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Cannabis-infused foods: Phytonutrients, health, and safe product innovations

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Abstract

Cannabis-infused foods are currently on the rise in markets all around the world. Meanwhile, there are concerns over the health implications for consumers. Studies have explored the therapeutic potential and nutritional and economic benefits of cannabis usage. Yet, the phytonutrients, processing methods, and health implications of cannabis-infused foods have not been well explored. This review evaluates existing evidence on the nutritional, processing, safety, and phytonutrient composition of cannabis-infused food products and their medicinal and functional prospects. Cannabis seeds contain the highest amount of dietary nutrients, while flowers contain the highest amount of bioactive constituents. Oils, butter, seeds, flowers, and leaf extracts are the plant forms currently incorporated into food products such as beverages, baked products, cooking ingredients, functional foods, nutraceuticals, and nootropics. Cannabis-infused foods have been found to offer therapeutic benefits for pain management, brain function, gut health, and certain cancers. Findings also show significant constraints associated with cannabis-infused foods regarding dosage guidelines, limited research, efficacy, and long-term health effects on consumers. This is further worsened by the lack of policies that regulate the industry. To realize the full potential of cannabis use in the food and health industries and in research, regulatory guidelines are needed to control dosages and improve its efficient use in these industries. This will go a long way to ensure the safety of cannabis users and enhance responsible production, marketing, and distribution.

KEYWORDS
cannabis-infused foods, medicinal benefits, nutritional benefits, phytonutrients, safety risks

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1 | INTRODUCTION

The evolution of the cannabis plant from a forbidden substance to a highly valued plant has significantly influenced the food industry (Rasera et al., 2021). This shift is largely influenced by the increasing legalization of cannabis in many countries across the globe. This has increased acceptance of cannabis-infused food products as promising alternatives with both dietary and medicinal benefits (Charlebois et al., 2018). Consumers' demand and high expectations for healthy, safe, and sustainably produced natural foods have also accelerated research efforts worldwide to explore these alternative food products to meet this ever-increasing demand (Hassoun et al., 2022).

Cannabis-infused food products cover a wide range of products such as chocolates, concentrates, cooking ingredients, baked goods, savory snacks, tinctures, candies, and beverages (White et al., 2021). These products are made by incorporating extracts from the flower, leaves, or seed of the cannabis plant into several food matrices (Krüger et al., 2022). Generally, the cannabis leaves, flowers, or seeds are dried, stored for use in these foods, or further processed into extracts, tinctures, oils, and butter (Lazarjani et al., 2021).

Different parts of the cannabis plant such as flowers, seeds, leaves, and extracted oils offer benefits including neuroregulation, relief from nausea, pain management, appetite stimulation, and treatment of sleep disorders, epilepsy, cancer, and neurodegenerative diseases (Amin & Ali, 2019). Therefore, the growing acceptance of cannabis food products, as well as the continuous search for novel therapeutic compounds, presents immense opportunities for the food, pharmaceutical, and other health industries to innovate and produce food products enriched with bioactive ingredients (Fike, 2016).

Besides, increasing scientific evidence shows that cannabis-infused food products can exhibit significant therapeutic and health-promoting effects, making them highly valuable in the commercial marketplace (Pathak et al., 2022). For instance, in one longitudinal study, edibles administered to glaucoma patients over 6 months improved their eyesight (Mahvan et al., 2017). A study found that optimizing cannabis strains in producing hemp seed cake resulted in functionally enhanced products that improved overall gut health (Aliferis & Bernard-Perron, 2020). Thus, incorporating cannabis into food ingredients allows manufacturers to create functionally improved products with enhanced health and nutritional capabilities such as nootropics and nutraceuticals (Leonard et al., 2020). Improvements in the formulation, manufacturing processes, and safety considerations of cannabis-infused food products also provide enhanced flavors and increased bioactive benefits for consumers' health (Lindsay et al., 2021).

Despite the potential benefits, there is a need for comprehensive reviews on the extraction and processing methods of cannabis-infused foods, health implications, and types of cannabis-infused foods. While some studies have focused on applications of hemp and hemp extracts (Al Ubeed et al., 2022; Cerino et al., 2021), others have provided general overviews of cannabis food products on the market (Rasera et al., 2021). Lachenmeier and Walch (2005) analyzed cannabinoids in hemp food products, while Bakowska-Barczak et al. (2020) examined the application of flax and hemp seeds in several food matrices. However, an in-depth knowledge of these foods, their composition, bioactive constituents, preparation, safety considerations, and particularly health implications is of the essence. This paper addresses these gaps by exploring the forms of cannabis-infused foods, assessing their phytonutrient and health implications, and evaluating innovations and challenges in developing effective, consumer-safe products.

2 | COMPOSITION OF THE CANNABIS PLANT

Cannabis, a member of the *Cannabaceae* family, is commonly referred to as "marijuana," "weed," and "hemp" (Small, 2015). Historical evidence points out that cannabis use dates back 10,000 years to ancient civilizations in Asia, for its medicinal and industrial properties (Pisanti & Bifulco, 2019). The distinctive aroma, flavor, and exceptional taste of cannabis can be attributed to cannabinoid compounds, such as tetrahydrocannabinol (THC) or cannabidiol (CBD), terpenes, and phenolics, which contribute to its numerous applications (Cerino et al., 2021).

The cannabis plant is documented primarily for its "psychoactive" compounds and to a lesser extent for its dietary nutrients (Fathordoobady et al., 2019). *Cannabis sativa* is classified into two: drug type (marijuana) and industrial type (hemp) (Cerrato et al., 2021). The flowers of drug-type cannabis plants are typically harvested and dried for consumption through smoking, vaporizing, or ingestion. The cannabinoid compounds, such as THC or CBD, are well-documented for their ability to induce effects such as euphoria, relaxation, and altered perception (Carvalho et al., 2022). The industrial cannabis varieties are valued for their sturdy stalks, which can be processed into a range of industrial and commercial products (Kraszkiewicz et al., 2019). For example, hemp fibers are used in industries for textiles, paper, construction materials, and biofuels. Hemp seeds are consumed directly or processed to obtain hemp

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oil, which finds application in food products, cosmetics, and dietary supplements (Rehman et al., 2021).

Not all cannabis strains are specifically bred with a focus on increasing the THC levels (Johnson, 2019). Certain varieties have been selectively bred to have low THC levels simultaneously with higher concentrations of CBD or other cannabinoids, such as cannabinol (CBN), that do not cause intoxication (Mostafaei Dehnavi et al., 2022).

The hemp seeds and cannabis seeds differ significantly in terms of CBD and nutrients; however, the hemp seeds contain the highest nutrients and lowest contents of "CBD". This makes the seeds the most desired in terms of dietary nutrients for animal and human consumption. On a dry weight basis (per 100 g), the seeds are rich in proteins (24%), fiber (35%), oil (30%), crude fat (37%–44%), and minerals (4.8%) (Cital et al., 2021). The seeds are most often converted to hemp oil and used for cannabinoids and their nutritional benefits (Silver et al., 2021).

The flowers known as buds are the most wanted part of the cannabis plant and contain the highest concentration of cannabinoids, made up of THC (10%–30%) and CBD (1%–45%), which are responsible for the plant's psychoactive and therapeutic effects (Silver et al., 2021). The resinous trichomes present in the flowers are the source of these compounds in addition to terpenes and flavonoids. Aside from the dried flower extracts, the flowers are also frequently harvested for resin-based products processed in the pharmaceutical industries (Valizadehderakhshan, 2022). Cital et al. (2021) identified that although the flowers contain a considerable amount of proteins (5%–15% dry weight) and carbohydrates, they are barely used as a source of nutrition.

Cannabis leaves generally have lower cannabinoid levels (1%–3%) compared to the flowers. However, they contain terpenes and flavonoids, albeit in smaller amounts (Bruci et al., 2012). Just like the flowers, leaves are not considered a suitable daily nutritional source due to their low content of carbohydrates, proteins, and minerals. Thus, after the removal of the cannabinoids (90%), the remaining plant material is used for animal feed as outlined by Yalcin et al. (2018).

The stems of the cannabis plant contain fibrous material and provide structural support, although they are not typically harvested for their medicinal properties. Some studies show they contain trace amounts of cannabinoids and other therapeutic compounds (Zimniewska, 2022). However, there is currently no substantial evidence regarding the amount of fiber, protein, or fats in the stem. In contrast, the stalks (main structural support) of the cannabis plant are considered an essential component of fiber, although there is very limited information regarding its usage as feed for animals or as a dietary source of nutrients for humans (Crini et al., 2020).

The plant's roots are the plant's least explored components, especially as a nutritional ingredient. Current evidence demonstrates that they contain therapeutic compounds with considerable applications in the medical field for the treatment of skin ailments, inflammation, fever, and tumors (Ryz et al., 2017). The roots have been reported to contain low concentrations of triterpenoids (7.5–21.3 mg/kg) (Sethi et al., 1977), alkaloids (0.3–2.5 mg/kg) (Elsohly et al., 1978), carvone, a monoterpene (77.7%), dihydro carvone, a monoterpene (23.3%) (Elsohly et al., 1978), and sterols (0.56%–1.5%) (Ryz et al., 2017).

2.1 | Bioactive constituents of cannabis

Cannabis as a genus is composed of a very diverse genetic profile containing hundreds of different cannabis strains, each with unique combinations of cannabinoids, terpenes, and other compounds. This genetic diversity contributes to the wide array of effects and therapeutic properties exhibited by different cannabis varieties (Addison, 2022). As of 2022, a total of 565 therapeutic compounds have been identified in cannabis, which includes 198 non-cannabinoids and 125 cannabinoids. These compounds include terpenes, flavonoids, and phytocannabinoids (Figure 1) and have therapeutic and biological effects (Al Ubeed et al., 2022). These are briefly discussed below.

