natural Fiber Composites. *Compos. Part A: Appl. Sci. Manuf.*, 2008, **39**, 1632-1637. [CrossRef]
90 Rice B. Hemp as a Feedstock for Biomass-to-Energy Conversion. *J. Ind. Hemp*, 2008, **13**, 145-156. [CrossRef]
91 Kolosov C.A. Evaluating the Public Interest: Regulation of Industrial Hemp under the Controlled Substances Act. *UCLA L. Rev.*, 2009, **57**, 237. [Link]
92 Da Porto C.; Decorti D.; Natolino A. Separation of Aroma Compounds from Industrial Hemp Inflorescences (*Cannabis sativa* L.) by Supercritical CO_2 Extraction and On-line Fractionation. *Ind. Crops Prod.*, 2014, **58**, 99-103. [CrossRef]
93 Ferrante C.; Recinella L.; Ronci M.; Menghini L.; Brunetti L.; Chiavaroli A.; Leone S.; Di Iorio L.; Carradori S.; Tirillini B.; Angelini P. Multiple Pharmacognostic Characterization on Hemp Commercial Cultivars: Focus on Inflorescence Water Extract Activity. *Food Chem. Toxicol.*, 2019, **125**, 452-461. [CrossRef]
94 Frassinetti S.; Moccia E.; Caltavuturo L.; Gabriele M.; Longo V.; Bellani L.; Giorgi G.; Giorgetti L. Nutraceutical Potential of Hemp (*Cannabis sativa* L.) Seeds and Sprouts. *Food Chem.*, 2018, **262**, pp.56-66. [CrossRef]
95 Nissen L.; Zatta A.; Stefanini I.; Grandi S.; Sgorbati B.; Biavati B.; Monti A. Characterization and Antimicrobial Activity of Essential Oils of Industrial Hemp Varieties (*Cannabis sativa* L.). *Fitoterapia*, 2010, **81**, 413-419. [CrossRef]
96 Van der Werf H.M.; Turunen L. The Environmental Impacts of the Production of Hemp and Flax Textile Yarn. *Ind. Crops Prod.*, 2008, **27**, 1-10. [CrossRef]
97 Schäfer T.; Honermeier B. Effect of sowing date and plant density on the cell morphology of hemp (Cannabis *sativa L.). Ind. Crops Prod., 2006, **23**, 88-98.* [CrossRef]
98 Amaducci S.; Scordia D.; Liu F.H.; Zhang Q.; Guo H. Testa G.; Cosentino S.L. Key Cultivation Techniques for Hemp in Europe and China. *Ind. Crops Prod.*, 2015, **68**, 2-16. [CrossRef]
99 Kolodziejczyk P.; Ozimek L.; Kozłowska J. The Application of Flax and Hemp Seeds in Food, Animal Feed and Cosmetics Production. In *Handbook of Natural Fibres,* 2012, 329-366. Woodhead Publishing. [CrossRef]
100 Dhakal H.N.; Zhang Z. The Use of Hemp Fibres as Reinforcements in Composites. In *Biofiber Reinforcements in Composite Materials,* 2015, 86-103. Woodhead Publishing. [CrossRef]
101 Amaducci S.; Pelatti F.; Bonatti P.M. Fibre Development in Hemp (*Cannabis sativa* L.) as Affected by Agrotechnique: Preliminary Results of a Microscopic Study. *J. Ind. Hemp*, 2005, **10**, 31-48. [CrossRef]
102 Amaducci S.; Colauzzi M.; Zatta A.; Venturi G. Flowering Dynamics in Monoecious and Dioecious Hemp Genotypes. *J. Ind. Hemp*, 2008, **13**, 5-19. [CrossRef]
103 Höppner F.; Menge-Hartmann U. Yield and Quality of Fibre and Oil of Fourteen Hemp Cultivars in Northern Germany at Two Harvest Dates. *Landbauforsch Volk*., 2007, **57**, 219–232. [Link]
