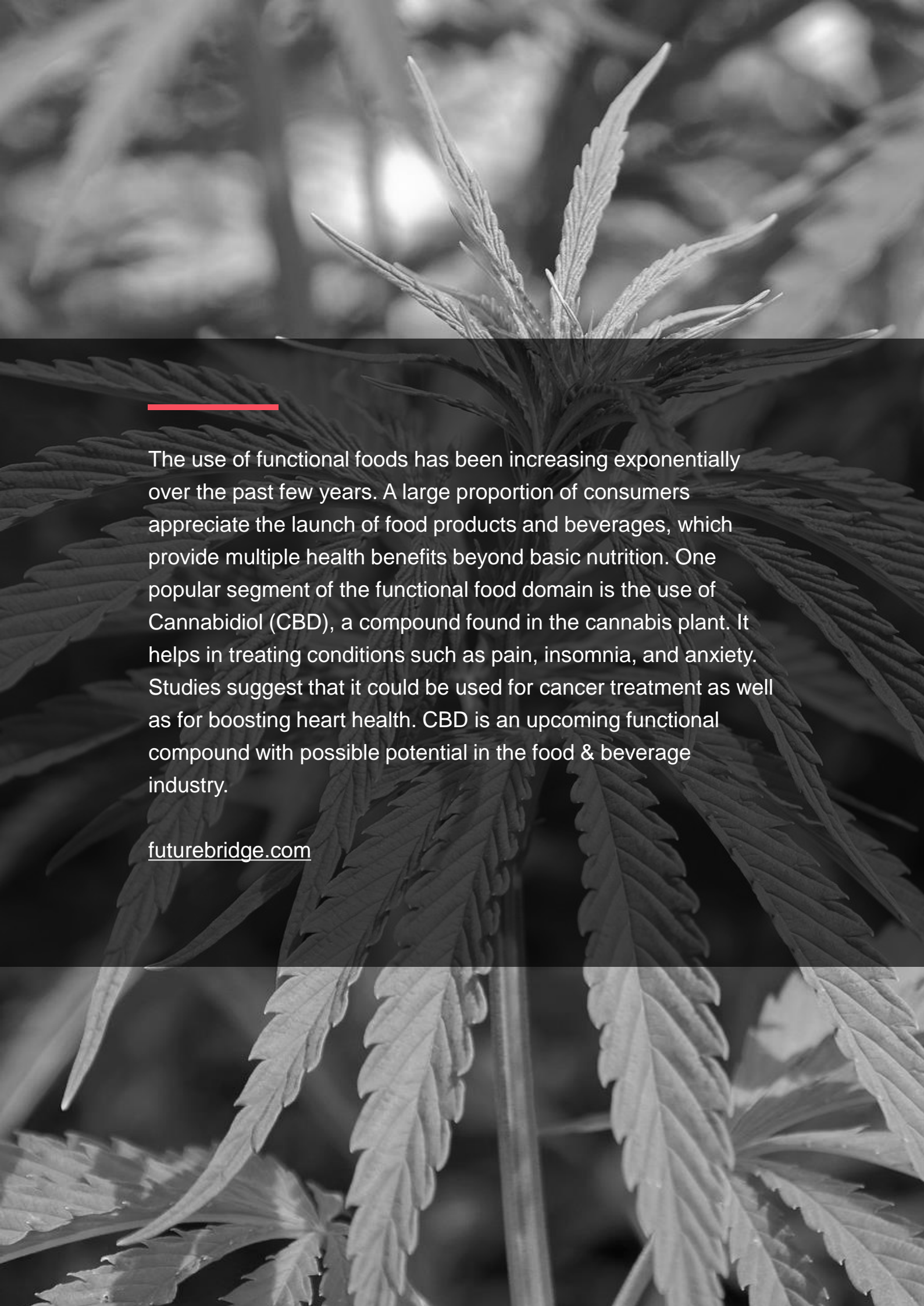




WHITE PAPER

Cannabidiol – Towards a Propitious or Bleak Future?