2.1.1 | Cannabinoids

Cannabinoids are a group of compounds found primarily in the flower of the cannabis plant and contribute to the plant's psychoactive effects (Atakan, 2012). The plant contains over 100 cannabinoids, with THC, CBD, and CBN being the most predominant compounds observed in the plant profile (Swift et al., 2013).

THC widely known to be present in the plant is responsible for the feelings of euphoria and intoxication that are commonly associated with its use (Drennan et al., 2021). Certain cannabis strains have been specifically bred to have concentrations of THC ranging from 15% to 30% (Chandra et al., 2017). Over time, THC has gained popularity due to its potential for pain relief in patients with conditions such as AIDS, cancer, epilepsy, and certain neurological disorders such as Huntington's disease, epilepsy, Parkinson's disease, and multiple sclerosis (Breijyeh et al., 2021). Chemically, THC's core structure consists of three hydroxybenzene units known as a resorcinol ring connected to two side chains—one a pentyl and the other a propyl moiety. This unique structure gives THC its ability to dissolve in fats and oils, making it lipophilic (Mechoulam et al., 2019). The synthesis of THC

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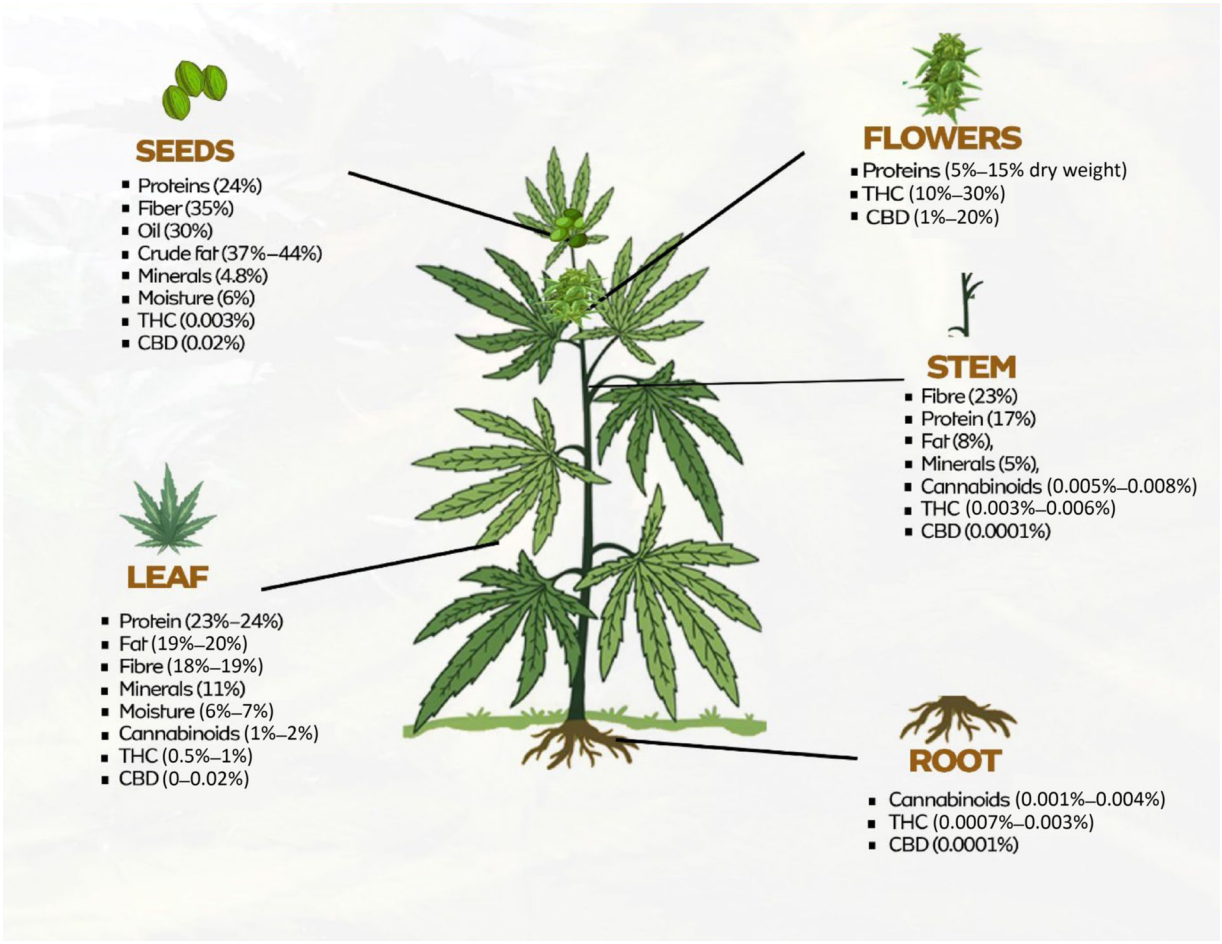

FIGURE 1 Dietary and bioactive constituents of cannabis. CBD, cannabidiol; THC, tetrahydrocannabinol. Source; Edited from Xu *et al.* (2022)

involves a series of reactions starting from cannabigerolic acid (CBGA) a precursor in cannabinoid synthesis. CBGA undergoes a series of enzymatic reactions to produce THC. For example, CBGA is converted into tetrahydrocannabinolic acid (THCA) by the action of the enzyme THCA synthase, which, upon decarboxylation (removal of a carboxyl group), becomes THC (Degenhardt et al., 2017).

In contrast, CBD's central structure consists of a resorcinol moiety, linked to geranyl pyrophosphate, a monoterpene unit. Enzymatic transformations within the plant lead to the production of cannabinoids using this core structure (Bouloc et al., 2013). CBD is derived from an acid (CBGA), a major precursor in the pathway. CBGA undergoes enzymatic conversion into cannabidiolic acid (CBDA) by CBDA synthase. CBDA is then decarboxylated to produce CBD (Sunda & Arowolo, 2020).

Unlike THC, ingestion of CBD does not cause intoxicating effects. However, it has gained attention for its anti-inflammatory, pain-relieving, and anxiety-reducing effects (Kicman & Toczek, 2020). Similarly, low concentrations of THC have also been reported to enhance the therapeutic properties of CBD (Sunda & Arowolo, 2020).

CBN forms from the degradation of THC over time through oxidative processes influenced by exposure to heat, light, or air during storage or aging periods. CBN's chemical structure is similar to that of THC and consists of carbon, hydrogen, and oxygen atoms symbolized by the chemical formula $C_{21}H_{26}O_2$ (Meija et al., 2022). Both THC and CBN are fat soluble and get absorbed by fatty tissues in the body. Thus, aged cannabis can be a good source of elevated CBN for applications in food and other health products-related formulations (Iversen, 2001). CBN is generally considered to have a milder effect compared to THC and is associated with the "couch lock effect," calmness, and drowsiness (Baron, 2018). Research on CBN is still limited compared to that of THC and CBD; therefore, its specific effects are not yet fully understood. Yet, limited evidence suggests its interaction with the body's system in ways similar to that of THC or CBD (Devinsky et al., 2014).

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2.1.2 | Terpenes

Terpenes are a class of over 30,000 compounds found in cannabis (Sommano et al., 2020). Each terpene has a distinct structure resulting in different subclasses (monoterpenes, diterpenes, triterpenes, sesquiterpenes) that account for the characteristic aroma of cannabis. These compounds work individually or synergistically with cannabinoids to enhance the plants' properties creating what is known as the "entourage effect." For instance, myrcene, a mono-terpene, is known for its soothing qualities, whereas limonene is linked to a citrus aroma and the possibility of uplifting one's mood (Booth et al., 2017). In several studies, terpenes have been found to possess specific therapeutic properties, such as anti-inflammatory, analgesic, or anxiolytic effects (Giese et al., 2015). Thus, terpenes are of great interest in developing cannabis-infused edibles or therapeutics. It is anticipated that terpenes will overtake cannabinoids as cannabis-infused therapeutics in a few years to come.

2.1.3 | Phenolics

Phenolics are a class of compounds in cannabis that include resorcinol and pyrocatechol known for their antioxidant properties (Hu et al., 2006). These compounds comprise a benzene ring with a hydroxyl (OH) group attached (Pollastro et al., 2018). Several subclasses of phenolic compounds include flavonoids, phenolic acids, lignans, stilbenes, and tannins. The phenolic acids are particularly recognized to contribute to the anti-inflammatory properties of cannabis (Pollastro et al., 2018), whereas ferulic, *p*-coumaric, and caffeic acids have been reported to demonstrate antioxidant and anticancer activities in renal, squamous, and somatic cells (Celińska-Janowicz et al., 2018).

Flavonoids are arguably the most reported phenolics in cannabis with different subclasses of flavonoids including flavones, flavanols, and anthocyanidins. Flavonoids are found in the glands called trichomes located on the flowers and leaves of plants and chemically consist of carbon, hydrogen, and oxygen atoms arranged as two phenyls and a three-carbon heterocyclic ring (A, B, and C) containing the oxygen atoms (Duke et al., 2000). These ring structures (C_6—C_3—C_6) undergo a wide range of modifications, resulting in the formation of many distinct compounds with different biological properties (Alamgir, 2018b).

