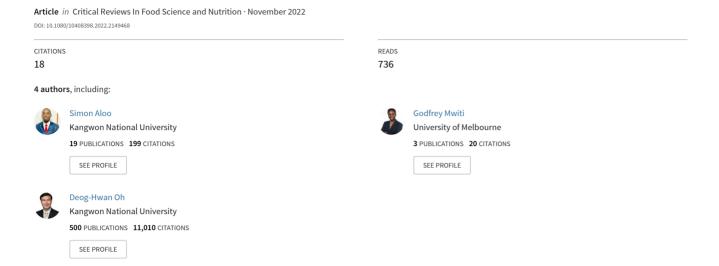
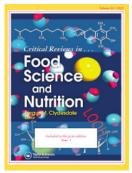
Uncovering the secrets of industrial hemp in food and nutrition: The trends, challenges, and new-age perspectives





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Uncovering the secrets of industrial hemp in food and nutrition: The trends, challenges, and new-age perspectives

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ABSTRACT

Hemp is a valuable crop with a wide range of use, from applications in foods and textiles to pharmaceuticals. Over recent years, the use of hemp as food and food ingredients has drastically increased. The growth is driven by numerous health benefits hemp possesses and its wide range of applications in the food industry. This review provides the scientific literature concerning the benefits of industrial hemp in the food industry. The relevant historical context of use, recent applications in the food industry, health benefits, various development challenges, and the global market outlook for hemp-based food products have been analyzed. Evidence suggests that today hemp is widely consumed as food or an ingredient in the food. Hemp-based foods are marketed as having various health benefits, although their reception by target consumers and success varies. Besides, scientific research on hemp-derived foods has dramatically increased over recent years. Numerous in vitro and in vivo studies have investigated the health benefits of hemp-based foods. Therefore, there is a promising growth trend in producing novel foods from industrial hemp. Nevertheless, due to health concerns related to THC, there is a general need for regulatory compliance when integrating hemp into foods to ensure product safety before use.

KEYWORDS

Functional ingredient; health benefits; hemp-based food market; industrial hemp

Introduction

Hemp is a high-niche dicotyledonous plant belonging to the genus Cannabis of the Cannabaceae family in the order, Rosales (Muzammal et al. 2021). The plant has wide applications in the food, pharmaceutical, agrochemical, energy, cosmetic and textile industries (Ranalli and Venturi 2004; Rupasinghe et al. 2020). Over decades, man has used hemp as food, making clothing, and medicine. Despite its long history of utilization, the taxonomic classification of the plant has remained one of the most inconclusive research areas with varying phases of nomenclatural attempts (Hazekamp, Tejkalová, and Papadimitriou 2016; Koren et al. 2020). Until recently, classification attempts had primarily relied on the level of intoxication possessed by the plant and domestication status, such that we have the wild type, domesticated, psychoactive and non-psychoactive Cannabis. Most legal definitions of industrial hemp have also been based on the intoxication potential of the plant. Since delta-9-tetrahydrocannabinol (THC) is the primary psychoactive component of the Cannabis genus (Atakan 2012), it then appears that most legal and earlier scientific basis of distinguishing industrial hemp from other varieties of the plants in the genus have been chemo phenotypic based, with a wide acceptance of industrial hemp as cultivars containing <0.3% THC and recreational Cannabis as having

>1% THC (Sgrò et al. 2021). This has, however, failed to consider other vital details such as domestication status in various regions, genetics and guidelines on botanical naming (Barcaccia et al. 2020). Although this review does not center on the nomenclature of Cannabis sativa, we find it essential to appreciate what exactly constitutes industrial hemp, more so because the production and usage of the plant have been undergoing a renaissance. Though various detailed research has dealt with hemp taxonomy (Carboni et al. 2000; Clarke and Merlin 2013), we find the work by Small to be among the most comprehensive and widely appreciated in this regard (Small 2015). Small align his work with International Code of Nomenclature (ICN) for algae, fungi and plants guidelines while trying to marry both the level of psychoactive content and domestication status to group existing Cannabis cultivars into six major groups as follows: (1) Non- psychoactive plants cultivated mainly for seed and fiber in Western Asia and Europe contain low amounts of THC and high cannabidiol (CBD); (2) Non-psychoactive cultivars from East Asia (mainly China) containing low to moderate THC and high amounts of CBD; (3) Psychoactive varieties from South Central Asia are composed mainly of THC as the dominant cannabinoid; (4) Psychoactive varieties found in Afghanistan and surrounding countries containing high THC and CBD; (5) Hybrids of 1 and 2, and (6) Hybrids of 3 and 4. Thus, it is important to emphasize that

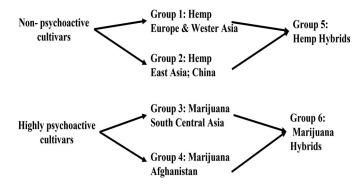


Figure 1. Classification of *Cannabis sativa* varieties according to Small 2015. *Cannabis sativa* plants can be grouped into 6 main groups depending on region of origin and psychoactive component composition with 2 hybrid categories. Group 1: Non- psychoactive plants cultivated mainly for seed and fiber in Western Asia and Europe contain low amounts of THC and high cannabidiol (CBD). Group 2: Non-psychoactive cultivars from East Asia (mainly China) contain low to moderate THC and high amounts of CBD. Group 3: Psychoactive varieties from South Central Asia are composed mainly of THC as the dominant cannabinoid. Group 4: Psychoactive varieties are found in Afghanistan and surrounding countries containing THC and CBD. Group 5: Hybrids of 1 and 2 and Group 6 comprising of Hybrids from groups 5 and 6.

there are only some cannabis plants that can be classified as industrial hemp. Therefore, hemp-based food products are products from hemp cultivars that meet certain specifications to allow them to be used as food items. Therefore, even though there exist numerous ways through which the definition of hemp can be approached, for the purpose of this review, "industrial hemp" has been used to refer to the non-psychoactive cultivars of the *Cannabis* plant referred to in groups 1, 2 and/or 5 above. Figure 1 summarizes the six proposed definitions related to common terminology used in the hemp marketplace (as described above).

In recent decades, hemp utilization as food and ingredient in various foods has been on the rise, owing first to a shift in its legal status, a widely health-conscious public, and the suitability of hemp as both a nutritious and healthy plant food and food ingredient. However, despite this positive trajectory, hemp-based products may contain THC above the limit, which is of concern for safety and regulatory compliance. As mentioned earlier, the currently accepted limit for THC in industrial hemp is 0.3% or less. Thus, the safety limit of hemp-derived food products and their potential concerns based on available analytical data is essential to offer a strong foundation for the use of hemp as a food item. A recent study performed in Germany found out that, for products such as hemp leaf tea, calculated exposures to THC may not be considered critical; however, this finding may probably be due to the absence of intoxication reports in the scientific literature (Steinmetz, Nahler, and Wakefield 2022). The study further disclosed that a safety limit of 11.9 µg/kg/day is proposed for most hemp-based foods. Most importantly, the authors' examination of hemp seed oils, the most common hemp-derived food products, revealed that 4 of the 102 samples investigated posed a low-to-moderate risk for inducing toxicity, confirming the general need for safety regulation of the food products (Steinmetz, Nahler, and Wakefield 2022).

Thus, while for most hemp-derived foods, safety concerns for the general public may be considered low, this may not be the case for some hemp-based products. There is a general need for regulatory compliance for the safe integration of hemp into foods. This article mainly analyzes industrial hemp as an essential raw material in the food industry. A brief history of its utilization during ancient times, legalization progress, health benefits, and market trends for hemp-derived foods have been reviewed. Therefore, the term 'uncovering,' as used in the title of this article, means disclosing or revealing the latest findings related to the utilization of hemp, with emphasis on its use as a food or food ingredient, as well as global market trends for hemp-based food products. Accordingly, this article provides an understanding of the role of industrial hemp in the food industry and, thus, aims to hasten public knowledge about industrial hemp as a food material.

A general history of hemp domestication and utilization in the ancient world

Considerable evidence from historical and archaeological sources suggests that hemp has been in use by humanity for thousands of years. Nevertheless, every region of the world depicts a distinct historical perspective on hemp cultivation and use. The earliest evidence of the crops' domestication dates back to the third millennium. It indicates that hemp primarily originated from the Asian continent in countries such as Japan, Korea, and China (Koltai and Namdar 2020), even though there is also information that the crop was first domesticated in Europe (McPartland and Hegman 2018). The earliest archaeological proof of the origin of hemp was first discovered in Japan, followed by China. However, from different research findings, it is believed that hemp had first gone to Korea and was brought by merchants to Japan's southern island of Kyushu (Olson 1997). A neolithic cave painting from coastal Kyushu depicts this proof by demonstrating a tall stalk with hemp-shaped leaves (Olson 1997). In China, evidence shows that the ancient Chinese domesticated hemp and integrated it into a cultivated crop (Koltai and Namdar 2020). The oldest Chinese agricultural article, the Xia Xiao Zheng, written during the 16th century BC, names hemp as one of the major crops grown in ancient China (Koltai and Namdar 2020). In fact, the remains of hemp seeds were reportedly found in major archeological sites such as the Yellow and Yangtze Rivers in China (Koltai and Namdar 2020), suggesting that the ancient Chinese sowed hemp seeds.