FutureBridge



The use of functional foods has been increasing exponentially over the past few years. A large proportion of consumers appreciate the launch of food products and beverages, which provide multiple health benefits beyond basic nutrition. One popular segment of the functional food domain is the use of Cannabidiol (CBD), a compound found in the cannabis plant. It helps in treating conditions such as pain, insomnia, and anxiety. Studies suggest that it could be used for cancer treatment as well as for boosting heart health. CBD is an upcoming functional compound with possible potential in the food & beverage industry.

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Executive Summary

The domain of functional foods is the trend that is maturing at a very rapid pace. Large consumer population across the globe are constantly on the lookout for novel food products, supplements, and beverages, which are developed with innovative ingredients to enrich their health.

The use of Cannabidiol (CBD) is a growing segment within the functional foods domain. Owing to its therapeutic, and beyond metabolic functional benefits, the compound is entering the market swiftly in the form of supplements, snacks, and as infusions. However, despite all the commotion surrounding its benefits, the compound is still lacking regulation for use in product development and distribution, owing to its ill-famed psychoactive cousin, Tetrahydrocannabinol (THC). Few, yet distinct challenges are present in the development of CBD-infused products; however, these challenges have not deterred players from using the functional ingredient in novel product formulations.

A majority of players involved in the functional foods domain are startups and small companies, spread across the globe; these companies develop products containing broad-spectrum, full-spectrum, and CBD isolates. Established companies are slowly, yet steadily entering the market with launches of CBD supplements, in regions with less regulatory constraints.

What is Cannabidiol?

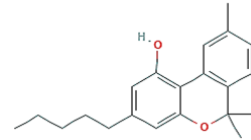
Cannabidiol (CBD), is a non-psychoactive compound obtained naturally from the cannabis species of plants, also known as marijuana plants. It is the second most prevailing compound in the plant, following THC. CBD has been medically proved to possess properties, such as being anti-proliferative, anti-angiogenic, and pro-apoptotic. It makes up about 40% of the cannabis plant extract and is currently being studied actively for use in food supplements and as a new drug. Currently, CBD has been approved for use as a drug by the name of [Epidiolex](#), which is preferred for the treatment of seizures accompanying Lennox-Gastaut syndrome and Dravet syndrome. In recent years, several CBD-infused food products have been observed entering the food & beverage market in the form of snacks, beverages, and supplements, despite the legal constraint of considering CBD as a dietary supplement.

EXHIBIT 1: Scientific Make-up of Cannabidiol

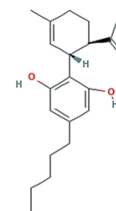
Cannabis Plant



Delta9-tetrahydrocannabinol



Cannabidiol



Source: PubChem

Regulatory hurdles surrounding CBD

Though CBD does not induce a “high” feeling upon consumption, it is increasingly disputed considering the source material also provides THC, a psychoactive compound. According to a report by the World Health Organization (WHO), in humans, CBD exhibits no effects indicative of any abuse or dependence potential. The claimed negative aspects of CBD are usually due to the presence of THC, causing psychoactive effects, such as paranoia and increased stress. This, in turn, has caused multiple regulatory hurdles regarding the use of CBD as a food ingredient.

“According to the Federal Food, Drug, and Cosmetics Act, the addition of compounds used as drugs is strictly prohibited in human or animal food. This is inclusive of substances approved as drugs, as well as those under clinical investigations.”

The only FDA approved product is a drug named Epidiolex, which contains the purified form of CBD. Owing to the consideration of CBD as a novel drug, the FDA has concluded that CBD products are blacklisted from the definition of a dietary supplement, under the Federal Food, Drug, and Cosmetic Act (FDCA). However, despite barring the use of CBD in food supplements, the 2018 U.S. Farm Bill approved the legalization of hemp containing less than 0.3% of THC. According to the bill, hemp would presently be cultivated as a regulated crop for personal as well as industrial production, thereby excluding hemp from the definition of “Marijuana” under the Controlled Substances Act (CSA). The CSA prohibits the manufacturing, distributing, dispensing, or possessing cannabis with a THC content higher than 0.3% of THC.