About 0.266–1.20 mg/g of total phenolic acids have been found in whole hemp seeds, whereas dehulled seeds contain 0.66–1.25 mg/g (Alonso-Estaban et al., 2022). Although present in lower concentrations compared to cannabinoids and terpenes, flavonoids also play a role in the therapeutic effects of cannabis by interacting with other compounds synergistically. Some reported flavonoids include quercetin, kaempferol, apigenin, cannflavin A, and cannflavin B (Hartsel et al., 2016). Each flavonoid is reported to exhibit specific biological activities. For example, quercetin, apigenin, and kaempferol possess antioxidant, anti-inflammatory, and neuroprotective properties (Alamgir, 2018b). Alamgir (2017) reported that flavonoids possess significant health-promotive benefits, including the potential to treat or reduce the risks for cancer, diabetes, and microbial infections. Werz et al. (2014) demonstrated that sprouting improved the activity of anti-inflammatory compounds prenyl flavonoids cannflavins A and B in hemp sprouts.

2.1.4 | Sterols

Phytosterols are a subclass of compounds prevalent in cannabis plants. Chemically, they consist of a hydrocarbon tail and a sterol nucleus that is made up of four fused rings (Alamgir, 2018a). Phytosterols like the other predominant phytochemicals reported in cannabis are primarily found in the trichomes of the cannabis flowers and leaves (Andre et al., 2016). Beta-sitosterol is a key phytosterol found in cannabis and is structurally similar to cholesterol found in animals. Other phytosterols found in cannabis include campesterol and stigmasterol. Phytosterols are typically present in low amounts in cannabis, but they are very effective in their health-promotive effects at these low concentrations (Sommano et al., 2022). Phytosterols in cannabis have been linked with benefits such as anti-inflammatory and antioxidant properties, reducing cholesterol levels, and regulating the immune system (Kornpointner et al., 2021).

2.1.5 | Alkaloids

Alkaloids are another important class of compounds (nitrogen-containing) found in plants. However, the concentration of alkaloids in cannabis is relatively low, similar to many of the other phytochemical subclasses (Kukula-Koch & Widelski, 2017). Currently, only two alkaloids have been identified and isolated. In 1975, the first alkaloid was isolated from the methanolic root extract of a Mexican variant and named cannabisativine (Latter et al., 1975). The total alkaloid yield was 0.003%. In the same year, cannabisativine was isolated from ethanolic stem and leaf extracts of a Thai variant (El Feraly & Turner, 1975). Anhydrocannabisativine, another alkaloid, was isolated from

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stems and dry leaves of a Mexican variety (Elsohly & Turner, 1977).

These alkaloids have demonstrated analgesic, anti-inflammatory, and anticancer properties and other therapeutic applications (Taura et al., 2007). However, research on cannabis alkaloids is currently limited.

3 | CANNABIS EXTRACTION AND PROCESSING METHODS

The most important aspect of cannabis food preparation is the form of extract used. Most parts of the plants such as seeds, flowers, and leaves require minimal processing, while the oils require extensive processing through extraction (Baldino et al., 2020). Because of the volatile nature of THC and CBD, some studies point out that factors such as oxygen, light intensity, floral maturity, air, temperature, and harvest time affect the recovery of these secondary metabolites during extraction (Lazarjani et al., 2021). For example, THC in resin samples has been reported to be rarely degraded when placed in light or dark rooms. However, acidic and neutral THC extracts degraded significantly when exposed to light (Lindholst, 2010).

Besides, cannabis contains at least 80% water and can easily be inhabited by unwanted microorganisms upon harvest. Therefore, drying is a very important postharvest step for improving the safety of cannabis products and extracts for most food applications (Chasiotis et al., 2022). Thus, the dried form of cannabis is most desirable in these applications because drying influences long-term storage and shelf life stability, while preserving the bioactivities, sensory, and therapeutic properties, of cannabis-infused food products (Hawes & Cohen, 2015). Different parts of the cannabis plant dry at different rates, and separating buds from stems has the potential to result in a product with a more consistent flavor (Hawes & Cohen, 2015). The use of gravity during drying is an important consideration because delayed or uneven drying will result in water from the top part of the plant absorbing into the bottom parts. To expedite the process, fans, heaters, and dehumidifiers can be employed (Namdar et al., 2019). However, fast and slow drying are important factors to consider because slow drying does result in smoother-tasting products, while fast drying may result in harsher flavors when used for food applications. Furthermore, hastening the drying process can prevent the plant from reaching its peak potency during the curing process (Hawes & Cohen, 2015).

Another important postharvest processing is curing, which ensures that the unique flavor of the plant is retained (Klumpers & Thacker, 2019). Hawes and Cohen (2015) reported that storing cut flowers in a closed container in a dark space for a month while intermittently opening the cover each day for 6 h improves flavor development.

Extraction is another method employed to enhance the purity and concentration of phytochemicals for applications in producing cannabis-based products. To obtain the maximum flavor, the temperature, extraction time, rate of agitation, particle size, the mass of biomass, size distribution, and the type of solvent used are important (Fathordoobady et al., 2019). Solvent-based extraction methods including water extraction, rosin press extraction, Soxhlet extraction, maceration, ultrasonic extraction, and dried sieve extraction have all been recorded in the literature as suitable methods (Fathordoobady et al., 2019).

3.1 | Preparation and food safety considerations for cannabis-infused products

Several factors impact the bioavailability and accessibility of THC when ingested. The pharmacokinetics of THC are impacted by concerns with impaired gastrointestinal (GI) function, fat malabsorption, interactions with other dietary ingredients, and encapsulation strength (Light & Karboune, 2022). Heat naturally decarboxylates phytocannabinoids before incorporation into food products (Beal, 2019). The application of heat causes the conversion of nonpsychoactive THCA and CBDA into their psychoactive forms, THC and CBD. Yet, Tonoyan et al. (2022) found that prolonged temperatures cause cannabinoids to degrade, whereas Wolf et al. (2017) demonstrated that at 300°F and at different time intervals, THC and CBD remained stable in the brownie matrix.

In preparing food products, cannabis extracts are usually infused through encapsulation, emulsification, direct addition (powder/coarse extracts), and preheating (Marangoni & Marangoni, 2019). The batch size of the intended product and the formulation method determine the amount of cannabis added. For instance, in preparing brownies, 1 g of dried cannabis (8–10 mg THC) was infused with 100 g of ingredients such as flour, baking powder, sugar, and so forth. In another recipe, cannabutter (2–5 mg THC) was added to butter before mixing it into a 500-g brownie mixture (Lavorato, 2021). In producing cake, Mezher (2023) hand-grinded cannabis and baked it for 45 min while stirring intermittently every 15 min before adding it to the cake mixture.

For beverage production, usually 5–30 mg of tinctures, syrups, or water-based emulsions of THC/CBD are added to a base beverage mixture of at least 1-L solvent (Van Tran et al., 2021). This formulation can be used to prepare soft drinks. Although most cannabis beverage manufacturers use already prepared liquid extracts, some also tend

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to prepare their tinctures using buds and ethanol-based solvent extraction methods. Buds are typically added to ethanol, where THCA is decarboxylated to THC and kept in a dark place for 2–4 weeks until it turns a dark green color (Andrews, 2022). In some other cases, cannabis oil is encapsulated to create a lipid-soluble complex in water-based drinks (Marangoni & Marangoni, 2019). In other cases, the oil turns semisolid during cold temperatures and therefore is liquefied at temperatures between 70–80°C and emulsified in a carrier oil before being added to a beverage (Romano & Hazekamp, 2013).

For chocolate preparation, a dried cannabis extract is incorporated in melted cocoa butter before final addition to other chocolate ingredients such as cocoa mass, sugar, milk, and lecithin (Romano & Hazekamp, 2013). Due to the complex crystalline nature of chocolate, extracting the cannabis plant directly into edible oil produces a fat-based complex that limits the eutectic effect of the cocoa butter. This affects the final chocolate bar produced, which tends to be soft and lusterless (Beal, 2019).

Cannabis plants can be contaminated by molds, fungi, metals, pesticides, mites, and microbial diseases; some of which naturally exist in the environment (McPartland & McKernan, 2017). THC, CBD, and other cannabinoids are extracted from raw plant materials using solvents such as hydrocarbons and ethanol to create concentrated oils. As a result, concentrated cannabis oils may retain solvent impurities or leftover solvents and may contain concentrated levels of contaminants (Qamar et al., 2021). For instance, a study in Oregon discovered detectable pesticides in 55% of concentrate samples (compared to 29% of flower samples), with 46% of those samples failing to meet recommended limits (Maguire et al., 2019). THC is usually activated by cooking for 30–45 min at 220°F or 104°C. However, some producers might be enticed to cook at lower temperatures, which might not satisfy the required internal temperatures to kill microbial contaminants, because heating above the minimum THC temperature may cause some degradation (Evans, 2020).

Typically, test batches of cannabis edibles are sent to external laboratories for testing potency, mycotoxins, yeast and mold, foodborne pathogens such as Shiga toxin-producing *Escherichia coli* and *Salmonella*, residual solvents, metals, and pesticides (Kosa et al., 2017). Pathogen and residue testing and the creation of extraction techniques for a wide array of edible goods continue to be difficult tasks. Limited access to testing, inadequate licensed laboratories to meet testing volume, insufficient methods for THC extraction from all potentially edible food matrices, and testing accuracy not independently validated by the state are just a few of the limitations of laboratory testing that still exist to varying degrees and largely dependent on the state (Peralt et al., 2022).