In Europe, the earliest evidence of hemp was attributed to its fiber product, and it predates back to the Neolithic era. This evidence is associated with the Gravettian culture in the 25,000 BCE, consisting of low-resolution woven netting pottery discovered in the Czech Republic (McPartland and Hegman 2018). Moreover, a study conducted in Lithuania at Šventoji recovered a piece of string from the olden days identified as hemp fiber revealing the domestication of the crop in Europe (McPartland and Hegman 2018). Are these pieces of evidence proving that hemp

domestication's origins are traced from Europe or Asia? Perhaps this is a concern for many other common crops, such as millet, maize, and other major grains. Nevertheless, a compressive study by McPartland and Hegman on this subject concluded that neolithic Europeans neither cultivated nor domesticated hemp and that even though wild harvesting of hemp took place, it happened at a small scale that does not offer substantial proofs to the archaeological record of hemp origin in Europe (McPartland and Hegman 2018). Finally, and more recently is the evidence of hemp cultivation in North America. In the colonial era, farmers were allowed to legally grow hemp and process it into other products in the United States (Crini et al. 2020). It is believed that the first American flag was made from hemp, and the declaration of the country's independence was drafted on hemp paper in 1776 (Crini et al. 2020). All this evidence confirms that hemp was being cultivated without restrictions in North America, in countries such as the United States.

Ancient man used the hemp plant for different purposes. Hemp fiber was used to weave cloth; until cotton was introduced in China from 960 to 1127 AD, hemp was the primary raw material for cloth worn by the ancient Chinese (Lu and Clarke 1995). Many of the accounts of hemp utilization in textiles are described in the ancient Chinese texts contained in archeological discoveries, which demonstrate that during the Western Zhou dynasty, the hats of nobles were mainly crafted from hemp fiber (Lu and Clarke 1995). Hemp was also an ingredient for making paper, commonly known as washi (Lu and Clarke 1995). Moreover, hemp was also used as medicine throughout the ancient history of man. From a scientific point of view, ancient man was well aware of the health benefits of hemp components. For instance, during the second century AD, a Chinese surgeon, Hua, is claimed to have successfully used an anesthetic derived from hemp seeds and wine to treat an abdominal wound (Wai 2004). Besides its use as medicine and in textiles, the use of hemp as food, although not common, dates back to the olden days. Archeological sources, mainly in China, indicate that among the sacrificial crops during ancient ceremonies were seeds, including hemp, rice, millet, and wheat seeds, signifying the importance of these grains as food crops to early man (Chang 1977).

A shift from old to new era: evolution of hemp from prohibition to regulation, to being incorporated as a food material

Prohibition of hemp consumption

As already been described above, hemp was cultivated and consumed without restrictions in the olden days. Nonetheless, the clear turning point of legal hemp cultivation happened during post-world war II when it came to a complete halt. Before this period, the Marijuana Tax Act of 1937 was adopted by the United States as the first step by the federal government to restrict Cannabis cultivation. The act was passed on 2 August 1937 (Musto 1972). The Marijuana Tax Act of 1937 was primarily enacted to increase taxes on the use of marijuana-related products and subject its possession to some regulations; however, it did not entirely stop its cultivation. The passage of the Marijuana Tax Act of 1937 was immediately followed by the introduction of a series of post-world II hemp prohibition regulations. The first of such regulations was the 'Japanese Cannabis Control Act of 1948. In 1948, an American general, Douglas MacArthur and his colleagues rewrote the Japanese constitution, including the Hemp Control Act, commonly known in Japanese as 'Taima Torishimari Ho' (Olson 1997). The act effectively banned all Cannabis cultivation and possession in Japan. Subsequently, thirteen years later, a Single Convention on Narcotics was signed by over 73 states on 30 May 1961, which effectively led to a comprehensive global control for crops such as opium, coca, and Cannabis bringing international narcotics under a single prohibitive framework (Pryor 2013). During this period, there was no clear distinction between hemp and marijuana. Thus, in just a mere half-century, the marijuana Tax Act of 1937, MacArthur's Marijuana Regulation Law of 1948, Single Convention on Narcotics treaty of 1961, and subsequent anti-hemp-related legislations were able to wipe away the good memories of hemp culture, which then continued for several years to the recent times.

Several reasons might explain why hemp was prohibited. Chiefly, the taxonomic similarities between all plants that belong to the Cannabis genus made it difficult to distinguish their chemical components using unsophisticated and nonspecific ancient analytical techniques; thus, the cultivation of hemp as an independent crop was not entirely possible. Plants of the genus Cannabis, such as marijuana, was and still is one of the most commonly consumed illicit drugs in the world and they remain illegal globally. Due to their high levels of psychoactive compounds, there is strict control of Cannabis products under drug control agencies (Farinon et al. 2020). Consequently, hemp production was frowned upon due to its association with other cannabis plants; most international laws, especially in the United States, restricted any plant in the Cannabis genus group regardless of its purpose (Pryor 2013). In this context, it was believed that legalizing the use of hemp could jeopardize international bureaucracies that prohibited cannabis crops, thereby increasing the production of illegal plants (Pryor 2013). Another explanation for the hemp prohibition is economic in nature. Due to the discovery of alternative sources of fibers, such as cotton, there were efforts to abandon hemp in favor of the newly invented substitutes such as cotton (Pryor 2013). Even though this explanation serves as a "null hypothesis," it may be one of the primary reasons that led to changes in the regulations that have so far caused the decline of hemp cultivation.

A new shift to regulation instead of prohibition and the gradual reintroduction of hemp as a food item

Meanwhile, after a long period of prohibition, over the past few years to recent times, a new dramatic shift in global viewpoint and perception about hemp has been on course, aided by scientific knowledge. Science has led to new techniques and machines that can quantify plant compounds, thereby increasing plant chemical composition knowledge. The current understanding of biochemical and biomolecular features of Cannabis Sativa species has made it possible to accurately quantify the levels of compounds such as THC in Cannabis plants to distinguish between crops with high and low contents, thanks to the discoveries of analytical techniques such as mass spectrometry. Cannabis contains plants such as marijuana and hemp, belonging to distinct varieties. While marijuana is characterized by high THC content ($\geq 0.3\%$), industrial hemp (C. sativa L.) has been shown to contain less than 0.3% THC (Malone and Gomez 2019). Scientific research has discovered that consumers cannot become intoxicated by the level of THC contained in industrial hemp (Malone and Gomez 2019). These new findings have led to a shift in the current global trend and perception of hemp cultivation as pro-hemp legislations are being enacted to regulate rather than prohibit the crop's consumption. A rather thorough analysis of these new hemp legislations' scope is summarized elsewhere (Farinon et al. 2020).

Canada was among the first country to re-legalize hemp production in 1994. In 1994, the Canadian government began to re-issue licenses to grow industrial hemp only on an experimental basis. Then, two years later, the progress in legalizing hemp took a new positive trajectory in Canada, and a hemp regulation act was adopted. According to the 1996 hemp regulation act, all commercial production for varieties of C. sativa L. with less than 0.3% THC were licensed under the new law (Vantreese 2002). Further, on this act, farmers marketing hemp or hemp as a food supplement were allowed to do so, but under stringent security checks, including providing GPS coordinates of the plots to confirm THC levels in the said product. By 12th March 1998, however, a lesser stringent law was proposed; the Canadian government legalized industrial hemp production under licenses issued by Health Canada (Laate 2012). This action was prompted by research findings and lobbying from the business community. Nevertheless, up to 2002, beyond providing and defending the regulatory environment, the Canadian government did not offer or provide any direct monetary support for hemp production or hemp-based food processing (Vantreese 2002). To date, there are many Canadian companies, such as Hemp Oil Canada Inc., Fresh Hemp Foods Ltd., Ruths Hemp Foods, and Natures Path, working to develop hemp-based foods including snack foods, hemp meal and flour, and edible oils (Laate 2012).

In the EU and UK, under the Psychoactive Substances Act, a psychoactive compound is one that triggers psychoactive behavior in a person by depressing the person's central nervous system. Historically, products from the *Cannabis* plant containing more than 0.3% THC content have been considered psychoactive substances (United Nations 1971). However, according to the current regulations in the UK, products such as hemp protein are exempt substances and are ordinarily consumed as foods (Tallon

2020). This exemption does not cover hemp extracts such as isolated CBD; thus, consuming such compounds as foods is illegal and prosecutable under the UK's Psychoactive Substances Act (PSA) 2016 (Tallon 2020). Additionally, in Europe and the UK, the adoption of the Novel Food Regulation (NFR) on 11th January 2016 substantially influenced the consumption and marketing of hemp-based foods (de Boer and Bast 2018). The NFR, which has been in use since 1st January 2018, stipulates that novel foods would be subject to a premarket notification assessment before their full release for consumption. It further asserts that any food developed using a "new" technique in which the production method causes significant changes in its composition or structure, thereby altering its nutritional value, functionality, or level of undesirable substances, the food is considered "novel" (de Boer and Bast 2018). Therefore, foods produced by novel techniques such as supercritical carbon dioxide and purification may be considered as novel products and thus, must undergo a premarket test to ascertain their safety. The exemptions from this regulation are foods including hemp-based foods that have a long history of safe food use within the UK or EU. Such hemp-derived foods must include the foods produced from the hemp varieties allowed for food consumption and must have been obtained through similar traditional propagating practices that are known to be in use within the UK or EU before 15 May 1997 (Tallon 2020). Therefore, it can be argued that the EU and UK hemp regulatory guidelines concerning hemp have so far been made less stiff compared to decades earlier.