“When hemp was removed as a controlled substance, this lack of research, and therefore evidence, to support CBD’s broader use in FDA-regulated products, including in foods and dietary supplements, has resulted in unique complexities for its regulation, including many unanswered questions related to its safety.”

– **Norman “Ned” Sharpless**

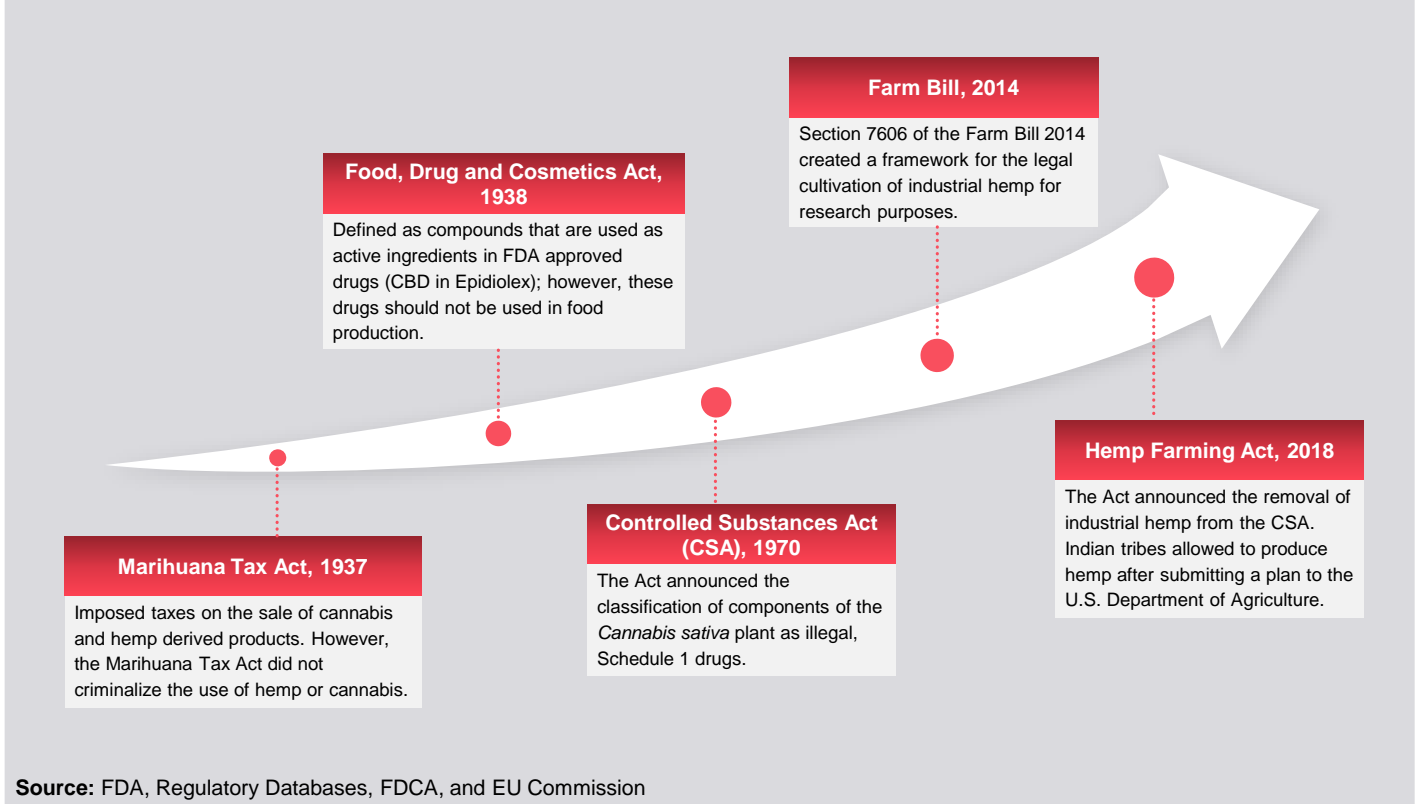
Acting Commissioner, U.S. Food and Drug Administration