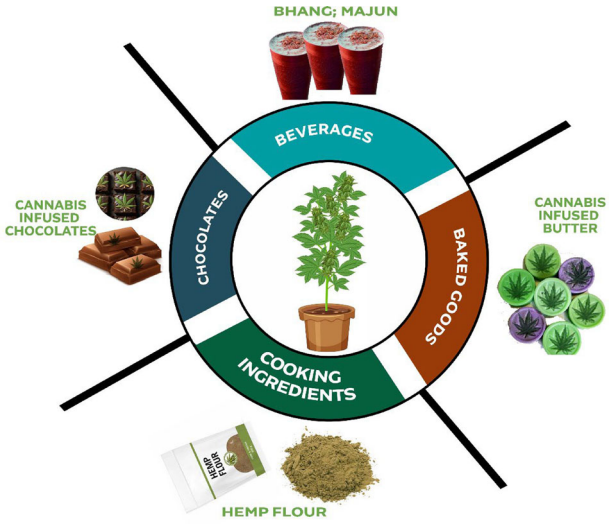

FIGURE 2 Examples of cannabis-infused foods.

Consumers can purchase edibles at retail or medical dispensaries after they have been packaged, labeled, and delivered according to established criteria by primary regulators. For example, the universal symbol, ingredient list, production date, expiration date, refrigeration statement, nutrition facts panel, serving size, and total active THC statement are all required on labels in Colorado (Subritzky et al., 2017). An edible product's potency, quality, and safety may be impacted by storage at the manufacturing plant, retail location, or consumer's house. Inadequate ventilation is a major safety risk that can lead to humid conditions well known to facilitate mold growth. There are also possible safety risks related to individual use, such as accidental use, excessive consumption, and off-label use (Larkin Jr., 2018).

3.2 | Types/forms of cannabis-infused food products

Cannabis food products are commercially referred to as "edibles" by consumers. They are usually administered orally and include a wide range of products such as candies, baked products, lozenges, and beverages (Figure 2) (Peng & Shahidi, 2021). All food products depending on the processing method are made using different forms and parts of the cannabis plant (Klein, 2017). For instance, extracts and concentrates, such as oils, tinctures, and waxes, are obtained through extraction processes that isolate compounds, like THC from the plant parts including flowers, seeds, leaves, and stems. Hard candies are usually made from cannabis tinctures produced using ethanol-based solvent systems (Barrus et al., 2016). In various countries, where the plant has achieved full/partial

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FIGURE 3 Cannabis-infused beverages.

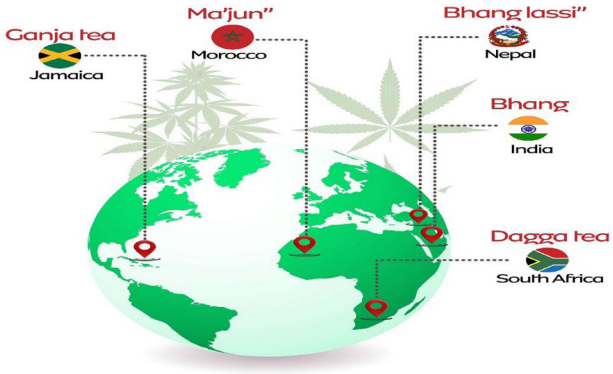

FIGURE 4 Examples of cannabis-infused cultural beverages across geographic regions.

legal status, edibles are majorly classified under beverages, cooking ingredients, nutraceuticals/functional foods, baked goods, chocolates, and confectionaries (Lamy et al., 2016). In the United States and Canada, the most frequently consumed infused food products are baked goods, such as cookies and brownies, as well as confectionaries, such as candies (Charlebois et al., 2018). Similarly, in Jamaica and France, the most consumed products are baked goods and to a lesser extent candies (Bouquié et al., 2018; Davenport & Pardo, 2016).

3.2.1 | Beverages

There are many different types of beverages infused with cannabis, including teas, coffees, sodas, flavored water, fruit juices, energy drinks, and some alcoholic beverages (Figure 3). These beverages are made with cannabis extracts or oils and offer a refreshing way to consume cannabis (Evans, 2021). In various cultures in Pakistan and India, cannabis leaves are crushed, ground, and mixed with either milk, or nuts, and served as a beverage (Figure 4) (Sen, 2004; Waheed et al., 2023). In India, for instance, the consumption of *bhang*, a cannabis-infused beverage, has deep cultural and religious roots (Bennett, 2010). Bhang is traditionally consumed during the festival of Holi and other celebrations (Bennett, 2010). It is prepared by grinding cannabis leaves and flowers into a paste and then mixing it with milk, ghee (clarified butter), and a variety of spices. Bhang is believed to have medicinal and spiritual properties and has been used in Ayurvedic practices for centuries (Koenigs, 2022). In Jamaica, "ganja tea" or "ganja-infused punch" is made by steeping cannabis leaves and flowers in hot water along with various herbs and spices. Ganja tea is enjoyed for its relaxing and therapeutic effects (van Solinge, 1996). In Morocco, the traditional drink called "ma'jun" or "majoun" is made by combining ground cannabis with honey, nuts, and various spices to create a thick, sticky paste (Feng et al., 2009). In Nepal, the drink known as "bhang lassi" is made by blending cannabis leaves and flowers with yogurt, milk, and spices like cardamom and nutmeg (Jha et al., 2019). In certain regions of South Africa, a traditional beverage called "dagga tea" is prepared using cannabis leaves and stems (Gordon, 1996).

3.2.2 | Baked foods

In both Northern America and Europe, cannabis-infused baked goods have gained significant popularity with consumers as a socially acceptable form of consuming cannabis-based products (Figure 5). These include cookies, brownies, cakes, muffins, and pastries (Lawrence, 2019). To make these products, the recipes use butter or oil derived from seeds. Among them, cannabis-infused brownies are particularly well-known and consumed in high amounts in Europe and North America. These products are made by adding cannabis-infused butter or oil (and sometimes ground/leaves) to the brownie batter, which often consists of chocolate as an ingredient (Krüger et al., 2022).

There are also cookie options infused with cannabis in different flavors such as chocolate chip, oatmeal, and sugar cookies. For cake lovers, there is a range of cannabis-infused options from simple pound cakes to decadent layer cakes. On the go, individuals can enjoy the convenience of cannabis-infused muffins and a scone with flavors like blueberry, banana, or cinnamon (Casey & Kraynak, 2019). Cannabis-infused pastries bring a touch of sophistication with a range of choices, like croissants, Danish pastries,

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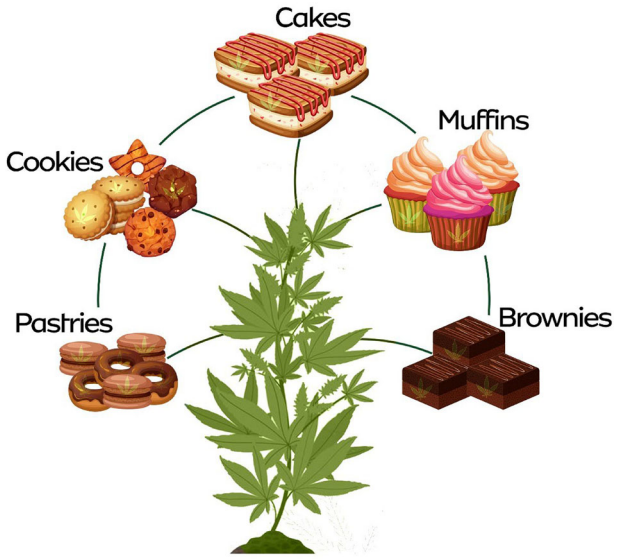

FIGURE 5 Examples of cannabis-infused baked foods.

and different savory flavor-inspired turnovers (Matheson & Le Foll, 2020).

3.2.3 | Chocolates, snacks, and sweets/confectionaries

Cannabis-infused chocolates, truffles, gummies, caramels, and other confectionery items are also popular choices among consumers. These products often come in various flavors and shapes, providing a delicious, convenient, and enjoyable way to consume cannabis (Lo, 2022). The popularity of cannabis-infused gummies, chocolates, and other sweet treats has increased particularly in Canada since the legalization of cannabis (Louis, 2018). Various brands offer a wide selection of cannabis-infused candies like gummies and chocolates (Louis, 2018). The Netherlands, famous for its coffee shops, also provides a range of cannabis-infused confectionery products such as lollipops and chocolate bars (Perlmutter, 2019).

As the first country to fully legalize cannabis, Uruguay has seen the emergence of cannabis-infused confectionaries as well. Products like cannabis gummies, chocolates, and fruit chews can be found in licensed dispensaries (Hall & Lynskey, 2020). In Jamaica, where cannabis has a cultural and spiritual significance, cannabis-infused candies can be found in specialized establishments. These include traditional tamarind balls and other locally made sweets infused with cannabis (Pretorius, 2006). Other foods classified as snacks include items like chips, pretzels, popcorn, granola bars, and trail mixes. These products are more popular in the United States and some European countries such as the Netherlands and Belgium (Grotenhermen et al., 2001). Cannabis-infused ice cream and stewed June plum identified in one study are some of the popular snack foods consumed in Jamaica (Lindsay et al., 2021).

3.2.4 | Cannabis-infused cooking ingredients

People who enjoy cooking take advantage of cannabis-infused cooking ingredients such as oils, butter, and tinctures as additives in different food recipes. These additives allow individuals to personalize their recipes to include cannabis as an ingredient. From meals to dressings, sauces, glazes, and so forth, there are endless possibilities. Hempseeds, for example, offer valuable nutritional properties and can be utilized to create flour and oil with various applications (Lo, 2022). Additionally, raw hemp sprouts, flowers, and leaves can be used in salads and juices, broadening the spectrum of possible uses for hemp in food (Kolodziejczyk et al., 2012).