In the US, by 1777, hemp cultivation was already in progress. By 1800 hemp was accepted as a medium of exchange in the USA, and it became the most used crop until 1937. As noted above, the United States was one of the first countries to prohibit hemp cultivation in the post-world war era. The subsequent significant change in hemp regulation occurred in the United States in 1970 when the Controlled Substances Act (CSA) was enacted to distinguish between hemp and marijuana (Malone and Gomez 2019). Hemp fiber, seed oil, and seed cake were differentiated by the act while viable hemp seeds were not fundamentally distinct from marijuana. The act further allowed hemp production under licenses provided by the US Drug Enforcement Agency (DEA), but under strict control. Thus, from the 1970s until 2014, hemp production existed in the United States but under a highly regulated grey area (Malone and Gomez 2019). Beyond 2014 to date, in the US, public policies surrounding hemp have been changing rapidly, and the support for legal industrial hemp production is gaining momentum in all parts of the US political spectrum. The legitimacy of industrial hemp research was introduced in the Agricultural Act of 2014, which legally allowed state governments and research institutions to conduct research on industrial hemp (Malone and Gomez 2019). In late 2018, the US under the FDA indicated that hemp seeds do not naturally contain THC, which is present in other parts of the Cannabis plant. Thus, hemp seed products, including hulled hemp seed, hemp seed protein powder, as well as hemp seed oil, were legally allowed to be used in the US

food production. Since then, several states have permitted small-scale production of hemp in an effort to evaluate its potential in the market. To date, eight states, including New Mexico, Hawaii, Kentucky, Maryland, Minnesota, Montana, North Dakota, and Virginia, have authorized limited industrial hemp production. Still, none has fully legalized commercial hemp production (Malone and Gomez 2019).

In Africa, while not indigenous to Africans, the consumption of hemp has a long history in the continent. The history of the crop traces from Ethiopian pottery during the 14th century, but some studies suggest that it was used in this region even before then (Carrier and Klantschnig 2018). Today, Cannabis is by far the most widely consumed and the most traded illegal substance in Africa. Despite the positive global changes on hemp, the African continent has largely remained conservative in its posture concerning hemp; the crop is regarded as illegal by governments and is also vehemently opposed by various religious groupings. Taking Kenya as a reference, even in the contexts where politicians and other interested groups have pushed for the legalization of hemp and its products, little to no progress has been made on introducing a new law that regulates rather than prohibits hemp consumption in Kenya (Ndanyi 2021). In 2018, a Kenyan politician named Kenneth Okoth introduced a Marijuana Control Bill in parliament (Ndanyi 2021). The bill sought to legalize the cultivation and use of industrial hemp, establish a system for the licensing of Cannabis growers and users, and increase public awareness of Cannabis (Ndanyi 2021). However, the bill was turned down by other members of parliament (Ndanyi 2021). Thus, hemp farming and utilization undoubtedly remain illegal even though a profitable venture under Kenyan law. Nevertheless, despite this stiff prohibition, since 1980, farmers in Kenya have been desperate for income from Cannabis cultivation, and the product continues to be illegally grown in the country and even elsewhere in the African continent, but only for other purposes other than utilization as a food or food ingredient (Ndanyi 2021). Lesotho was the first African country to allow issuing an administrative license for the commercial cultivation of hemp for medical and scientific use in 2017 (Information available at: https://businesstoday.co.ke/prof-wajackoyah-meet-the-man-o n-a-mission-to-legalize-marijuana-in-kenya/. Last accessed on 24 July 2022). Since then, other African countries such as Zimbabwe, South Africa, Malawi, Zambia, Uganda, and Rwanda have joined the suit.

Finally, in the context of the Asian continent, the latest country to review its hemp legal status is Thailand which began it in late 2021 to early 2022 (Sommano et al. 2022). Even though the distribution and possession of C. sativa (including hemp) largely remain illegal in the country, the current revision to Thailand's Narcotics Act (B.E. 2563) allows the country's corporations to produce Cannabis for therapeutic purposes as well as for research. According to this latest development, Thailand's narcotics board has potentially removed some elements of industrial hemp which relate the crop to narcotics and also projects to remove them entirely by the end of 2022, paving the way for the use of hemp in a low-restricted zone (Sommano et al. 2022). Thailand hemp's legalization ambitions are seen as opportunities for businesses or individuals looking to benefit from this plant, both as food and as a medical drug in Asia and the Middle East. In Korea, South Korean government created a local hemp trade free zone to facilitate research and spearhead legislation strategies of hemp. Andong (an area located in the Gyeongbuk province in Korea) was designated as a "regulation-freezone" that will be used for management and production; although the emphasis is currently on medical hemp (Kim, Shin, and Pan 2022). The South Korean government is looking to monitor the hemp production system by deploying the block-chain technologies to ensure safety, transparency, and fasten legalization (Kim, Shin, and Pan 2022). Figure 2 highlights significant global policies regarding pro and anti-hemp utilization.

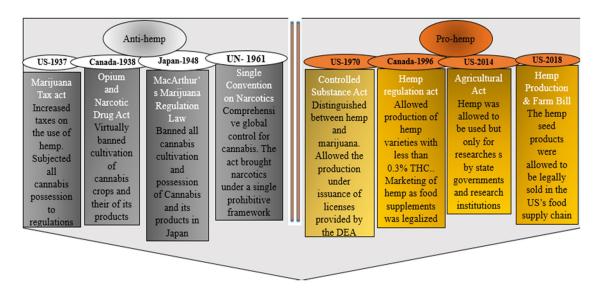


Figure 2. The major global legislations that led to the prohibition and reintroduction of industrial hemp as food material. DEA: Drug Enforcement Agency; US: THC: delta-9-tetrahydrocannabinol; United States; UN: United Nations.



Figure 3. Parts of industrial hemp with the potential for use as raw material for food processing.

Applications in food industry: hemp as an emerging source for food and food ingredients

Due to the gradual restoration of its cultivation, hemp containing THC levels of 0.3% or below, also known as industrial hemp, is of interest to humanity, especially in the food sector, where it is considered a nutritious product, thanks to its diverse nutritional composition. Today, numerous publications highlight the benefits of hemp as a food or an ingredient in food. Flowers, seeds, and leaves are the significant parts of hemp considered to be nutritious and, thus, possess a potential utilization in the food industry (Figure 3).

Hemp as a food item

Seed is arguably the most nutritionally complete food source originating from hemp, and it is the only part of hemp currently allowed for use as a food item. Hemp seeds can be consumed as whole, hulled or dehulled seeds (Farinon et al. 2020). Seed processing techniques such as germination have been reported to promote changes in the phytochemical profile of seeds and have drawn interest in the commercial development of sprouts enriched in specific phytochemicals (Werz et al. 2014). In the context of hemp-derived foods, studies have also assessed the nutritional benefits of hemp sprouts. Werz et al. reported that sprouting enhanced the anti-inflammatory compounds such as prenylflavonoids cannflavins A and B, indicating that hemp sprout can be a novel anti-inflammatory food material (Werz et al. 2014). Another study reported an increased polyphenol, flavonoid contents, antioxidant activity, and protein concentration of hemp sprouts produced under blue (B) light-led emitting diode compared to raw seed (Livadariu, Raiciu, Maximilian, & Capitanu, 2019). Additionally, a study noted interesting findings-that hemp sprouts possess no hallucinogenic effects, do not contain high delta-9-tetrahydrocannabinol, and thus can be consumed without any concerns of negative health impact (Moon et al. 2020).

Hemp seed can be processed into products, including hemp oil, nuts, and cakes which can be further manufactured into foodstuffs such as high-moisture meat analogues and hemp milk. A high-moisture meat analogue is a meat substitute that has been developed mostly from seeds such as soybean but is not widely available on the market yet; other dominant meat substitute in the market include tempeh, seitan, mycoprotein, and texturized vegetable protein (Zahari et al. 2020). The method for developing a high-moisture meat analogue from hemp was described by (Zahari et al. 2020). Meanwhile, there is also a possibility of developing high-quality and nutritious hemp milk from seeds. Such milk contains about 25-30% protein and 35% fatty acids with an optimum essential omega-3 and omega-6 fatty acid content (Vahanvaty 2009). Other parts of hemp, such as leaves and flowers, are also edible and contain vital health-beneficial compounds such as cannabinoids. Thus, hemp leaves and flowers are also regarded as potential raw materials for food products even though they are not yet entirely allowed for food-related applications at the moment (Kwaśnica et al. 2020; Valizadehderakhshan et al. 2021). Collectively, these findings demonstrate that hemp can be an excellent nutritional source for humans. Figure 4 provides a summary of existing hempseed-based food products.

Hemp as an essential nutritional supplement/ingredient in foods

The benefit of hemp as a nutritional supplement is that it can enrich the consumer's diet. Hemp extracts such as CBD are currently used as dietary supplements (Cerino et al. 2021). According to some studies, CBD as a supplement can be administered from 6000 mg/day but can be increased to 5 mg/kg or even up to 20 mg/kg/day (Cerino et al. 2021). In the US, food and Drug Act (FDA) has prohibited the marketing of CBD as a nutritional supplement which appears to contradict the settings in Europe, where CBD-containing products, including CBD-enriched hemp oil, have been classified as novel foods and are sold in the market (Cerino et al. 2021). CBD is an interesting pharmaceutical and food supplement and can be added to foods to complement nutritional value. Moreover, very recently, industrial whole hemp seeds have increasingly gained prominence in the food supplement industries. Attempts to combine hemp seed or leaf products (either in the form of oil, flour, cake etc.) with other products to produce enriched and nutritionally improved foods have been in progress. Such efforts have been reported for the production of hemp-supplemented bread (Rusu et al. 2021), extruded rice (Norajit, Gu, and Ryu 2011), and gluten-free biscuits (Korus et al. 2017), among other foods. In most of these studies, food supplemented with hemp was found to have a higher nutritional value and elevated levels of essential nutrients and functional components such as proteins and macro- and microelements, as summarized in Table 1. Notable companies such as Ready Pac Foods Inc. in the United States recently launched two salads featuring hemp seeds (available at: https://www. readypac.com/newsroom/ready-pac-innovates-fresh-food-o fferings-first-ever-salad-kit-bistro-bowl-featuring-hemp-ingredients/. Last accessed on 17 May 2022). Another food production involving hemp as a supplement has been reported for the production of mead, a traditional drink produced via fermentation (Romano et al. 2021). Thus, the rapidly rising popularity of industrial hemp has attracted research

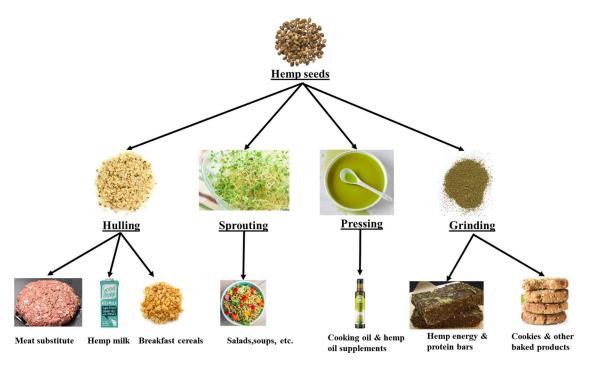


Figure 4. Food products derived from hemp seed.

interest across various sectors of food industry; food scientists and processers believe that the crop is a niche for novelty in food production and beyond. Table 1 summarizes studies evaluating hemp products as food supplements.