104 Jarabo R.; Fuente E.; Monte M.C.; Savastano Jr H.; Mutjé P.; Negro C. Use of Cellulose Fibers from Hemp Core in Fiber-cement Production. Effect on Flocculation, Retention, Drainage and Product Properties. *Ind. Crops Prod.*, 2012, **39**, 89-96. [CrossRef]
105 Maiolo S.A.; Fan P.; Bobrovskaya L. Bioactive Constituents from Cinnamon, Hemp Seed and Polygonum Cuspidatum Protect against H_2O_2 but not Rotenone Toxicity in a Cellular Model of Parkinson's Disease. *J. Tradit. Complement. Med.*, 2018, **8**, 420-427. [CrossRef]
106 Devi V.; Khanam S. Comparative Study of Different Extraction Processes for Hemp (*Cannabis sativa*) Seed Oil Considering Physical, Chemical and Industrial-Scale Economic Aspects. *J. Clean. Prod.*, 2019, **207**, 645-657. [CrossRef]
107 Fiorini D.; Molle A.; Nabissi M.; Santini G.; Benelli G.; Maggi F. Valorizing Industrial Hemp (*Cannabis sativa* L.) By-products: Cannabidiol Enrichment in the Inflorescence Essential Oil Optimizing Sample Pre-Treatment Prior to Distillation. *Ind. Crops Prod.*, 2019, **128**, 581-589. [CrossRef]
108 Montserrat-de la Paz S.; Marín-Aguilar F.; García-Gimenez M.D.; Fernández-Arche M.A. Hemp (*Cannabis sativa* L.) Seed Oil: Analytical and Phytochemical Characterization of the Unsaponifiable Fraction. *J. Agric. Food Chem.*, 2014, **62**, 1105-1110. [CrossRef]
109 Cheng C.W.; Bian Z.X.; Zhu L.X.; Wu J.C.; Sung J.J. Efficacy of a Chinese Herbal Proprietary Medicine (Hemp Seed Pill) for Functional Constipation. *Am. J. Gastroenterol.,|* 2011, **106**, 120-129. [Link]
110 Rodriguez-Leyva D.; Pierce G.N. The Cardiac and Haemostatic Effects of Dietary Hempseed. *Nutr. Metab.*, 2010, **7**, 1-9. [CrossRef]
111 Yu L.L.; Zhou K.K.; Parry J. Antioxidant Properties of Cold-Pressed Black Caraway, Carrot, Cranberry, and Hemp Seed Oils. *Food Chem.*, 2005, **91**, 723-729. [CrossRef]
112 Kiralan M.; Gül V.; Kara S.M. Fatty Acid Composition of Hempseed Oils from Different Locations in Turkey. *Span. J. Agric. Res.*, 2010, **8**, 385-390. [CrossRef]
113 Cai P.; Fu X.; Deng A.G.; Zhan X.J.; Cai G.M.; Li S.X. Anti-Aging Effect of Hemp Seed Oil, Protein and Lignanamide of Bama on Old Mice. *Cent. South Pharm.*, 2010, **8**, 165. [Link]
114 Gowran A.; Noonan J.; Campbell V.A. The Multiplicity of Action of Cannabinoids: Implications for Treating Neurodegeneration. *CNS Neurosci. Ther.*, 2011, **17**, 637-644. [CrossRef]
115 Chen T.; He J.; Zhang J.; Li X.; Zhang H.; Hao J.; Li L. The Isolation and Identification of Two Compounds with Predominant Radical Scavenging Activity in Hempseed (Seed of *Cannabis sativa* L.). *Food Chem*., 2012, **134**, 1030–1037. [CrossRef]
116 Moldzio R.; Pacher T.; Krewenka C.; Kranner B.; Novak J.; Duvigneau J.C.; Rausch W.D. Effects of Cannabinoids Δ (9)-tetrahydrocannabinol,

Δ (9)-tetrahydrocannabinolic acid and Cannabidiol in MPP+ Affected Murine mesencephalic Cultures. *Phytomedicine*, 2012, **19**, 819-824. [CrossRef]
117 Lin Z.M.; Chen L.M.; ZM L.; Xia X. The Effect of Different Extracts from Hemp Seed in Mice with Experimental Alzheimers disease. *Pharmacol. Clin. Chin. Mater.*, 2016, **32**, 130-133. [Link]