For instance, a research study conducted on hempseed flour revealed that the "Fedora" variety contained 7.9% moisture, 30.7% protein, 13.6% lipids, 41.6% carbohydrates, and 6.2% ash and can be used in several food applications (Cerino et al., 2021). When 10% of hempseed flour was substituted with wheat flour, there was no impact on dough stability or strength; instead, it resulted in increased nutritional value by boosting protein and mineral levels (Cerino et al., 2021). Another study explored the use of hemp flour in gluten-free bread production. The addition of hemp flour to starch resulted in improved flavor, color, and nutritional value, including increased fiber and protein content (Korus et al., 2017). Crackers produced from hemp flour also demonstrated enhanced nutritional value in terms of crude fiber, protein, minerals, and fatty acid content (Radočaj et al., 2014).

Hempseed oil is widely used as an edible cooking ingredient and is particularly popular in the culinary industry. Hempseed oil is rich in unsaturated fats, comprising essential fatty acids that remain stable at high temperatures (Xu et al., 2022). Available cooking oils deliberately maintain levels of omega-3 fatty acids to enhance stability because the presence of three double bonds in omega-3 fatty acids can lead to quick oxidation and rancidity (Farag et al., 2021). Another examination focused on hempseed oil quality reported to be derived from select cultivars that contained total unsaturated fatty acid content ranging from 82% to 86%. Among these fatty acids, linoleic acid accounted for around 51.9%–55.7%, while alpha-linolenic acid varied between approximately 12.3% and 15.3%. The study also found variations in gamma-linolenic acid—a type of omega-6 fatty acid ranging from approximately 0.8% to 2.46% (Dimić et al., 2009).

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TABLE 1 Allowable limits for THC- and CBD-infused food products.

Country	Allowable limit for THC	Allowable limit for CBD
Canada[a]	10 mg THC per package	No specific limit
Switzerland[a]	1% THC	No specific limit
United Kingdom[a]	1 mg THC per product	No specific limit
Australia[b]	2 mg THC per serving	No specific limit
Germany[b]	0.2% THC	No specific limit
Netherlands[a]	5 mg THC per product	No specific limit
Uruguay[c]	9% THC	No specific limit
United States[c]	0.3%	No specific limit
Spain[d]	0.2% THC	No specific limit
Italy[d]	0.6% THC	No specific limit
New Zealand[d]	2 mg THC per serving	No specific limit
South Africa[d]	0.001% THC	No specific limit
Mexico[d]	1% THC	No specific limit
Argentina[d]	1% THC	No specific limit

Abbreviations: CBD, cannabidiol; THC, tetrahydrocannabinol.
[a]Hazemkamp (2018).
[b]Deville et al. (2020). Deville et al.(2020)
[c]Steigarwald et al. (2018).
[d]McGregor et al. (2021).McGregor et al. (2020)

3.2.5 | Nutritional and value-added functional substances

These refer to specific components obtained from cannabis that provide certain nutritional content or additional health benefits. Currently, there is ongoing research regarding the use of cannabis extracts as nutritional supplements, functional ingredients, and nutraceuticals. The high nutritional content of hemp seeds is well documented. Mineral constituents vary from 4.7% to 5.8% for most cultivars. Cultivars such as Finola contain as high as 28% proteins, while Crag contains 32.3% oil. Anka, juta, and fedora cultivars have been found to contain as high as 38% fiber (Leonard et al., 2020). In one study, dehulled hemp seeds, also known as hemp hearts, were reported to be a good protein source that is commercially available as food products (Table 1). The hulls from the seeds are also consumed for their fiber content, which improves gut health (Ely & Fike, 2022). In another study, the whole seed was used as a feed concentrate for poultry, which increased the meat quality (Crini et al., 2020).

Norajit et al. (2011) formulated energy bars by substituting different percentages of whole hemp and defatted hemp seed powders with rice flour. The researchers observed that increasing levels of both hemp powders increased flavor, alcohol compounds, and phenolic and antioxidant contents. The identified constituents, particularly antioxidant content, can reduce inflammation and improve overall health as documented in serval studies (Lanzoni et al., 2023). Nissen et al. (2022) also demonstrated that hemp seed-based drinks have nutritional and functional properties. The researchers observed that, after prolonged fermentation with a mixture of bifidobacteria and lactobacilli, the levels of amino acids, proteins, carbohydrates, vitamins, minerals, and organic acids and compounds increased while pH remained stable. In another study, Nissen et al. (2020) investigated the nutritional content of hemp seed-based drinks. The study found a correlation between hemp terpenes and antimicrobial activity. It also found a correlation between saturated and unsaturated fats with high levels of alpha-bergamotene and beta-myrcene. Compounds such as octadecane, 2-heptanal, 2-butanone, 2,3-butanedione, nonanal, and decanal were also found to be associated with improved flavor and other sensory attributes of hemp-based drinks (Ascrizzi et al., 2020).

Despite the widespread use of CBD in nutritional supplements, there is not enough evidence in literature particularly in clinical studies regarding its properties as a dietary ingredient. However, some studies report its use as a therapeutic oil for the treatment of pain, arthritis, inflammation, anxiety, and sleep (Burstein, 2015). The use of cannabis in clinical settings is currently ongoing. For instance, Epidiolex (pure CBD) and Sativex (THC and CBD in a 1:1 ratio) are among the uses for which it has received authorization (Chopra et al., 2022). Epidiolex, an approved supplement, obtained from hemp with reported wide therapeutic abilities and a generally favorable safety profile, is presently available in the market. Epidiolex has gained approval from agencies like the European

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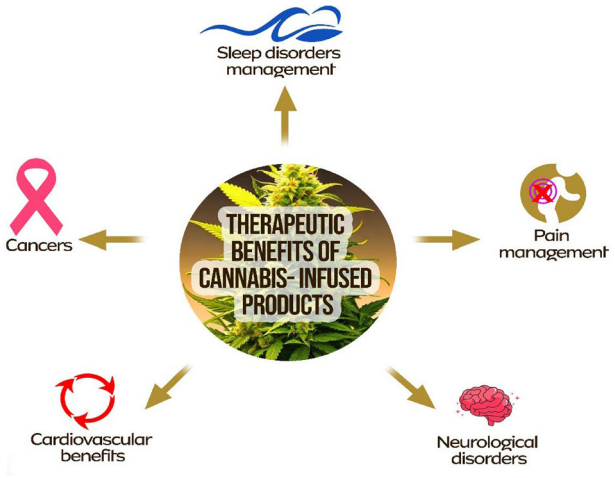

FIGURE 6 Proposed treatments or benefits sought by consumers from consuming cannabis-infused products.

Medical Agency (EMA) and the Food and Drug Administration (FDA) for treating seizures linked to Lennox Gastaut or Dravet syndrome in individuals aged 2 years and above. This approval is based on established evidence from controlled experiments (Martínez et al., 2020). It is believed that the appropriate CBD supplement dose for adults may range between 5 and 10 mg/day with a limit of 350 mg/day. This dosage range could be considered for testing CBD hemp supplements as part of a healthy diet (Cerino et al., 2021).

4 | THERAPEUTIC AND FUNCTIONAL APPLICATIONS OF CANNABIS-INFUSED FOOD PRODUCTS

As already established, cannabis-infused products offer a range of therapeutic benefits due to the presence of cannabinoids, such as THC and CBD, and other compounds found in the cannabis plant (Figure 6). The therapeutic advantages of cannabis-infused products have been widely discussed to include both cannabinoids and non-cannabinoid-based phytochemicals that show several benefits in humans and animals. These include pain relief in conditions such as fibromyalgia, arthritis, and sclerosis (Mishra et al., 2022). Currently, THC and CBD show promise in managing inflammation-related conditions like bowel disease, rheumatoid arthritis (RA), and certain skin conditions (Evans, 2020). Food products infused with both THC and CBD have been found to have anxiety-reducing effects and are a potential therapeutic source to aid stress reduction and anxiety management (Iftikhar et al., 2021). When used in appropriate doses, cannabis-infused products containing THC may induce relaxation and a sense of calmness (Skelley et al., 2020). The status of CBD has experienced a significant rise in the marketing and consumption of CBD-infused food products driven by consumer interest in using CBD/THC for various medical conditions (Carhart-Harris & Goodwin, 2017).

However, studies on food products infused with non-cannabinoids such as flavonoids, terpenes, phenolic acids, and alkaloids are still at the infantile stage. Due to restrictions, a lack of scientific studies, and the classification challenges of metabolomics characterization of cannabis-infused food products, research on their therapeutic potential and optimal usage has been limited.

There is still a lack of research regarding how cannabinoids and other compounds in these food products interact with the body at a cellular level. In addition, there is limited knowledge about how the body absorbs, distributes, metabolizes, and eliminates these components. These gaps in understanding hinder our insights into the timing, effective dosing, duration, and intensity of their effects (Klumpers & Thacker, 2019). There is also a scarcity of research examining the prolonged effects of cannabis food products as treatments, and specifically, the long-term effects are not well-understood (Grant et al., 2003). Current short-term data indicate that CBD is generally well-tolerated and has minimal adverse side effects. Yet, there is still constant demand for these products driven by consumer interest in using CBD/THC for various medical conditions (Crippa et al., 2018). Some of these conditions are summarized below.