Hemp as a valuable component for enriching physicochemical properties of foods

Nowadays, there is an immense interest in controlling the functionality of processed foods in relation to their rheological properties (Lin, Pangloli, and Dia 2021). There is an interrelationship between the process, structure, rheology, and function of foods. Thus, the rheology of food determines its functional characteristics because of its influence during the entire food processing up to the moment of consumption and digestion (Moelants et al. 2014). The structure of food, texture, size, and morphology are key rheological properties that influence food functions. Since the structure of plant-tissue-based products changes during processing, the rheological parameters of the final products are simultaneously altered (Moelants et al. 2014). Lately, the addition of external ingredients in foods has been found to influence the final product's rheology significantly. These ingredients may help to retain moisture, form films, or improve freeze-thaw stability, thereby enhancing the quality of the final food product (Lin, Pangloli, and Dia 2021). Besides being used as food or a food supplement, the influence of hemp-derived products such as hemp powder or oil on physicochemistry of other foods has been dubbed as an essential aspect to enhance the rheological properties of the final food product. Evidence from scientific research established that adding 15% of hemp seed oil to the bread dough modified rheological properties by reducing the

modulus of viscosity and elasticity (Ropciuc et al. 2022). It also improved the dough's hardness, springiness, cohesiveness, and adhesiveness (Ropciuc et al. 2022). Taken together, these findings demonstrate that adding hemp derivatives into foods may help improve the rheological properties of processed food, thereby improving their functional properties.

Hemp as a modifier of sensory characteristics of foods

Sensory characteristics such as color, flavor, and taste are essential to the consumer's acceptance of a specific food product/ingredient. One of the major hurdles in utilizing natural plant products in mainstream food applications is the unpleasant sensory property they may render to final products. Interestingly, hemp as a food item has been shown to possess a pleasant and unique sensory characteristic, such as flavor, mainly from its terpenoid content (Shen et al. 2021). Some volatile compounds such as α -pinene, β -pinene, α-humulene caryophyllene, myrcene, and terpinolene from hemp inflorescences can also promote its utilization as flavoring ingredient in food (Shen et al. 2021). Shen et al. (2021) comprehensively discussed flavor compounds of industrial hemp. As a result of their abundant volatile compounds, hemp-derived products have been extensively studied for their potential to influence the final food products' sensory characteristics positively. For instance, a research study obtained grayish-green powder with brown particles, a pleasant nutty taste, and a slight crunch when hemp flour was added into bread dough (Lukin and Bitiutskikh 2017b).

Merlino et al. used hempseed flour to fortify gnocchi, a typical Italian potato-based fresh pasta and investigated its influence on the final product's sensory characteristics (Merlino et al. 2022). Merlino and colleagues disclosed that

Table 1. Impact of hemp supplementation on the nutritional properties of food products.

Supplemented products	Purpose/objective of the study	Supplementation process	Resultant benefit on nutritional value	References
Hemp supplemented bread	To describe the advanced nutritional characteristics of hemp flour supplemented bread samples	Supplemented with hemp flour in different proportions (5%, 10%, 15%, and 20%)	Improved protein, total amount of unsaturated fatty acids, and mineral content	(Rusu et al. 2021)
Extruded rice	To investigate the effect of adding hemp powder on physicochemical properties, nutritional compounds and antioxidant activity of extruded rice flour.	Extruded rice was mixed with mixtures of hemp powders at varying hemp levels (0%, 20%, 30%, and 40%).	Improved total phenolic and flavonoid content as well as radical scavenging effect of extruded rice.	(Norajit, Gu, and Ryu 2011)
Gluten-free biscuits	To evaluate the effect of substituting corn flour with hemp flour on the nutritional, health value, and sensory properties of gluten-free biscuits	Substituted 20–60% of corn flour with hemp flour	Increased total polyphenols content (143%), antioxidant activity (114%), and sensory score.	(Korus et al. 2017)
Gluten-Free Crackers	To assess the impact of hemp seed oil press-cake on functional properties of gluten-free crackers.	Brown rice flour was replaced by 0–40%, hemp oil press-cake flour	Addition of hemp flour significantly increased fiber content (39% to 249%) but decreased carbohydrate content (8.4% to 42.3%) in crackers.	(Radočaj, Dimić, and Tsao 2014)
Pork loaves	To assess the effect of adding different hemp constituents on pork loaves	Added hemp seeds (5%), de-hulled hemp seeds (5%), hemp flour (5%), and hemp protein (5%).	Enhanced magnesium, manganese, iron, and copper content of pork loaves	(Zając et al. 2019)
Gluten-free cookies	To study the potential use of hemp flour in the making of Gluten-free cookies	Added hemp flour of different contents (90%, 80%, 70%, 60%, and 50%)	Improved organoleptic properties of the cookies	(Lukin and Bitiutskikh 2017a)
Durum wheat pasta	To determine the effect of hemp addition on the physicochemical properties, cooking quality, and sensory properties of durum wheat pasta	Wheat pasta was fortified with 5–40% of hemp flour or 2.5–10% of hemp cake	Addition of hemp seed increased the protein, dietary fiber, ash and fat content in the pasta samples.	(Teterycz et al. 2021)
Hemp flour supplemented bread	To examine the possibility of hemp seed cake supplementation of bread and the effects on processing quality and nutritive value of dough	Hemp flour was mixed with wheat flour at different hemp/wheat flour ratios (0/100, 5/95, 10/90 and 20/80).	Hemp flour supplementation improved nutritional value by enhancing the levels of important nutrients such as proteins and macro- and microelements such as iron	(Pojić et al. 2015)
Enriched chopped semi-finished meat products	To assess the possibility of using hemp flour in producing enriched chopped semi-finished meat products	Supplemented chopped semi-finished meat products with 10% of hemp flour	Increased contents of magnesium (2.4 times), iron (1.5 times), lipid (22%)	(Naumova, Lukin, and Bitiutskikh 2017)
Chapatti	,	0–40 g/100 g whole hempseed flour was added to wheat flour used in making chapatti	Protein content was increased from 12.39 to 18.29 g/100g while fiber was enhanced from 11.78 to 18.55. polyunsaturated fatty acid content was improved 58.1 to 73.5, and the essential fatty acids ratio improved by 4.6 fold	(Sharma and Prabhasankar 2021)

adding hemp seed flour to gnocchi improved the sensory attributes to some extent; however, the bitter taste of hemp negatively affected the final product, reducing its overall acceptability (Merlino et al. 2022). Hemp cake is a by-product of cold-pressing oil from hemp seeds. It is a nutritious ingredient that has been studied for its health benefits and impacts on the sensory characteristics of reformulated foods. An investigation indicated that adding hemp cake reduced fat oxidation and improved the textural and color attributes of meatballs stored in refrigerated environments (Kotecka-Majchrzak et al. 2021). In the most recent study, the effects of adding hemp seed on the taste desirability of poultry pâté were evaluated (Augustyńska-Prejsnar et al. 2022). The study found that pâtés with 24% added hemp seed, amaranth and flaxseed mixtures had their desirability improved compared to the control (Augustyńska-Prejsnar et al. 2022). Other studies on the effects of hemp on the sensory attributes of food have been summarized in Table

Table 2. Effects of hemp supplementation on sensory attributes of foods.

Enriched product	Hemp ingredient	Impact on sensory property	References
Pasta	Hemp flour	The organoleptic characteristics, that is, appearance, color, smell, springiness, hardness and adhesiveness were improved	(Teterycz et al. 2021)
Bread	Hempseed oil	The supplemented bread samples scored higher in sensory evaluation assessment, depending on the concentration of added hemp seed oil (i.e. samples with 5% hemp oil scored 7.66; 10% hemp oil scored 8.20; addition of 15% scored 7.12). The authors did not specify the tested sensory attributes	(Ropciuc et al. 2022)
Potato chips	Hempseed cake	Addition of hemp seed cake significantly decreased the lightness of potato chips, with a higher level of hemp cake supplementation resulting to a darker color of the final product. However, for the redness of the chips, hempseed cake supplementation significantly enhanced compared to the control.	(Feng, Sun, and Fang 2022)
Bread	hemp flour, seeds, and oil	Breads containing 25% of added hemp flour had a distinctive dark brown color whereas those with hemp oils (8% addition in dough) showed a darker color than the control	(Liliana, Livia, and Laura 2018)
Gnocchi	Hemp flour	Fortified <i>gnocchi</i> tasted less sweet and more bitter compared to the control. However, the fortified samples recorded a favorable score in terms of odor, appearance, and texture.	(Merlino et al. 2022)
Bread	Hemp flour	Supplemented bread had grayish-green powder, a pleasant nutty taste, and a slight crunch	(Lukin and Bitiutskikh 2017b)

2. All these studies demonstrated that the use of hemp-derived products could be a promising strategy in the reformulation of foods with improved sensory qualities.