118 Luo J.; Yin J.H.; Wu H.Z.; Wei Q. Extract from Fructus cannabis Activating Calcineurin Improved Learning and Memory in Mice with Chemical Drug-Induced Dysmnesia. *Acta Pharmacol. Sin.*, 2003, **24**, 1137-1142. [Link]
119 Saberivand A.; Karimi I.; Becker L.A.; Moghaddam A.; Azizi-Mahmoodjigh S.; Yousefi M.; Zavareh S. The effects of *Cannabis sativa* L. Seed (hempseed) in the Ovariectomized Rat Model of Menopause. *Methods Find. Exp. Clin. Pharmacol.*, 2010, **32**, 467-473. [Link]
120 Rezapour-Firouzi S.; Arefhosseini S.R.; Mehdi F.; Mehrangiz E.M.; Baradaran B.; Sadeghihokmabad E.; Mostafaei S.; Fazljou S.M.B.; Torbati M.A.; Sanaie S.; Zamani F. Immunomodulatory and Therapeutic Effects of Hot-nature Diet and Co-Supplemented Hemp Seed, Evening Primrose Oils Intervention in Multiple Sclerosis Patients. *Complement. Ther. Med.*, 2013, **21**, 473-480. [CrossRef]
121 Darkovska-Serafimovska M.; Serafimovska T.; Arsova-Sarafinovska Z.; Stefanoski S.; Keskovski Z.; Balkanov T. Pharmacotherapeutic Considerations for use of Cannabinoids to Relieve Pain in Patients with Malignant Diseases. *J. Pain Res.*, 2018, 837-842. [CrossRef]
122 Shannon S.; Opila-Lehman J. Effectiveness of Cannabidiol Oil for Pediatric Anxiety and Insomnia as Part of Posttraumatic Stress Disorder: A Case Report. *Perm. J.*, 2016, **20**. [CrossRef]
123 Zanelati T.V.; Biojone C.; Moreira F.A.; Guimarães F.S.; Joca S.R.L. Antidepressant-like Effects of Cannabidiol in Mice: Possible Involvement of 5-HT1A Receptors. *Br. J. Pharmacol.*, 2010, **159**, 122-128. [CrossRef]
124 Sales A.J.; Crestani C.C.; Guimarães F.S.; Joca S.R. Antidepressant-like Effect Induced by Cannabidiol is Dependent on Brain Serotonin Lvels. *Prog. Neuro-Psychopharmacol. Biol. Psychiatry*, 2018, **86**, 255-261. [CrossRef]
125 Shrivastava A.; Kuzontkoski P.M.; Groopman J.E.; Prasad A. Cannabidiol Induces Programmed Cell Death in Breast Cancer Cells by Coordinating the Cross-Talk Between Apoptosis and Autophagycbd Induces Programmed Cell Death in Breast Cancer Cells. *Mol. Cancer Ther.*, 2011, **10**, 1161-1172. [CrossRef]
126 McAllister S.D.; Christian R.T.; Horowitz M.P.; Garcia A.; Desprez P.Y. Cannabidiol as a Novel Inhibitor of Id-1 Gene Expression in Aggressive Breast Cancer Cells. *Mol. Cancer Ther.*, 2007, **6**, 2921-2927. [CrossRef]
127 Oláh A.; Tóth B.I.; Borbíró I.; Sugawara K.; Szöllõsi A.G.; Czifra G.; Pál B.; Ambrus L.; Kloepper J.; Camera E.; Ludovici M. Cannabidiol Exerts Sebostatic and Antiinflammatory Effects on Human Sebocytes. *J. Clin. Invest.*, 2014, **124**, 3713-3724. [CrossRef]
128 Tan J.K.; Bhate K. A Global Perspective on the Epidemiology of Acne. *Br. J. Dermatol.*, 2015, **172**, 3-12. [CrossRef]
129 Chagas M.H.N.; Zuardi A.W.; Tumas V.; Pena-Pereira M.A.; Sobreira E.T.; Bergamaschi M.M.; dos Santos A.C.; Teixeira A.L.; Hallak J.E.; Crippa J.A.S. Effects of Cannabidiol in the Treatment of Patients with Parkinson's Disease: An Exploratory Double-Blind Trial. *J. Psychopharmacol.*, 2014, **28**, 1088-1098. [CrossRef]