4.1 | Pain management

THC is widely acknowledged for its benefits in providing pain relief. It interacts with the body's entire system as a regulator of pain perception (Passie et al., 2012). THC binds to receptors in both the brain and nervous system to alleviate pain sensations and provide comfort. THC has displayed potential in managing symptoms such as queasiness and vomiting in individuals undergoing chemotherapy or facing symptoms associated with specific medical conditions (Donvito et al., 2018). In addition, THC has been thoroughly researched for its capacity to stimulate appetite, making it especially advantageous for individuals experiencing reduced appetite due to conditions like HIV/AIDS or cancer leading to emaciation. These are conditions that significantly reduce the effectiveness of many frontline treatments to control and manage these diseases. By activating receptors in the brain, THC can amplify the feeling of hunger and encourage food consumption in these individuals (Greineisen & Turner, 2010). There is promise in utilizing cannabis-infused food products to alleviate symptoms such as nausea, pain, and loss of appetite among AIDS patients. For instance, a study published recently discovered that cannabis-infused chocolate contributed to improved appetite and weight gain among

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patients living with HIV (Bonn-Miller et al., 2019). Few studies have explored the use of cannabis-infused edibles as a form of therapy to manage symptoms induced by chemotherapy. These symptoms encompass nausea, vomiting, and diminished appetite, which can impact the quality of life for individuals battling cancer (Turgeman & Bar-Sela, 2019).

According to a study conducted in 2021, researchers investigated the use of cannabis-infused edibles for cancer patients undergoing chemotherapy (Abu-Amna et al., 2021). The researchers found that it helped alleviate nausea and improved their appetite. This positive effect contributed to enhancing the treatment experience for these patients (Abu-Amna et al., 2021). A study published in 2012 examined the benefits of cannabis extract for individuals with pain conditions. It revealed that those who consumed the extract experienced a reduction in pain intensity and an improvement in their quality of life (Witkop et al., 2012).

Studies have indicated that CBD oil and powders can be beneficial in managing pain associated with arthritis. For instance, in a rat model, applying CBD topically resulted in reductions in swelling, pain levels, thickness of the synovial membrane, immune cell infiltration, and inflammation markers. These effects were observed to vary depending on the dosage (John et al., 2020). CBD has displayed antianxiety properties based on both preclinical and clinical research by positively influencing the prefrontal cortex of the brain associated with emotions when ingested (Singh et al., 2020).

Although cannabis-infused food products have shown effectiveness in relieving pain, a significant obstacle to using them for treating these health ailments is the availability of long-term studies (Naeem et al., 2023). In folk medicine, hemp seed oil has traditionally been used to alleviate chronic knee pain in individuals with RA and poor blood circulation (Khaleghi, 2020). Recent research also indicates that hemp seed oil stimulates the production of reactive oxygen species (ROS), promotes lipid storage, and increases markers of endoplasmic reticulum stress. These factors act as rheumatoid agents in following processes leading to improved blood circulation and providing additional relief to RA patients (Rong et al., 2017). The synergistic interaction between terpenoids and phytocannabinoids found in hemp milk drinks has also been shown to alleviate pain and inflammation (Nissen et al., 2022).

4.2 | Management of sleep disorders

The effects of cannabis on sleep are complex and can vary depending on the specific cannabinoids and dosage used. There are mixed opinions about the benefits of these compounds for sleep (Kaul et al., 2021). Acute cannabis use has been linked with improvements in sleep, while chronic use is more commonly linked to sleep deficits (Angarita et al., 2016). Edibles are the most reported cannabis food products and have shown promise in managing sleep disorders (Connor et al., 2021). Edibles such as biscuits, brownies, and cakes have been reported to assist in the sleep disorders of geriatric and older patients (Bidwell et al., 2024; Kaufmann et al., 2023). To illustrate, Babson et al. (2017) conducted a study to examine the impact of the dose of CBD and THC edibles on sleep. The researchers observed that administering a controlled amount of THC infused in brownies led to reduced time taken to fall asleep, which improved sleep and increased subjective satisfaction with sleep quality. These findings suggest that using THC under control might have effects on promoting better sleep. It has also been observed that continued use of cannabis edibles as a sleep aid over consecutive days may result in the development of tolerance to any initial positive effects, leading to habituation and potentially negative sleep outcomes (Maddison et al., 2022).

Some studies also indicated that presleep administration of cannabis in oil or powder, typically in isolated or synthetic form, can lead to shorter sleep onset latency, longer and improved sleep maintenance, and increased subjective sleep satisfaction (Babson et al., 2017; Maddison et al., 2022). A study has pointed out that high-dose CBD and acute low-dose THC have shown potential therapeutic effects on sleep (Zhornitsky & Potvin, 2012).

Interestingly, among intermittent users, it is possible that those who use cannabis food products less frequently do not experience the same negative effects on sleep as daily chronic users. Edibles have shown promise in managing sleep disorders (Connor et al., 2021). Several studies have examined the impact of cannabinoids such as THC and CBD derived from cannabis on sleep patterns. Although further research is required, preliminary findings indicate that these cannabinoids might offer benefits in enhancing sleep quality and alleviating symptoms of insomnia (Babson et al., 2017; Kaul et al., 2021).

CBD oils have been associated with anxiety reduction and sedative effects. Despite not being psychoactive, CBD has shown the potential to enhance sleep (Urits et al., 2020). Another research investigation focused on the use of CBD in patients with anxiety and sleep disorders, highlighting its benefits in improving sleep quality. Specifically, the researchers found that CBD significantly improved sleep scores in the majority of participants throughout the study (Moltke & Hindocha, 2021). In addition, CBD has shown promising results in clinical trials for a range of other conditions including social phobia, sleep disorders, and posttraumatic stress syndrome (Orsolini et al., 2019). While phase I studies have tested CBD doses up

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to 6000 mg/day using Epidiolex (cannabis supplement), a recommended dose of 5 mg/kg has been approved, with the possibility of increasing it to 20 mg/kg/day (Cerino et al., 2021).

4.3 | Cardiovascular benefits

Hemp seeds provide several health benefits owing to their favorable ratio of omega-6 to omega-3 polyunsaturated fatty acids (PUFA). Hempseed proteins are highly valued because they contain sulfur-linked amino acids, like methionine and cystine (House et al., 2010). These specific amino acids have been reported to be responsible for improving conditions like blood pressure and heart failure, where the renin–angiotensin–aldosterone system (RAAS) is not working correctly (Girgih et al., 2014). Hemp seeds also provide significant amounts of arginine, an essential amino acid known for its cardiovascular benefits (Xu et al., 2021). Hydrolyzed hempseed proteins of cannabis seeds have been found to possess antihypertensive effects possibly attributed to their inhibition of angiotensin-converting enzyme and renin, which has prompted an ongoing human trial investigating the incorporation of hemp seed protein powder as a nutritional intervention for hypertension (Samsamikor et al., 2020). In another human trial study, the renin-inhibitory effect of hemp seed protein hydrolysate administered to patients was studied (Girgih et al., 2014). Additionally, hemp seed oil has become increasingly popular as a cooking oil substitute because of its taste, with a bitter undertone. Hemp seed oil is widely known for its impact on health (Dunford, 2015). Studies have indicated that consuming small amounts of hemp seed oil daily (2 g/day) did not significantly affect cholesterol levels, high-density cholesterol levels, triglyceride levels, platelet aggregation, or circulating markers in both healthy individuals and children with primary hyperlipidemia (del Bo et al., 2019). However, there have been intriguing findings from trials. For instance, one study involving 14 participants revealed that daily consumption of 30 mL of hemp seed oil led to an improvement in the ratio between cholesterol and high-density lipoprotein cholesterol when compared to flaxseed oil (Kontogianni et al., 2013).

In a study conducted by Schwab et al. (2006), they added 30 mL of hemp seed oil to the diets of human participants for 4 weeks. The results showed changes in the profiles of the participants, indicating potential benefits for cardiovascular health. When assessing the heart performance after ischemia–reperfusion injury, it was discovered that the PUFA content in hemp seeds played a role in aiding heart recovery. These findings imply that consuming hemp seeds can potentially contribute to health by influencing lipid profiles, enhancing heart performance, and reducing the risk of clot formation (Schwab et al., 2006). The impact of hemp flour on cholesterol levels has been investigated in obese mice. The study revealed that the high-density lipoproteins (HDLs), low-density lipoproteins (LDLs), triglycerides, and total cholesterol levels significantly reduced, indicating the potential of hemp flour as a hypocholesterolemic substance (Bouarfa et al., 2020). Hemp seed oils also reportedly show the potential to increase metabolism and reduce blood cholesterol levels (Aloo et al., 2024).

4.4 | Other benefits: Inflammation/gut health/allergy

There have been considerable strides in cannabis research toward inflammatory diseases, immune diseases, gut health (digestive issues), and metabolic syndrome. Terpenes in cannabis have been cited to have anti-inflammatory and antiallergic properties, which can help alleviate pain and act as powerful antioxidants (Nuutinen, 2018). Research conducted on mice has established that consuming hemp seeds can improve memory and learning (Zhou et al., 2018).

Zhou et al. (2018), demonstrated the anti-neuroinflammatory activities of hemp seed using a mouse model. The study revealed that the CBD component of hemp suppressed cellular and humoral immunity and triggered apoptosis in specific lymphocytes. These effects demonstrate the beneficial use of hemp seeds for treating or managing cancerous diseases (Nagarkatti et al., 2009). In another study, pre-emptive treatment with CBD extracted from seeds was proven to delay the beginning of type 1 diabetes in obese diabetic mice and significantly reduce leukocyte activation compared to standard treatment (Rupasinghe et al., 2020).

Plant-derived oils, like hemp seed oil, have gained attention not only for their potential as cooking and dietary ingredients but also for their medicinal and nutraceutical properties (Crini et al., 2020). These oils are being investigated for their potential to provide various health benefits, expanding their application beyond traditional culinary uses (Rupasinghe et al., 2020). Apart from its use as cooking oil, hemp seed has found applications as a valuable source of vegetable protein and dietary fiber in its milled form. This versatility has led to its incorporation into various food products such as energy bars, flavored yogurt, confectionery, chocolate, sauces, pralines, and baked goods (Łopusiewicz et al., 2022). Likewise, hemp seed powder has been investigated as a protein source, food additive, and supplement (Kolodziejczyk et al., 2012). Hemp seed and hemp seed oil incorporated

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into products such as bread, confectionery items, sauces, and pralines have been associated with improved digestive health (Colatruglio & Slater, 2014). Other studies report that hemp seed oil has therapeutic benefits and aids constipation (Crescente et al., 2018).