Characteristics that make hemp or hemp-derived products suitable for food applications

Film formation

One of the most significant challenges food processors encounter is the loss of quality of food products during storage. Edible packaging, such as film and coating, is known to reduce food losses. They can improve the shelf life of food by providing moisture or gas barrier properties (Suhag et al. 2020). Hemp products such as protein isolates possess great potential to be used in the protein film-making process. Yin and colleagues studied this characteristic of hemp. They demonstrated that hemp-based protein hydrolysate films have some superior features, such as a higher surface hydrophobicity as compared to soy protein hydrolysate-based films (Yin et al. 2007). Disulfide bonds of hemp proteins have been described as the main factor in the formation and maintenance of the hemp protein film network (Yin et al. 2007).

Emulsification

Emulsifiers improve the rheological properties of foods by reducing food stickiness and may also help foods to maintain a smooth texture and flavor. Therefore, these agents are crucial in improving the physicochemical properties of food products. An emulsifying activity index and emulsifying stability index of hemp-stabilized emulsions have been reported (Tang et al. 2006). Tang noted a lower emulsifying activity index and emulsifying stability index of hemp protein stabilized emulsions compared to soy protein (Tang et al. 2006). The enzymatically hydrolyzed version of hemp protein has also been investigated and found to possess an emulsifying ability (Yin et al. 2008). The emulsifying activity of hemp protein can be correlated to the solubility of its

protein which is a function of pH (Tang et al. 2006). The emulsification of hemp hydrolysates is attributed to the tendency of hemp protein to form covalent disulfide bonds between individual proteins and its subsequent aggregation at neutral or acidic pH (Tang et al. 2006). In a more recent study, ultrasonic treatment of 450 W was reported to effectively improve the properties of hemp oil emulsion activity (Li et al. 2022). Thus, Li et al. demonstrated that ultrasound treatment could be used to enhance the emulsification activity of hemp oil and possibly other hemp derivatives, too (Li et al. 2022) (Table 3).

Solubility

One of the essential properties in determining the potential of incorporating ingredients in food is their solubility. Most of the functional properties of food ingredients can be achieved only when they are fully soluble. Hemp isolates, such as hemp protein, have high solubility in certain foods when used as ingredients (Lin, Pangloli, and Dia 2021). However, this property of hemp protein is greatly affected by pH. For instance, at a pH of 2-10, the solubility of hemp protein in an aqueous solution is below 20%, but it gradually increases as pH increases from 10 to 12 (Lin, Pangloli, and Dia 2021). This high hemp protein solubility in extremely alkaline media has been attributed to its glutelin content which constitutes a major component of the protein in hemp (Lin, Pangloli, and Dia 2021).

Surface hydrophobicity

Products with high hydrophobicity can readily adsorb onto oil droplets and, thus, can effectively be used as emulsifiers with long-term stability action on dispersed particles (Garti and Reichman 1993). Hemp powder is a highly hydrophilic product. The high hydrophilicity of hemp powder might be due to the phenolic hydroxyls present in hemp (Zhang et al. 2018). This property limits their use as stabilizers in food, such as in the preparation of Pickering emulsions.

Table 3. General nutritional components of whole hemp seed and nutritional composition of 10 hemp cultivars.

			General nu	tritional compositi	ion and bioactive	components o	General nutritional composition and bioactive components of whole hemp seed				
DMC (mg/100 g) ^b	CPC (mg/100g) ^d	DMC (mg/100 g) ^b CPC (mg/100 g) ^d CFC (mg/100 g) ^d	DFC (mg/100g) ^b	CHO (mg/100 g) ^d	Ash (mg/100g) ^d	TPC (mg/g) ^d	CHO (mg/100 g) ^d Ash (mg/100 g) ^d TPC (mg/g) ^d Flavonols (mg/g) ^c		TFC (µg/mL) ^e	CBD (µg/mL)e TFC (µg/mL)e THC (µg/mL)e CBN (µg/mL)e	CBN (µg/mL) ^e
94.1-N/A	21.3–27.5	25.4–35.9	32.1-N/A	32.5–38.1	3.7-5.9	3.82-51.60 0.85-N/A	0.85-N/A	0.32-25.55	2.93-N/A	0.06-5.91	0.01-1.50
			Whole hem	empseed major an	pseed major amino acid content (mg/100g seed)	(mg/100 g seed	-				
Ala	Arg	Asp	Gly	Glut	Leu	Lys	Pro	Ser	Val	Thre	
0.94-1.28	2.28-3.10	2.13–2.78	1.02-1.24	3.74-4.58	1.47-1.72	0.84-1.28	0.89–1.15	1.12–1.27	0.68-1.28	0.79-1.01	
			Whole hem	ıempseed major fa	npseed major fatty acid content (mg/100g seed)	mg/100g seed	(
PAd	SAd	OA⁴	LΑ ^d	GLA ^d	ALA	SDA⁴	TSFA⁴	MUFA	PUFA⁴		
5.0-9.1	2.0-3.9	9.0–18.8	51.6–59.0	0.6–6.2	10.5–19.6	0.2–1.5	9.4–11.7	9.7-17.5	72.0-84.0		
	Mean nutritiona	Mean nutritional composition of 10 hemp cultivars (m	0 hemp cultivars	(mg/100 g seed)							
Cultivar ^a	DMCa	Protein ^a	Ash	Fiber	Lipid ^b						
Alyssa	98.87	241	26	37.3	300						
Anka	93.97	238	27	38.8	288						
CanMa	93.93	264	53	35.0	304						
CFX1	92.82	263	51	33.2	298						
CFX2	93.85	274	55	32.7	295						
CRS1	94.02	257	52	36.2	295						
Delores	94.01	245	26	37.5	269						
Finola	93.72	280	28	33.2	306						
Jutta	93.81	246	55	38.1	276						
Yvonne	94.01	248	54	35.2	286						
Average	93.80	256	54.7	35.8	292						
										: 1	i

^a(Vonapartis et al. 2015); ^b(Leonard et al. 2020); ^c(Frassinetti et al. 2018); ^a(Farinon et al. 2020); ^c(E. Jang et al. 2020). DMC, dry matter content, CPC, crude protein content; DFC, crude fat content; CHO, carbo-hydrocannabinol, CBD, cannabidiol; CBN cannabidiol; TPC, total phenolic compounds; TFC, total flavonoid content; DMC, dry matter content; CPC, crude protein content; CFC, crude fat content; CHO, carbo-hydrate; Stearic Acid (18:2, n-9); LA: Linoleic Acid (18:2, n-6); GLA: γ-Linolenic Acid (18:3, n-6); ALA: α-Linolenic Acid (18:3, n-3); SDA: Stearidonic Acid (18:4, n-3); SFA: Total Saturated Fatty Acid; Ma: alanine; Arg: asparagine; Cys: cysteine; His: histidine; Leu: leucine; Lys: lysine; Met: methionine; Phe: phenylalanine; Pro: proline; Ser: serine; Thr: threonine; Trp: tryptophan; Tyr: tyrosine; Glu: glutamate/glutamine; Val: valine; N/A: not available.



Table 4. List of the health benefits of hemp-based products.

Hemp product	Target condition/ activity		Treatment method/procedure	Effect of treatment related to the activity	References
Hemp milk	Anti-obesity	In-vivo	The rats were administered by hemp milk (28 ml/100 g body weight / day) for 21 days	Hemp milk significantly reduced serum triglycerides and cholesterol content.	(Chich-owska et al. n.d.)
Hemp leaves	Anti-fatigue activity	In-vivo	Mice were fed hemp leaves water extract twice a day (6h a part) at the dose of 6 g/kg for 14 days.	Compared with the control group, the glutathione peroxidases activity of mice in hemp extract-fed group increased by 29.62%. Hemp extract also decreased the accumulation of lactic acid in mice	(Zhu et al. 2021)
Hemp oil enriched in cannabidiol	Anti-cancer activity	In-vitro	The cells were treated with CBD-enriched hemp oil of various concentration (5, 10, 15, 20, 25 and 30 µg CBD/mL).	At a concentration of 15 µg CBD/ mL, CBD-enriched oil induced apoptosis of cancer cells in ROS-independent mechanisms	(Petrovici et al. 2021)
Hemp oligopeptides	Anti-diabetic activity	In-vitro	Different concentrations (0.1 mg/ml, 0.5 mg/ml, 5 mg/ml, 20 mg/ml and 100 mg/ml) of two novel with sequences of Leu-Arg (287.2 Da) and Pro-Leu-Met-Leu-Pro (568.4 Da) were tested for ability to inhibit α-glucosidase and α-amylase	At the tested concentrations, both the peptides showed a higher α-glucosidase and α-amylase inhibition compared to the control	(Wang et al. 2020)
Hemp leaf and seed extracts	Anti-bacterial activity	-	The bacteria in BHI agar plates were treated with 20 µI of the extracts at the final concentration of 10 mg/ ml.	At the tested concentration, both hemp seed and leaf extracts inhibited Streptococcus mutans, Staphylococcus aureus and Propionibacterium acne	(Manosroi et al. 2019)
Hemp seed extract	Anti-inflammatory activity	In-vivo	Protective effects was investigated on isolate mouse skin specimens, which were exposed to the extract (1–500 μ g/mL).	Reduced hydrogen peroxide-induced l-dopa turnover and kynurenine/ trypt pophan, thus corroborating anti-inflammatory/antioxidant effects	(di Giacomo et al. 2021)

Interestingly, studies on the hydrophobicity of hemp powder revealed that the surface hydrophobicity of the powder can be chemically improved by the application of compounds such as sodium hydroxide (Zhang et al. 2018). The application of these chemicals can modify phenolic hydroxyls by partially converting them into phenolic ethers (Zhang et al. 2018). According to Zhang et al. the modified powder can be effective as an emulsion stabilizer since sodium hydroxide can easily balance the surface hydrophilicity-hydrophobicity of the hemp powder (Zhang et al. 2018).