130 Watt G.; Karl T. In vivo Evidence for Therapeutic Properties of Cannabidiol (CBD) for Alzheimer's disease. *Front. Pharmacol.*, 2017, **8**, 20. [CrossRef]
131 Jadoon K.A.; Tan G.D.; O'Sullivan S.E. A Single Dose of Cannabidiol Reduces Blood Pressure in Healthy Volunteers in a Randomized Crossover Study. *JCI Insight*, 2017, **2**. [CrossRef]
132 Rajesh M.; Mukhopadhyay P.; Bátkai S.; Patel V.; Saito K.; Matsumoto S.; Kashiwaya Y.; Horváth B.; Mukhopadhyay B.; Becker L.; Haskó G. Cannabidiol Attenuates Cardiac Dysfunction, Oxidative Stress, Fibrosis, and Inflammatory and Cell Death Signaling Pathways in Diabetic Cardiomyopathy. *J. Am. Coll. Cardiol.*, 2010, **56**, 2115-2125. [CrossRef]
133 Mikulec A.; Kowalski S.; Sabat R.; Skoczylas Ł.; Tabaszewska M.; Wywrocka-Gurgul A. Hemp Flour as a Valuable Component for Enriching Physicochemical and Antioxidant Properties of Wheat Bread. *LWT*, 2019, **102**, 164-172. [CrossRef]
134 Callaway J.C. Hempseed as a Nutritional Resource: An Overview. *Euphytica*, 2004, **140**, 65–72. [CrossRef]
135 Galasso I.; Russo R.; Mapelli S.; Ponzoni E.; Brambilla I.M.; Battelli G.; Reggiani R. Variability in Seed Traits in a Collection of *Cannabis sativa* L. Genotypes. *Front. Plant Sci.*, 2016, **7**, 688. [CrossRef]
136 Siudem P.; Wawer I.; Paradowska K. Rapid Evaluation of Edible Hemp Oil Quality Using NMR and FT-IR Spectroscopy. *J. Mol. Struct.*, 2019, **1177**, 204-208. [CrossRef]
137 Porto C.D.; Decorti D.; Natolino A. Potential Oil Yield, Fatty Acid Composition, and Oxidation Stability of the Hempseed Oil from Four *Cannabis sativa* L. Cultivars. *J. Diet. Suppl.*, 2015, **12**, 1-10. [CrossRef]
138 Aluko R.E. Hemp Seed (*Cannabis sativa* L.) Proteins: Composition, Structure, Enzymatic Modification, and Functional or Bioactive Properties. In *Sustainable protein sources*, 2017, 121-132. Academic Press. [CrossRef]
139 Korus J.; Witczak M.; Ziobro R.; Juszczak L. Hemp (*Cannabis sativa* subsp. sativa) Flour and Protein Preparation as Natural Nutrients and Structure Forming Agents in Starch Based Gluten-Free Bread. *LWT*, 2017, **84**, 143-150. [CrossRef]
140 Švec I.; Hrušková M. Crumb Evaluation of Bread with Hemp Products Addition by means of Image Analysis. *Acta Univ. Agric. Silvic. Mendel. Brun.*, 2013, **61**, 1867-1872. [Link]
141 Ivan S.; Marie H. Properties and Nutritional Value of Wheat Bread Enriched by Hemp Products. *Potravinarstvo*, **9**, 304–308. [CrossRef]
142 Kladar N.; Čonić B.S.; Božin B.; Torović L. European Hemp-Based Food Products–Health Concerning Cannabinoids Exposure Assessment. *Food Control*, 2021, **129**, 108233. [CrossRef]
143 Yanchev I.; Jalnov I.; Terziev J. Hemp's (*Cannabis sativa* L.) Capacities for Restricting the Heavy Metals Soil Pollution. *Rasteniev" dni Nauki*, 2000, **37**, 532-537. [Link]