Through this development, the United States Patent and Trademark Office (USPTO) would permit the registration of goods encompassing cannabis or CBD. An additional aspect considered was that the use of hemp in the production of food or dietary supplements, without the approval from the FDA, would violate the FDCA and the production would be denied. Thus, a clash in regulations is observed between the FDCA and the CSA. Recently, the New York State Department of Health announced a ban on the use of CBD food products in bars and restaurants.

Till date, no clear regulations have been laid out concerning the production and distribution of CBD-infused products in the U.S. The European Commission has reclassified CBD as a novel food, thereby implying its illegality in the production of food products and beverages. According to the EC’s Working Group of Novel Foods, the extracts of *Cannabis sativa L.* and its derived products are considered as novel, owing to the absence of a history of consumption. The European Food Safety Authority (EFSA) takes on the regulatory development that would be considered a novel food application in case of CBD infused products, with a daily intake of 130mg per day in adults.

Regulatory challenges associated with CBD are depicted in the *Exhibit 2* below:

EXHIBIT 2: Regulatory Challenges Associated with the Growth of the CBD Segment



What is the Current Market Trend?

Despite the constant flux in regulations, a large number of CBD-infused food products and beverages are entering the market (depicted in *Exhibit 3*). Products are developed primarily in the form of beverages, coupled with natural compounds that boost an individual's cognitive capabilities. Other forms of products include CBD oils, gummies, and shots.

Multiple start-ups are being established in the field of nootropics using CBD as an active ingredient. CBD-infused beverages are further divided into fruit infusions and sparkling water ranges, wherein CBD extracts are mixed along with natural fruit extracts and water, respectively. Several dispensaries are selling CBD products, mostly in the form of tinctures and oils. Moreover, the sale of CBD gummies and snack products are also increasing. CBD supplements are developed in the form of capsules with several health claims, such as stress relief, improving sleep qualities, and increasing concentration.



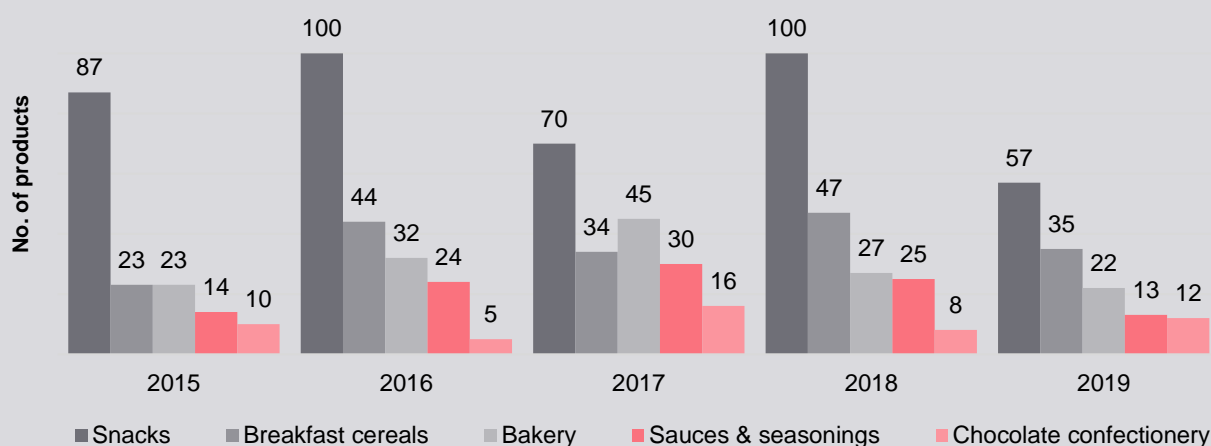
“The current industrial hemp market is valued at \$4.6 billion USD, and is expected to reach a value of 26.6 billion by 2025, with a CAGR of 34%”