The addition of hemp juice to alcoholic beverages has been shown to offer digestive benefits (Tireki, 2021). Some studies have highlighted that hemp sprouts and seeds have significant antioxidant activities in both in vitro and in vivo models (Aloo et al., 2023). This opens up possibilities for using hemp in culinary preparations, such as adding hemp sprouts, leaves, and flowers to raw juices or salads (Cerino et al., 2021). An additional advantage of hemp sprouts is their production of glucuronic acids, which play a role in the production of vitamin C. This adds to the significance of incorporating hemp sprouts into the diet (Malabadi et al., 2023). While there is potential for effects, further research is still needed to understand the range of benefits and determine the optimal usage or dose of cannabis food products including those formulated with hemp.

4.5 | Nutraceuticals

Nutraceuticals are substances that possess a double function—a nutritional component and a health-promoting component (Rupasinghe et al., 2020). Over the years, several bioactive compounds and nutrients have been identified and isolated from cannabis and explored as potential agents for human nutrition (Della Rocca & Di Salvo, 2020). Currently, several studies demonstrate that hemp is a valuable source of dietary nutrients and therapeutic compounds. There is currently a wide range of food products infused with CBD/THC such as beverages, cookies, milk, sports products, and breakfast cereals (Pisciottano, 2023). Although the development of nutraceutical products derived from cannabis is still in its infancy, hemp oil and seeds are promising nutraceutical agents with high minerals, fiber, essential fats, amino acids, proteins, and bioactive compounds (Xu et al., 2022).

Hemp oil is also used as a food supplement, dietary supplement, and cosmeceutical. In some studies, hemp seed oil has demonstrated its use as a source of dietary fiber and vegetable fiber (Cerino et al., 2021). Due to its health-promoting use in a milled form, hemp seed and oil have been incorporated into different food products such as baked goods, flavored yogurt, and energy bars. Secondly, Shim et al. (2009) report the use of hemp seed oil, seeds, and hemp seed flours as functional foods in reducing LDLs and glycerides and increasing HDLs. Hemp protein powder is also speculated to aid in the treatment of anemia (Shim, 2009). Besides, the leaves, seeds, flowers, and sprouts are added to juices, alcoholic beverages, and salads. The addition of these parts of the plant has been demonstrated to aid in digestion (Von Meer, 2014).

The high amino acid, PUFA, and mineral contents of hemp seeds examined in various studies serve as a suitable addition to the daily dietary requirement (Mihoc et al., 2012). In increasing protein concentration, another study demonstrated the effect of *Bacillus subtilis* in the fermentation of hemp seed meal (Zhang et al., 2023).

The seeds were revealed to be rich sources of bioactive, antioxidant, and antimutagenic compounds. In the study by Frassineti et al. (2018), seeds and sprouts exhibited excellent antioxidant activity both in vitro and in vivo. The bioactive constituents identified as cannabisin A, B, and C and caffeoyl tyramine were also found to exhibit antimutagenic activity against *Saccharomyces cerevisiae*. Upon further analysis, bioactive compounds, gluconic acids, and linoleic acids were found to exhibit nutraceutical potential (Frassinetti et al., 2018). In the study by Cerino et al. (2021), terpenes identified in hemp seeds were found to be antiallergic, antioxidant, and anti-inflammatory while containing considerable levels of fiber and protein. In another study, ultrafiltration was used to concentrate and encapsulate bioactive compounds and isolate essential amino acids and polysaccharides from hemp fiber meal. Isolated compounds were found to be concentrated with protein, increasing its superiority to other protein products in the market (Belščak-Cvitanović et al., 2018).

In another study, the in vivo anti-neuroinflammatory activity of phenyl propionamide found in hemp seeds was evaluated. The levels of inflammatory cytokines were found to decrease with increasing concentrations of phenyl propionamide, which led to a reduction of neuronal damage in mice (Zhou et al., 2018). Rodriguez-martin (2019) evaluated the anti-neuroinflammatory and inflammatory activity of hemp protein isolated from hemp seeds. At the transcriptional level, inflammatory cytokines were downregulated, which suggests the nutraceutical potential of the seeds. Porto and Tubaro (2011) found that seed samples contained high levels of linoleic acid (59.6%), omega-3 fatty acids (3.4%), omega-6 fatty acids (18%), and PUFA (81%). These properties of the seeds are suggested to be anti-inflammatory and antilipidemic activity.

Seven hemp variants of seeds were evaluated for their phytochemical constituents and nutritional and antioxidant properties. The study demonstrated high levels of protein and oil content, the presence of bioactive constituents, and high antioxidant properties (Irakli et al., 2019). Hemp seed protein hydrolysates were evaluated for their anti-hypoglycemic, anti-hypotensive, immunomodulatory, and antioxidant properties in vitro. These evaluated properties demonstrate hemp seed hydrolysates as dietary supplements, functional foods, and treatment of

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metabolic diseases such as hypertension, diabetes, and metabolic syndrome. Other studies have also reported anticancer, neuroprotective, antifatigue, antihypertensive, hypercholesterolemia, and lipid metabolism regulatory properties (Chen et al., 2023). Methanolic extracts of seed oil extracted from hemp were found to possess phenols, flavonoids, α-linolenic acid, and linoleic acid. Further investigation showed that the presence of these compounds suggests the nutraceutical and antioxidant potential of the seed oil (Rashid et al., 2021). A nanoemulsion of CBD-rich hemp oil was revealed to increase the bioavailability of CBD. The study further demonstrates the potential of CBD-rich hemp oil used as a functional food product (Zheng et al., 2022). The antihypertensive and antioxidant activities of protein hydrolysate and hemp seed peptides are also well-reported in the literature (Girgih et al., 2014). Other studies suggest that hemp sprouts can be promising candidates for anti-inflammatory agents, as sprouting and germination processes induce the production of anti-inflammatory compounds, including flavonoids such as prenyl flavonoids cannflavins A and B (Werz et al., 2014).

4.6 | Nootropics

Nootropic substances, either natural or synthetic, have been demonstrated to stimulate memory, cognition, and concentration (Lorca et al., 2023). Several empirical evidence pinpoint cannabis as a promising candidate for improving cognitive function in both animals and humans (Cassano et al., 2020). O'Brien et al. (2021) identified that CBD-rich edible cannabis influences motor coordination, memory, cognition, and pain perception. However, the exact mechanism of action is still unknown. The findings of Abdel-Salam et al. (2013) point out the impact of cannabis extracts on inducing neurotransmitters in the brain. Induced neurotransmitters increased the levels of serotonin, dopamine, and noradrenaline. The use of edible cannabis continuously for a year has been linked to reducing depression, anxiety, insomnia, and stress (Stith et al., 2020).

On the other hand, other evidence points to cannabis as a memory-impaired substance. Studies by Niloy et al. (2023) found that edible cannabis causes short-term memory in Wistar rats. In 2018, another study found that cannabis's effects on memory impairments persist for a very long period, making it difficult to recover cognitive functions even after several weeks of abstinence (Schuster et al., 2018). Crean et al. (2011) found that extensive use of cannabis is a risk factor for low cognitive function and affects the ability to remember new information. Impaired memory function is also reported after ingestion of hashish in a dose–concentration relationship (Zuurman et al., 2009). CBD-administered extract appeared to induce memory impairment in other findings (Egashira et al., 2012). In the same study, the author demonstrated that Δ9-THC influences memory impairment and activates cannabinoid receptors (Egashira et al., 2012).

Other studies also suggest that prefrontal dopamine receptors are involved in impaired memory processes (Fadda et al., 2006). In studying the combined effect of scopolamine and cannabis, Smith et al. (2002) demonstrated a dose-related response of cognitive impairment evident after the initial administration. Several in vivo experiments of CBD-ingested extracts demonstrate mixed results regarding memory. While some studies demonstrate CBD's ability to distort memory after a training session, other studies found that CBD-ingested extracts improve memory during a training session (Giordano et al., 2023). These findings further demonstrate that CBD-ingested extracts are dependent on the time of administration and could possess nootropic benefits. Similarly, another study in 2023 evaluated the potential benefits of CBD extract and found that treatment with CBD increased hippocampal neuroplasticity and decreased hippocampal neurodegeneration (Aychman et al., 2023). The nootropic efficacy of cannabis was evaluated in a double-blind study for healthy adults. The study findings demonstrated the ability to influence cognitive flexibility and synaptic plasticity (Lanni et al., 2008).