Nutritional value and bioactive components of hemp seed

Being the only constituent of hemp allowed to be used as a food item, hemp seeds have proven to be of great nutritional value. More than 40 hemp cultivars have been identified and reported, but they slightly differ in their nutritional content; however, finola is the most commonly cultivated hemp cultivar for commercial use. The nutritional composition of whole hemp seed and 10 hemp seed cultivars is shown in Table 4. Generally, the seed is composed of 250-350 g/kg lipids, 20-25 g/kg protein, and 20-30 g/kg carbohydrates (Oliver and Joynt 1999). Hempseed contains two significant proteins: albumin (33%) and edistin (65%) (Norajit, Gu, and Ryu 2011). The seed contains essential amino acids with exceptionally high arginine levels (Norajit, Gu, and Ryu 2011). On the other hand, hempseed has various fatty acid components, such as palmitic acid, stearic acid, oleic acid, linoleic acid, and arachidic acid. Concerning

the essential fatty acids, hemp seeds of different varieties contain an average of 56.07% (linoleic acid) and 15.98% (alpha-linolenic acid) of total fatty acid content (Vonapartis et al. 2015). Most of the carbohydrates found in hemp are located on the seed's outer shell. The whole seed contains about 30-40% fiber, although the dehulling process can eliminate most of these carbohydrates. Hemp is rich in bioactive components. Specifically, whole and dehulled hemp seeds are known for their high content of phenolic acids, majorly syringic acid and ferulic acid (Alonso-Esteban et al. 2022). A study by Alonso-Esteban et al. established that whole hemp seeds contain about 0.266-1.20 mg/g of total phenolic acids while the amount in the dehulled seeds ranged from 0.66 to 1.25 mg/g (Alonso-Esteban et al. 2022). Other groups of phenolic compounds such as terpenoids, alkaloids, and cannabinoids are also known as distinctive compounds in hemp seeds. The most-known cannabinoid is Δ^9 -tetrahydrocannabinol (Δ^9 -THC), which possesses a psychoactive activity and various medicinal properties (Alonso-Esteban et al. 2022; Jang et al. 2020). Research has also demonstrated that whole hemp seed is abundant in cannabidiol (CBD) and cannabinol (CBN), with promising natural benefits in the diet (Jang et al. 2020). In hemp seeds, the THC concentrations have been reported to range from 0.06 to $5.91 \,\mu\text{g/g}$, whereas CBD levels vary from 0.32 to 25.55 µg/g (Jang et al. 2020). Moreover, two predominant compounds have been identified as N-trans-caffeoyltyramine and cannabisin B have been reported to be responsible for the antioxidant activities of hemp extracts (Chen et al. (2012). Hemp, especially hempseed can be considered a



superfood material with a rich nutritional profile and bioactive compounds which could be added to dietary supplements to help prevent diseases.

Potential health benefits

Besides their nutritional value, hempseed, hemp-based foods, and other hemp-derived products are known for their health benefits. To date, many studies are appearing in mainstream journals describing the biological activities of hemp-derived foods in both in vitro and in vivo models. Studies have reported on anti-diabetic, anti-obesity, anticancer, anti-hypertension, and antioxidants, among other functions. These activities have been discussed as follows.

Anti-obesity properties

The world has in the past few decades seen an alarming up-spiraling of obesity which has led to growth in the breadth of research on its prevention and/or management. Food and bioactive ingredients have become the focal point of this owing to the vital role food play in metabolism and energy homeostasis. The impact of hemp has been studied both at this level and in hemp-specific evaluations of the biological activity of parts like seeds and hemp-derived phytochemicals. Using C. sativa seed flour, Bouarfa et al., sought to establish whether there is an effect of the flour on high caloric diet-induced obese mice (Bouarfa et al. 2020). Their findings revealed that mice fed on either 200 mg/kg or 300 mg/kg of the Cannabis seed flour had their body weight gain, epididymal and perirenal adipose tissue significantly decreased as opposed to mice fed on normal diets. In addition, the total cholesterol, HDL, LDL, and triglycerides were also significantly reduced, thus showing that seed flour could be used in the fight against obesity. Besides, hemp seed oils were shown to have an omega-6 to omega 3 ratio of 3:1 that is dimmed optimal for achieving various benefits in the body, such as increased metabolism and lowering of blood cholesterol levels (Leizer et al. 2000).

Antioxidant benefits

An evaluation of antioxidant properties of hemp seed protein hydrolysate found that both fractionated and unfractionated hemp protein hydrolysates have in vitro scavenging effect on hydroxy and DPPH radicals, although fractionated hydrolysate had a significantly better radical scavenging activity than the non-fractionated one (Girgih et al. 2011). More recently, by comparing 8 different fiber-based types of hemp cultivars, Andre and colleagues showed that the total phenolic content of the plant significantly correlated with the DPPH activity for all the cultivars tested and that the DPPH radical scavenging activity of these cultivars was significantly decreased over the maturation period of the crop (André et al. 2020). Another in vivo evaluation of the effect of C. sativa L. extract on the oxidative stress markers in the BALB/C mice showed a significant decrease in concentration of glutathione in mice blood by 26.81%, malondialdehyde

by 82.12% and 53.5% in brain and liver respectively while the doses oppositely increased the action of catalase in brain and liver by 64.79% and 72.37% respectively (Kubiliene et al. 2021). Hemp seed polysaccharides' modulatory effect on the Nrf2-Keap1 signaling pathway in CY mice was also shown as the underlying mechanism through which the polysaccharides protect against cyclophosphamide induced intestinal oxidative damage (Xue et al. 2020).

Antihypertensive effects of hemp

There has been a growing demand for the use of naturally derived bioactive peptides in the management of hypertension partly because of the side effects related to conventional antihypertensive drugs. Food protein hydrolysates, including those from hemp have that gained significant research attention in regard to the same. Girgih, and colleagues conducted both in vitro and in vivo investigation on the effect of hemp protein hydrolysate and its fractions on the activities of renin and angiotensin -1- converting (ACE) enzymes (Girgih et al. 2015). They reported that peptides present in the hydrolysate synergistically exerted antihypertensive effects though this was significantly reduced when the peptides were fractionated (Girgih et al. 2015). Besides, by administering 200 mg/kg body weight of hemp seed protein hydrolysate to spontaneously hypertensive rats, it was reported that 1% alcalase digest of hemp seed was most effective in lowering systolic blood pressure while pepsin digest produced a longer-lasting effect on systolic blood pressure reduction (Malomo et al. 2015).

Anti-cancer benefits

Part of the benefits attributable to hemp is anticancer effect which has been studied at various levels. Hemp protein hydrolysate, was for instance, evaluated by Wei et al. for its anticancer properties in Hep3B human liver cancer cells (Wei et al. 2021). The study showed that treatment of the cells with the hydrolysate may confer the cells with anti-proliferative and proapoptotic activity, possibly through modulation of the Akt/GSK/3B - Catenin signaling pathway through the phosphorylation of AKT, inactivation of GSK-3B and phosphorylation and breakdown of B - Catenin. Elsewhere, CBD-enriched hemp oil was demonstrated to have anticancer effects on malignant melanoma (MeWO), HeLa, HepG2, and HOS cells through selective modulation of gene expression of antioxidant enzymes, induction of apoptosis and reactive oxygen species (ROS) generation in the cells (Petrovici et al. 2021). Thus, it can be observed from these studies that there is potential for use of hemp in prevention and therapeutic efforts against cancer or its spread.

Antidiabetic effects

Several scholarly works have reported on the antidiabetic benefits of hemp or its components. In their study, Aslan, Sezik, and Yeşilada (2000) reported that the administration of 120 mg/Kg of ethanolic extracts from C. Sativa fruits gave 13-5-24.5% inhibition in blood sugar levels in Streptomycin-induced diabetic rats (Aslan, Sezik, and Yeşilada 2000). In a different study, dose-dependent intake of hemp protein was reported to produce a postprandial blood glucose reduction after 1h in comparison to intake of carbohydrates; with 40 mg of hemp protein raising both blood glucose and post-meal insulin response (Mollard et al. 2017). Treating diabetes with hemp products can thus, be one of the effective methods to curb the fast growing detrimental effects of the disease. Other health benefits that have been reported for hemp or its derivatives have been summarized in Table 4.

Current challenges in food formulation using hemp and new technological advances as solutions

The production of food products from hemp has been a challenge to food processors and nutritional specialists in formulating the final product. Myriad challenges limit the inclusion of hemp as a raw material in the food processing chain. First, hemp components, such as hemp oils utilized in food supplementations, contain a bitter taste accompanied by a "tar-like" viscosity (King 2019). In addition to their bitterness and viscosity issues, hemp-based food products possess an unusual dark color that originates from its original green color and is attributed to polymerization and oxidation reactions of polyphenols and chlorophyll during processing (Shen et al. 2021). The bitter taste, unusual color, and unappealing viscosity of hemp products significantly affect the palatability of hemp-derived foods

to the consumer. Nonetheless, food processors are recently advancing their processing techniques to overcome challenges associated with the sensory attributes of hemp-based foods. From a food processing standpoint, adding flavor-bearing ingredients has been found to reduce the bitter taste and produce a final product of hemp oil, which is more appealing to consumers (King 2019). Elsewhere, research has found that the application of either high or low temperatures can be used to reduce the bitter taste in foods (Stamenkovic et al. 2019). For instance, storage of olive oil at 5°C for 2-8 weeks reduced bitterness while heating decreased its acidity as reported by scientists (Stamenkovic et al. 2019). Though it has not been applied to hemp-based products, the varying temperatures can effectively reduce the bitter taste of hemp products (Shen et al. 2021). Food researchers have also been able to use techniques such as dehulling, micellization, and mixing hemp products (e.g., hemp oil) with compounds such as acetone (supposedly at a ratio of 1:10 w/v) to improve the color (Shen et al. 2021).