The growth is ascribed to factors such as

- Legalization of hemp cultivation
- Increased consumer demand for functional foods and beverages
- Rise of chronic disease incidences

– Market Research Report, Jun 2019

EXHIBIT 3: Number of Product Launches in the Top Five Food Categories (2015-2019)



Source: Mintel

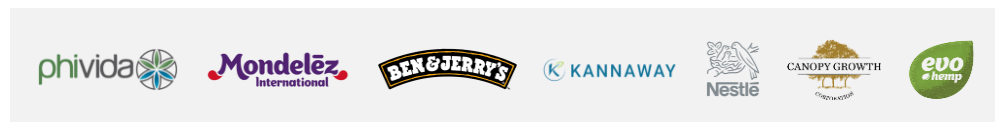
Established food & beverage company, Nestlé, announced the launch of first CBD oil extracts and supplement capsules under its ‘Garden of Life’ brand in the US, during the [Investor Seminar](#) in May 2019. The established player activity is lacking in the segment of CBD-infused products, mainly due to the lack of clear regulatory protocols. Several large players, including Coca-Cola, Mondelez, and Ben & Jerry’s, have revealed their intentions to enter the field after clear regulations regarding the manufacture and distribution of CBD-infused products have been laid out.

The U.S. and Canada have reported the highest activity surrounding CBD products within the North American region. However, cannabis is legalized in Canada for consumption as a food supplement or for medical purposes.

Who are the Active Players?

The rising demand for unique food functional products has prompted multiple start-ups and small companies to get involved in the manufacture of CBD food products and beverages. Unfazed by the regulatory dilemma, established players are also entering the domain, owing to the ever-rising consumer interest in CBD-related functional foods and beverages.

A key notable development in the field was that of ingredient developer, Amyris's joint venture with LAVVAN for the development, licensing, and commercialization of CBD as a food ingredient. Amyris is an established U.S.-based, ingredient developer, specializing in the production of zero-calorie sweetener solutions. Through the partnership, Amyris has revealed its plans to become a leader in the space of fermentation-based CBD development.



Canopy Growth is a Canadian multi-brand cannabis company that develops THC as well as CBD containing products, in the form of dried flowers, powders, or as soft gels. Several companies are developing reformulated snacking products to contain cannabinoids, including CBD and THC.

Tweed, a subsidiary under Canopy Growth, was the first company to introduce the concept of compassionate pricing to make medical cannabis affordable for patients, and also the first approved company to export dried cannabis to Germany. The company is involved in the development of novel cannabis products that are marketed through its brand, Spectrum Therapeutics.

Phivida, a Canadian company is a key startup that develops CBD-infused food and beverages through its brands, Vida+, and Oki. Vida+ is involved in the development of CBD capsules and tinctures, while Oki develops CBD-infused sparkling water and iced tea. Phivida has been working on developing its business model to launch & distribute Oki brand products via different distribution chains, including online retail stores as well as the supermarket chain, Safeway Stores.

It has been observed that start-ups and small companies are active in this segment of CBD-infused foods and beverages with launches of unique products like CBD-infused sparkling water and iced tea. Established companies are slowly showing interest in this segment and have announced their plans to develop CBD products, based on the safety validation by associated food authorities.

Case Studies

CASE 1: Novel product formulations containing full, broad-spectrum hemp extracts and isolates

Various new CBD-infused products are entering the market. Active players in this segment are developing new formulations to ensure maximum functional health benefits and gain consumer attention. The three most commonly used terms in CBD-containing products include full-spectrum, broad-spectrum, and CBD isolates.