5 | SAFETY OF CANNABIS-INFUSED FOOD PRODUCTS

The legal status of cannabis remains complex despite its extensive use and applications in food and medicine (Baron, 2015). Despite the illegality of cannabis in various countries, there has been an observed significant increase in the marketing of food products containing CBD/THC over the past 5 years (McGregor et al., 2020). These products include baked goods, infused beverages, candies, and snacks, with varying CBD doses. The cannabis market is currently $2 billion in sales in 2022 and is estimated to reach $5.98 billion by 2025, with a substantial portion attributed to edibles and beverages (Nyland & Moyer, 2022). However, concerns arise regarding the use of cannabis food products, particularly among vulnerable populations such as children and pregnant women (Haroutounian et al., 2021). The lack of basic packaging regulations also raises concerns about the physical, chemical, and sanitary integrity of these food items. It is crucial to have child-proof packaging and accurate labeling to minimize the risk of unintentional consumption of cannabis-infused foods, especially by unsuspecting

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individuals, including children, who may mistake them for regular and popular snacks (Lindsay, 2022). Edible cannabis products are sometimes packaged in a way that resembles regular sweets and candy, featuring colorful and attractive labels. Unfortunately, this can make them more appealing to children and increase the risk of accidental ingestion (Lindsay, 2022). Studies have shown that the labeling of edible products is often inaccurate. One study discovered that only 17% of retail products contained the exact dose of THC as indicated on the label (Parnes et al., 2018), whereas 23% of retail products contained at least 10% more THC than what was stated on the label (Parnes et al., 2018). Another study examined 88 CBD liquid products, including oil and vaporization liquids, from 31 companies. The study found that the median CBD levels in these products were 9.45 mg/mL, ranging from 0.10 to 655.27 mg/mL, lower than the median concentration stated on the labels, which was 15.00 mg/mL, ranging from 1.33 to 800.00 mg/mL (Bonn-Miller et al., 2017). In countries where the status is illegal such as Jamaica, there are no packaging and labeling requirements for cannabis edibles due to their illegal status (Lindsay et al., 2021).

Owing to the potential for significant adverse events and the need for precautions and warnings, as well as reported drug interactions at pharmacological doses, the FDA in the United States prohibited the publicizing of CBD as a component of nutritional supplements. The situation regarding CBD-containing products is also complex in Europe (Wagoner et al., 2021). Products like CBD-enriched hemp oil are classified as novel foods due to their limited historical use in Europe before 1997 (Aloo et al., 2024).

Determining a safe dosage of CBD involves the FDA considering both vigorous testing of toxicity and pharmacokinetics about intake, exposure, and consumption methods (Russo, 2016). Complicating matters further is the inconsistency in CBD extracts, which can likely contain other cannabinoids and exhibit different safety profiles individually or in combination with each other (Nyland & Moyer, 2022). Efforts are being made in the United Kingdom and Europe to address the problem by categorizing CBD food products as "novel foods" and necessitating authorization for the introduction or continued presence of such products in the market (Borgelt et al., 2013). The current process for obtaining research on CBD in the United States does not provide a comprehensive risk assessment or a clear pathway for approval (Li et al., 2021). While there are reports attesting to the safety of pure CBD, a specific quantity safe for consumption has not been quantified or identified. Typically, the safe amount of a food additive is determined as a percentage of the acceptable daily intake, considering the estimated daily intake (Nyland & Moyer, 2022). The lack of standardization in classifying CBD quantities per serving and specifying the forms of extracts used can lead to significant variability in CBD exposure and potential safety risks (Nyland & Moyer, 2022). The lack of consistent parameters and standards for CBD products, including the absence of clear information on extract types and quantities per serving across different jurisdictions, leaves consumers to assume safety regardless of the dose or extract type presented (Pavlovic et al., 2018). This lack of regulation can result in other safety risks. Hemp plants, by nature, absorb heavy metals from the soil, necessitating control measures. Unregulated CBD products may be polluted with chemicals used in plant cultivation, pesticides, heavy metals, mold, bacteria, extraction solvents, and synthetic cannabinoids (Kuzdzal et al., 2018). Therefore, food products with nonstandardized extracts may also contain other cannabinoids that have not been thoroughly studied for safety, such as Cannabigerol (CBG), Tetrahydrocannabivarin (THCV), CBDA, and THCA (Sarma et al., 2020). Moreover, CBD and synthetic materials can degrade under certain storage conditions, affecting their potency and label accuracy. Moreover, existing studies do not cover larger populations over lengthy periods, which is crucial for extrapolating risks to the general population (Citti et al., 2021). Although the increased exposure of CBD consumed with fats has been assessed, a range of doses applicable to various food applications has not been measured or identified as an established standard (Ujváry, 2023).

The increasing demand for CBD-based products has also led to evasive and misleading business practices, raising further concerns about product safety (Nyland & Moyer, 2022). In the past, some manufacturers added drugs/their equivalents to dietary supplements to enhance the perceived benefits of their products. There is a risk that manufacturers of such products may increase CBD dosages to achieve certain prescription levels, taking advantage of the availability of these widely accessible products (Bent, 2008). Some companies have advertised their products as containing "hemp extracts" rather than cannabinoids, which could be a warning sign of illegal additives and activities (White et al., 2021). Some companies have also found ways to work around national patents and trademark laws, which forbid CBD in food, by creating identical product lines without CBD to obtain intellectual property rights (Scheuer, 2020).

5.1 | Regulatory and legal landscape of cannabis products

Some regulatory bodies such as governmental bodies, for example, Colorado in the United States, support permitting up to 10 mg of THC per serving for any cannabis-infused food or drink products. The regulator's concerns for consumer safety and the lack of scientific evidence of effective

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TABLE 2 Examples of cannabis-based food ingredients and products.

Sources of cannabis	Food product
Fermented hemp seeds[a]	Seasoning sauce
Hemp seed and hemp seed oil[b]	Chocolate, pralines
Hemp seeds[c]	Hemp milk
Hemp seed powder[d]	Additive, protein powder
Hemp plant juice[e]	Beverage
Hemp Seed oil[f]	Additive

[a]Metz and Selg-Mann (2000).
[b]Steinbach (1997).
[c]Berghofer et al. (2003).
[d]Hu Guang Yuan (2004).
[e]Bisterfeld Von (2012).
[f]Devi and Khanam (2019).

doses of THC and other cannabinoids for minimum effect in many infused products influence decisions to restrict and use low dosages as a starting point (Lawrence, 2019). However, in terms of allowable limits for THC and CBD, there are major differences across the continent (Table 2). For instance, in Canada, the maximum THC per serving is 10 mg, while, in the United States (Oregon), the maximum serving is 5 mg per serving (Steigerwald et al., 2018). In countries such as Jamaica, THC levels range from 0.01 to 99.9 mg/100 g, while CBD can range from 0.001 to 69.2 mg/100 g (Lindsay et al., 2021). In Europe, according to the European Industrial Hemp Association (EIHA), the average daily intake of THC is 0.035 mg/kg of body weight; however, maximum limits are country dependent (Tsaliki et al., 2021). In New Zealand, an upper limit of 0.006 mg/kg of body weight has been set by the government (Beitzke & Pate, 2021).

Different types of cannabis food products are subject to varying regulations, with THC being more regulated than CBD due to its psychoactive effects. Concerns surrounding the health risks and misuse of THC have led countries to implement restrictions on its production, distribution, and use (Yang et al., 2017). Although CBD is not psychoactive, it is considered to have a risk profile and like THC faces stringent regulations in certain regions around the world (Mead, 2019).

In the United States, CBD regulations can be complex and vary at both the state and federal levels. CBD derived from hemp (containing more than 0.3% THC) was legalized through the 2018 Farm Bill (Mead, 2019). However, the FDA has regulations for CBD products marketed as supplements. State laws vary with CBD regulations, where some states have lenient access to CBD products, while others impose stricter regulations (Malone & Gomez, 2019). In Canada, both CBD and THC are regulated under the Cannabis Act. However, unlike THC, which has a limit set in place, there is no limit for CBD products (Hazekamp, 2018).

In the United Kingdom, CBD products must contain 0.2% THC and cannot be marketed with claims of medicinal benefits unless they have been permitted by the Medicines and Healthcare Products Regulatory Agency (MHRA) as a medicine (McGregor et al., 2020). Switzerland allows CBD-containing cannabis products with up to 1% THC to be sold as alternatives to tobacco. In addition, over-the-counter CBD products, as well as oils, extracts, and flowers, are widely accessible in Switzerland (Deville et al., 2020). In the Netherlands, CBD products containing less than 0.05% THC are considered legal and available without restrictions. However, there are regulations governing cannabis products that contain more than 5 mg of THC per item. These products can only be acquired from coffee shops (Hazekamp, 2018). Some of these allowable limits are summarized in Table 1.

6 | CONCLUSIONS

Cannabis-infused food products offer an alternative method of consumption for individuals who may prefer edible options over other forms of cannabis products. While significant progress has been made in exploring different cannabis food products and the potential benefits of cannabis-infused products for various diseases, our study also revealed notable constraints on the optimal dosing and long-term safety of cannabis-infused food products. The development of cannabis-infused foods as nootropics and nutraceuticals also holds promising potential for the food industry, medical industry, and consumers.

Overall, cannabis-infused food products as therapeutic and dietary products are promising but require continued research, regulatory guidelines, and responsible use to ensure their efficacy and safety in therapeutic food formulations to manage different health issues. Limited research on food formulations, along with in vitro and in vivo experiments, further presents an opportunity for researchers to bridge this gap. Therefore, with advancements in technology and research, there is an opportunity for developing more precise and standardized formulations of cannabis-infused food products. This includes controlling the dosage and ratio of active compounds, optimizing delivery methods, and processing to ensure consistent and effective therapeutic effects.

AUTHOR CONTRIBUTIONS

Eric Fordjour: Conceptualization; investigation; writing—original draft; methodology; validation; visualization; writing—review and editing; software; formal analysis; resources; data curation. **Charles F. Manful**:

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Investigation; methodology; validation; writing—review and editing; supervision. **Tarsaim S. K. Khalsamehta**: Writing—review and editing; software. **Abraham Armah**: Investigation; writing—review and editing. **Mumtaz Cheema**: Conceptualization; writing—review and editing; validation; visualization; methodology; supervision. **Raymond Thomas**: Conceptualization; investigation; funding acquisition; writing—review and editing; validation; methodology; supervision; project administration.

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CONFLICT OF INTEREST STATEMENT

The authors declare no conflicts of interest.

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