Besides challenges associated with sensory attributes, the public perception regarding hemp and hemp-based foods is generally a major drawback to using hemp as food or food ingredient. The debate over adding hemp to foods comes largely from its association with marijuana since both plants belong to the species C. sativa associated with psychoactive elements. There are plentiful ungrounded claims regarding the risk of using hemp in foods, including the possibility of causing drug addiction to consumers (Tourangeau 2012). Both religious and non-religious groups elsewhere in the world are strongly opposed to hemp and its derived products due to fear of causing drug abuse and addiction among the population (Mutangi 2008). For this reason, there is a need

Table 5. Effects of processing techniques on the nutritional quality of hemp and hemp-derived products.

Processing method	Hemp product	Nutritional-related impact	References
Fermentation	Hemp sourdough	Reduced anti-nutritional components: total saponin content (from 0.64mg/g to 0.30mg/g and phytic acid (60.3 g/kg to 21 60.3 g/kg)	(Nionelli et al. 2018)
Malting	Hemp seeds	Decreased anti-nutritional content, trypsin inhibitors (from 2900 TIU/mg to 2200 TIU/mg)	(Farinon et al. 2022)
Microwave heating	Hemp oil	Application of 900w for 3 min improved CBD content from 5 g/100 g to 8.5 g/100 g	(Fiorini et al. 2019)
Enzyme-assisted low-temperature pressing	Hemp seed cake	Improved the levels of cannabinoids and tocopherols, and also led to high oil yield	(Wen et al. 2019)
Enzyme hydrolysis	Hempseed oil	Improved the total amount of polyunsaturated fatty acids from 77% to 85% of the crude oil whereas the content of omega-6/omega-3 was enhanced by 29%	(Torres-Salas et al. 2014)
Sprouting	Hemp seed	Improved total phenolic content from 2.33 \pm 0.07 mg GAE/g DW to 5.04 \pm 0.04 mg GAE/g DW	(Frassinetti et al. 2018)
Dehulling	Hemp seed	Improved the composition of amino acids such as Histidine (29.03 against initial content, 25.22), Arginine (93.21 against initial content, 86.72), and proline (45.59 against initial content, 43.31	(Shen et al. 2020)
Roasting	Hempseed	Roasting for 14 minutes improved protein content from 15.91% to 23.66% whereas 7 minutes roasting for 21 min enhanced the level of oil yield from 27.81% to 3190%	(Babiker et al. 2021)
Freeze drying	Hempseed oil	Improved protein content and in vitro protein digestibility	(Lin, Pangloli, and Dia 2021)
Vacuum–microwave drying	Hemp flowers	Treatment with 240W increased production of volatile compound such as β-myrcene, limonene, and β-(E)-caryophyllene	(Kwaśnica et al. 2020)
Boiling	Hemp seed	Heat treatment of varying degree improved the levels of crude lipid content but decreased those of crude protein content	(HL. Jang, Park, and Nam 2018)



Figure 5. Global hemp-based food market share per regions, trend and income forecast up to 2027. (Reproduced from https://www.databridgemarketresearch. com/reports/global-hemp-based-foodsmarket).

for improved communication, education, and technology's influence to change public perception of hemp-based foods.

The demand for hemp as a food ingredient is just beginning to emerge from the shadow of *Cannabis* prohibition, which presents a legal challenge for food producers hoping to add hemp-derived materials to their products. By law, for instance, in the US, any final edible hemp-based product intended for consumption must not contain more than 0.3% THC content (King 2019). Furthermore, the US law requires that CBD from hemp can be infused into edible products at levels ranging from 10 to 1500 mg (King 2019). Thus, hemp regulations create challenges for hemp-based food producers who cannot meet these requirements. Such requirements cause anxiety to food producers who fear income losses for their products as they continue to scramble for the never-ending restrictions on hemp. Moreover, a high level of anti-nutrients in hemp limits their ability to be used as potential foods or supplements. Hemp has six major anti-nutrients: phytic acid, condensed tannins, cyanogenic glycosides, trypsin inhibitors, and saponins. These compounds have been shown to reduce feed intake and lead to an enlarged animal pancreas (Russo and Reggiani 2015). Reports have also demonstrated the deleterious effects of these compounds; hence, they are considered unwanted components of hemp even though some of them, such as saponins, possess positive health impacts (Russo and Reggiani 2015). Also even though hemp is considered as low-allergenic food source, there are reports that its derived products, especially proteins induce certain mild symptoms when consumed (Shen et al. 2021). At this stage, about five putative allergens have been identified in hemp: ribulose-1,5-biphosphate carboxylase/oxygenase, profilin, thaumatin-like protein, oxygen evolving enhancer protein, and Can s 3 (Shen et al. 2021). Nonetheless, to date, the effects of processing on allergenic compounds in hemp is still unclear. Therefore, further studies are required to investigate the allergenicity of different hemp-derived products (Shen et al. 2021). The only way to enhance public confidence in hemp-based foods is to reduce the levels of harmful

compounds such as psychoactive compounds, allergens, and anti-nutrients in hemp to acceptable levels.

Finally, nutraceutical and functional food markets are among the fastest-growing food segment in the food industry. The interest has been put on developing nutritionally enhanced foods using isolated ingredients or supplements (Naumovski, Mellor, and Ranadheera 2020). The beverage market for plant-derived products, including milk analogs, consists mainly of coconut milk, cocoa milk, soybean milk, and more recently hemp milk. These products are regarded as functional foods because of their active components, often correlated to their health-promoting impacts. Hemp-based milk is growing in popularity. The hemp-derived milk is known for its abundance in unsaturated fats, which may help reduce the risk of cardiovascular diseases (Curl, Rivero-Mendoza, and Dahl 2020). However, the major limiting factor in the acceptance of hemp-derived milk among consumers is its extremely low protein level per serving (Curl, Rivero-Mendoza, and Dahl 2020). There are reports that individuals, especially vegetarians who consume hemp milk, are challenged to obtain adequate protein from other alternative sources (Curl, Rivero-Mendoza, and Dahl 2020). There is a need to find methods to improve such nutrients in hemp-based milk. Table 5 describes some of the processing technologies currently employed to improve nutritional components such as protein and reduce anti-nutritional factors in hemp-based products. It is important to emphasize that most of these techniques have been reported only at a research level and not in the production of the actual product for consumption.

Hemp-based foods global market: Current outlook and trends

Consumer responses to hemp-based foods in the market place

Industrial hemp, C. sativa L. is facing an image problem. This is because it is often confused with other *C. sativa* crops, mainly marijuana, associated with drug use. Most often, brands offering hemp-derived food products use distinctive marks to allow consumers to identify permitted hemp for industrial use quickly. Hemp-based food is marketed to consumers as having several beneficial effects on health. Despite the increased knowledge about the supposed benefits, hemp-derived foods have not been able to infiltrate the global market fully. Nevertheless, since the beginning of a new era of reintroduction, the hemp-based food market is steadily growing. A study to evaluate the acceptance rate of hemp-based food products in the United States among Vermont residents showed a progressive change in hemp perception; more respondents indicated positive feedback in using hemp-based products during 2020 compared to 2019 (Kolodinsky and Lacasse 2021). The study pointed out that hemp's growing acceptance was intense in the marketplace, where consumers are more informed of the benefits of novel foods than in a market segment lacking such knowledge (Kolodinsky and Lacasse 2021). In Australia, among adults, a study revealed that most consumers are confused about distinguishing between hemp isolates such as CBD or THC and foods derived from industrial hemp (Metcalf et al. 2021). Based on these findings, authors elsewhere argued that the organizations responsible for determining the legal status of hemp have yet not clarified to the public the distinction between industrial hemp, isolated components such as CBD or THC, and other Cannabis crops (Kramer 2017). Consequently, this confusion naturally leads to hesitation among the public, contributing to the hostile posture of consumers toward hemp-based foods. Metcalf and colleagues suggested that public education may be an appropriate tool to allay the fears arising from the association between hemp-derived foods, purified compounds such as CBD or THC, and other Cannabis varieties prohibited by laws (Metcalf et al. 2021).

Hemp-based food market size, insights, and growth projections

Over the past decade, the hemp-based food market has had slow but steady growth. From 2010 to 2013, the production of hemp seeds in the EU increased from about 6000 to 11,500 tonnes (an estimate of 92% growth) (Carus and Sarmento 2016). Notably, this growth was driven by the increasing demand for hemp in the food market, prompting big supermarkets in the EU to begin supplying hemp-based food products (Carus and Sarmento 2016). The rapid growth was especially notable in countries such as Germany and the Netherlands, where it was estimated that more than 50% of the hemp seeds produced went into the food industry in 2013, compared to only 30% in 2010 (Carus and Sarmento 2016). In other places, such as in the US, in 2016, the hemp market was estimated at \$688 million, with 19% of this value originating from hemp-based food-related markets (Stansbury 2017). The market share of hemp-based foods is estimated to rise to USD 7.08 billion by 2027, as described in Figure 5. Global finance survey reports that the surging preferences for hemp-based foods among consumers are due to the increasing cases of related nutritional disorders, a growing number of vegan population across the globe, and the rising nutrition and health consciousness among consumers (available at:https://finance.yahoo.com/news/ insights-hemp-based-food-global-102300385.html?fr=sycsrp_ catchall. Last accessed on 21 May 2022). Additionally, the continual launch of innovative hemp-related products such as hempseed-based sauces, shakes, ice creams and desserts is a growth-inducing factor in hemp-based food market.