The differences between the three are highlighted below:

- **Full-spectrum CBD products:** These products are developed using plant extracts that contain flavonoids, natural fatty acids, terpenes, and other cannabinoids, including traces of THC. Most CBD products are developed as full-spectrum, as they produce an “entourage effect,” wherein therapeutic effects of all compounds are made available.
- **Broad-spectrum CBD products:** Broad-spectrum extract is similar to a full spectrum extract, with the difference being, it does not contain any trace of THC. Products developed using broad-spectrum CBD is devoid of the psychoactive risks associated with THC.
- **CBD isolate products:** It is the purest form of CBD and used for the development of products for consumers who are sensitive to other cannabinoids and are required to take high doses of CBD.

CASE 2: Research identifying hepatotoxicity of CBD in mouse models

A major challenge in the use of CBD as a food ingredient is the lack of information available on the long-term risk effects of the compound. In a recent article titled, “Hepatotoxicity of a Cannabidiol-Rich Cannabis Extract in the Mouse Model” by Igor Koturbash et al., 2019, the toxicity of CBD was measured using mouse equivalent doses of recommended human maintenance doses of CBD in the **Epidiolex** drug.

Non-psychoactive drugs are responsible for the down-regulation of 50 genes, many of which play a vital role in oxidative stress responses, lipid, and drug metabolism pathways. On performing acute and sub-acute toxicity tests, CBD was found to affect hepatocytes, resulting in increased liver-to-body weight ratios, plasma Alanine transaminase, Aspartate transaminase, and total bilirubin.

The active toxic effect on the liver and the down-regulation of various metabolic pathways have raised concerns regarding the safety of CBD usage. According to a report developed by the FDA, the reduced dosage of Epidiolex was observed to resolve the transaminase elevations. However, the use of CBD in food products becomes a potential threat to liver health.

Challenges in Production and Distribution

CHALLENGES		POSSIBLE SOLUTIONS
REGULATION	Since CBD is considered as a pharmaceutical ingredient, a regulatory clash is observed between the Food Drug and Cosmetics Act, which allows the use of hemp plants with <0.3% THC and Controlled Substances Act that prevents the use of such drugs in food applications.	The FDA has made exceptions for certain ingredients, indicating the possible establishment of a regulatory framework for the use of CBD in food production and distribution.
INADEQUATE RESEARCH DATA	Therapeutic and functional benefits of CBD have been made clear through active R&D by companies and research centers. However, data available concerning the toxicity and long-term risks are sparse.	Active research by means of investments for identification of toxic effects and long-term risk factors associated with the consumption of CBD as a food ingredient could be promoted.
SCREENING	One of the main reasons for uncertainty towards consumption of CBD is that it is derived from the same source as its psychoactive cousin, THC. CBD-infused products that contain THC result in hallucinations and cause other side-effects.	Effective screening technologies to ensure that CBD-infused food products and beverages are completely devoid of THC traces could be developed.
PUBLIC PERCEPTION	Despite the popularity gained by CBD, a considerable percentage of consumers perceive it as an illegal product, as both CBD and THC come from the same source.	Clean labeling of CBD-infused products with reliable claims could be provided. Functional benefits about CBD must be conveyed to consumers.

Conclusion

Consumers are constantly on the lookout for products that provide something more than just nutrition. Increased consumption of products infused with CBD signifies the acceptance of this novel compound. Its availability in the form of snacks such as bars, gummies, cookies, and beverages make it more attractive to consumers. The restorative characteristic of CBD is one of the prime reasons for its rising popularity among the health-conscious population. Despite the fame that CBD has gathered across the globe, there exists a constant unease towards its production and distribution. The fact that CBD is currently being marketed as a drug, muddles the regulatory protocols required to consider it as a food supplement/ingredient.

However, even without the establishment of a regulatory framework, multiple start-ups and small companies are launching unique products that might appeal to consumers. Established players too plan to enter this segment; however, these companies are currently holding back due to regulatory concerns revolving the CBD usage. At present, CBD has a huge potential in the food & beverage industry. However, a complete review of the compound's short and long-term effects is required to ensure complete safety for use in food products. Thus, the use of CBD can be concluded as that of a double-edged sword, with both positive and negative aspects, the positive being its health improving properties and the negative being its toxicity and possible THC presence.

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