Hemp-based food market competitive landscape

Reports by the Data Bridge analyses indicate that the major players in the hemp-based foods global market include companies such as Hempco Inc., Elixinol., Cool Hemp, Hemp Foods Australia Pty Ltd, Canada Hemp-based foods Ltd., Liaoning Qiaopai Biotech Co., Ltd., Naturally Splendid Enterprises Ltd., Elixinol Global Limited, Compass Group Management LLC, NAVITAS ORGANICS, Canopy Growth

Corporation, among other global players (available at https:// www.databridgemarketresearch.com/reports/global-hemp-based-foods-market. Last accessed 21 May 2022). The hemp-based food product market has been segmented into two major groups. The first segment is based on product type, which is composed of hemp seed oil, hemp protein powder, and hemp seed (both dehulled and hulled hemp seed). The second segment is based on the distribution channel. This market segment includes supermarkets, convenience, and hypermarket stores, among other distributors. Major countries covered in the hemp-based foods market reports are mainly in North America (mostly United States, Canada, and Mexico). They are projected to be the leading hemp producers globally by 2027 and beyond. On the other hand, the Asia-Pacific hemp market is expected to grow at the highest rate by 2027 due to the adoption of western food styles and the increasing demand for hemp-based foods because of their gluten free property (Figure 5). Thus, going forward, the hemp-based food market is expected to grow and the competition among major players and from other food substitute is expected to rise.

Safety and dietary exposure assessment of hemp foods

Industrial hemp has been defined as the plant of C. sativa L. with a THC concentration of not more than 0.3% on a dry weight basis. This level of THC is regarded as safe, and within the limit of consumption. Food Standards Australia New Zealand (FSANZ) conducted a dietary exposure assessment to guarantee that the proposed maximum permitted levels of THC within foods containing low THC hemp may not lead to dietary exposures greater than the tolerable daily intake (Montoya 2016). In its 2002 assessment of low-THC hemp as a food, FSANZ assessed the toxicity level of THC present in hemp foods following oral administration in order to establish a tolerable daily intake food (Montoya 2016). From the assessment conclusion at the time, FSANZ established that a tolerable daily intake of THC in hemp foods was 6µg per kg, body weight. In 2012 assessment, FSANZ examined the scientific literature and again confirmed 6 µg per kg, body weight as the valid level of tolerable daily intake of THC in hemp foods (Montoya 2016). Thus, FSANZ found that it is likely that no consumers in Australia or New Zealand would be at risk of intoxication by hemp-based foods. The report further stated that hemp-derived foods may not expose consumers to allergenic reactions. A separate dietary exposure assessment performed in Canada, several years back concluded that the levels of THC in hemp foods does not cause any psychoactivity, or any other adverse health effects to consumers (Grotenhermen, Leson, and Pless 2003). The study stated that the THC levels present in Canadian hemp-derived foods offer protection from such effects with a wide margin of safety, even for individuals who regularly and extensively consume hemp foods (Grotenhermen, Leson, and Pless 2003). Thus, regarding acute toxicity, there is no literature evidence supporting that hemp-based food consumption may induce death situations.

However, in some other studies, minor aspects of health concerns have been described for hemp-based foods (Steinmetz, Nahler, and Wakefield 2022). Steinmetz et al., conducted a study to evaluate what is known about safe dose in hemp-derived food, and determine what data is still needed to inform regulated limit (Steinmetz, Nahler, and Wakefield 2022). Examination of different hemp seed oils discovered that 4 of the 102 samples investigated posed a low-to-moderate risk for inducing toxicity (Steinmetz, Nahler, and Wakefield 2022). Findings from the assessment also established that safety limit of 11.9 µg/kg/day is proposed for most hemp-based foods. Nonetheless, the study included an emphasis on safety limit and regulatory measures as key factors for preventing toxicity that may arise from consuming hemp-based foods (Steinmetz, Nahler, and Wakefield 2022). Based on these findings, we recommend the following: (1) Determining risks and what research and regulations are needed to address them is crucial to ensure confidence in hemp-derived foods. (2) To avoid confusion related to hemp-derrived foods, labeling requirements for all countries should be consistent. The labeling should accurately reflect THC content of the specific hemp cultivar used to produce foods as well as the product composition, and how it was processed. Thus, legal jurisdictions and strict adherence to good manufacturing practices are needed to safeguard consumers against any potential risk associated with hemp-derived products, and have not been established. (3) Authorities should facilitate a conditional product registration with its detailed parameters clearly stated. We recommend a corporate research program in each country that would include representatives from consumers and all stakeholders involved, including food manufacturers and regulators to verify adherence to quality and safety standards, product analysis, and sharing of safety data on hemp-based foods. Such efforts could optimize quality and safety control measures to ensure confidence in industrial hemp as a food item.

Research limitations and perspectives

While there has been a fast-changing stance in the legalization and usage of hemp globally, the anecdotal health benefits of hemp-based foods are largely unexplored at the clinical level (Cooper et al. 2021). Thus, there is a need to evaluate new and existing hemp-based food products at the population level to ascertain already known and unknown health benefits. Moreover, the continued launch of innovative products, such as hemp seed-based sauces, shakes, ice creams and desserts, require that proper clinical trials and safety assessment are performed and reports published to confirm the products' safety and health benefits before their official use. Also, in some in vitro and in vivo hemp-related studies, there are still inconclusive findings on the underlying mechanisms for purported benefits of hemp-derrived compounds (Turck et al. 2022). For instance, as per the above-cited statement by EFSA's expert panel, there are several cases of toxicity attributable to CBD-the most investigated and the primary bioactive molecule taunted for various benefits in hemp-based products. All these provoke a need for more significant research on hemp particularly that which shall bring into light the underlying effects of hemp components that possess beneficial claims, such as CBD. As more studies unfold and the legalization of hemp expands to more countries and regions, a comprehensive regulatory framework with precise definitions about what encompasses hemp-based food or Cannabis edibles will need to be formulated and sufficiently relayed to the public and all players involved in the hemp-based food business (Marcu 2022). As noted above, labeling of hemp foods should accurately reflect THC content of the specific hemp cultivar used to produce the food, product composition, and intake limits to guarantee long-term safety. This action will facilitate the public understanding of hemp-based foods by distinguishing them hemp isolates such as CBD, THC, and other hemp cultivars not allowed for food use.

The upcoming research needs to utilize novel and/or existing techniques to improve the quality of hemp during processing and incorporation in foods without compromising on nutritional quality, functionality, safety and overall acceptability of hemp-based foods. Notably, there is a need to research more on innovative techniques that can be used to reduce to acceptable limits the main psychoactive component of hemp, THC in different hemp cultivars. This will help reduce safety concerns about hemp and hasten the legalization of industrial hemp as a food item in different countries. Besides THC, as already been discussed above, about five allergens have been identified in hemp products, but research has not revealed yet the effects of processing on these compounds (Shen et al. 2021). Therefore, further studies are needed to investigate the effects of different processing techniques on allergenicity of hemp-derived products.

Moreover, hemp is a diverse crop that produces raw materials mainly in two distinct categories: food components and fiber. Within the food component category, hempseed (with a THC content of 0.3% or less) is considered a raw product for food processing and can be improved by multiple avenues of research. For example, due to the diversity of industrial hempseed cultivars (such as finola, alyssa, anka, canMa, CFX1 etc.), research targeting the understanding of which hempseed cultivar possesses a better yield of some particular food-derived ingredients will improve the ability to enhance the production of such products from the seed. Seed and oil research will enrich the understanding of which hempseed cultivar has a higher yield of oil production. Furthermore, hempseed produces a diverse array of nontoxic phytochemicals including cannabinoids, terpenes, and phenolic compounds with potential benefits for health. Studies targeting metabolite yield will expand insights into specific compounds that can be derived from particular hempseed cultivar. Thus, unlike the currently CBD-centered research, studies targeting other beneficial compounds in different hemp cultivars will improve our comprehension of the health benefits of such cultivars. Methods involving untargeted metabolomics using techniques such as UHPLC-MS/MS and UPLC-MS/MS analysis will provide a hint into the diverse nature of beneficial



compounds in different hemp cultivars and give a lead for the selection of hemp cultivars containing high levels of the target compound. Finally, more studies have yet to investigate the flavors of different hempseed cultivars. In a review elsewhere, authors suggested that different hemp cultivars possess distinct flavors ranging from weak to strong (Schluttenhofer and Yuan 2017). The study suggested that more work is needed in this area to allow the identification of the different tastes of hempseed cultivars. Information from the investigations will assist in expanding the use of hemp seed in human and animal food products.

Conclusion

Historically, hemp has been a valuable raw material for producing various consumable products such as food, clothes, and medicine. Recently, the use of industrial hemp as food and food ingredients has dramatically increased. Industrial hemp has been found to possess numerous properties, especially its high nutritional value that allows its wide application in the food industry. The crop has been applied to produce new functional food products, including beverages, oil, and bread. Foods containing hemp constituents are currently marketed worldwide as beneficial to human health. These health claims have been widely investigated in both in vitro and in vivo studies, proving hemp as an essential food item. Moving forward, studies are required to design techniques that can enhance the quality of hemp-based food products, such as improving the final product's sensory features and reducing THC levels of hemp seeds to improve acceptability among consumers.

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