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Clearing the Smoke on Cannabis

Edible Cannabis Products, Cannabis Extracts and Cannabis Topicals

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This is the seventh in a series of reports that reviews the effects of cannabis use on various aspects of human functioning and development. Other reports in this series address the link between regular cannabis use and mental health, regular cannabis use and cognitive functioning, maternal cannabis use during pregnancy, cannabis use and driving, respiratory and cardiovascular effects of smoking cannabis, and the medical use of cannabis and cannabinoids. This series is intended for a broad audience, including health professionals, policy makers and researchers.

Canadian Centre on Substance Use and Addiction

Evidence. Engagement. Impact.

Key Points

- Edible cannabis products, cannabis extracts and cannabis topicals have unique health and safety risks that are not inherent to dried cannabis.
- High-potency cannabis extracts increase the risk of over-intoxication more than dried cannabis. Although limited, the available evidence indicates that frequent use of these products is associated with problematic cannabis use, cannabis use disorder and mental health disorders.
- Edible cannabis products can increase the risk of over-consumption and subsequent over-intoxication and impairment. Because when unpackaged they look like ordinary food and beverage products, edible cannabis products also increase the risk of unintentional ingestion, especially by children.
- Research on cannabis topicals, including the use of topical and transdermal cannabidiol products, is limited. There is, however, growing interest among dermatologists and consumers in these cannabis products.
- The health impacts associated with long-term use of edible cannabis products, cannabis extracts and cannabis topicals are not known.
- Public education efforts will play an important role in mitigating the harms associated with new cannabis products.

Background

On October 17, 2019, Canada legalized the production and sale of several new cannabis products, including edible cannabis products (or "edibles"), cannabis extracts and cannabis topicals. Legalization will increase accessibility to a wide variety of products and methods of consumption for individuals who choose to use cannabis. While these products might look, smell and taste different from dried cannabis, "cannabis is cannabis." In other words, most of the short- and long-term health impacts associated with the use of dried cannabis also apply to edible cannabis products, cannabis extracts and, to a lesser extent, cannabis topicals. However, these new cannabis products also are accompanied by several additional health and safety risks that are not inherent to dried cannabis.

What are cannabinoids and terpenes?

Cannabinoids are the chemical compounds found in the cannabis plant, some of which can affect the mind and body when consumed. ***THC (Δ⁹-tetrahydrocannabinol)*** *is the best known cannabinoid. This cannabinoid has intoxicating and impairing effects, with high doses leading to severe anxiety, panic, heart palpitations and symptoms of psychosis (e.g., paranoia). Research is ongoing to determine whether THC has medical benefits for certain health conditions.* ***CBD (cannabidiol)*** *) is a cannabinoid that has gained increased attention for its therapeutic potential, although more research is needed to confirm its usefulness and effectiveness for medical purposes. CBD does not produce the characteristic high that is attributed to THC, but it appears to have sedative properties. The cannabis plant has at least one hundred more cannabinoids, about which little is known. Among other constituents, the cannabis plant also has terpenes, which are substances that contribute to the smell and taste of cannabis. It has been suggested that terpenes modulate the effects of THC and CBD on the mind and body (referred to as the entourage effect), although this suggestion has yet to be extensively examined. .*

This report reviews the available, albeit limited, scientific evidence on edible cannabis products, cannabis extracts and cannabis topicals, with a particular focus on what distinguishes these new products from dried cannabis. It provides an overview of current and anticipated cannabis products based on information available in Canada and the United States. The range of products available will likely continue to grow as the market evolves and updates to this report will be made accordingly. The report will assist healthcare practitioners, policy makers and public heath organizations in developing public education resources and harm reduction strategies related to the use of edible cannabis products, cannabis extracts and cannabis topicals. It also draws attention to the evidence gaps in this relatively new area of research.

Cannabis Extracts

A cannabis extract can, in essence, be any product that contains cannabinoids that have been extracted from the cannabis plant. Cannabis extracts vary greatly in their appearance and consistency, taste and smell, and in their THC and CBD (and other lesser known cannabinoids) concentrations. The term "concentrate"[1] has been applied to cannabis extracts that contain high concentrations (e.g., ~ 60%) of THC (Raber, Elzinga, & Kaplan, 2015). A recent study of the Washington State legal cannabis market found that cannabis concentrates are now averaging 70% to 80% THC (Davenport, 2019). While it is possible to create concentrated CBD products (e.g. CBD oils), these are typically not referred to as concentrates. Cannabis extracts are commonly smoked or vaporized ("vaped"), alone or mixed with dried cannabis. They can also be ingested, alone or in capsule form, or administered sublingually (i.e., under the tongue). Dabbing is becoming an increasingly popular method of inhaling concentrates, particularly among youth (Stogner & Miller, 2015). To get a sense of the diversity of cannabis extracts being used and produced, Table 1 provides a brief description of some of the more common products.

What is dabbing?

Dabbing is a relatively new way to vape concentrates. Dabbing is a method of vaporizing solid concentrates. A small piece or "dab" of concentrate is placed against a hot surface, such as the nail in a dab rig or coil in a wax pen (two specialized accessories used for dabbing). Once the concentrate has vaporized, all of the vapor is usually inhaled in a single breath.

Dabbing and maintaining a dab rig can be complicated and is not recommended for beginners. However, data from the United States shows that dabbing is becoming increasingly popular, especially among younger populations (Stogner & Miller, 2015). This trend is concerning because dabbing increases the risk of over-intoxication (Pierre, Gandal, & Son, 2016) and cardiovascular toxicity (Rickner, Cao, Kleinschmidt, & Fleming, 2017). Regular dabbing also increases the risk of cannabis-related problems, including tolerance and dependence (Meier, 2017; Loflin & Earleywine, 2014). In a national online survey in the United States, individuals who used dabs regularly indicated that they were more worried about their use of these cannabis products relative to those who tried dabs but did not use them regularly (Sagar, Lambros, Dahlgren, Smith, & Gruber, 2018).

[1] Canadian *Cannabis Regulations* state that a "cannabis concentrate means a substance that has a concentration of greater than 3% [weight per weight] of THC, taking into account the potential to convert THCA into THC" (Government of Canada, 2018).

Table 1. Summary of cannabis extracts

Product	Description	Method of Use	Average Levels of THC and CBD[2]
Hash			
	Hash or hashish is the oldest and best-known type of cannabis extract. It is a light to dark brown substance composed of compressed or purified trichomes, which are the stalked resin glands that contain most of the cannabinoids present in the cannabis plant. Hash that has been pressed is usually solid, whereas water-purified hash develops a paste-like consistency and is often called "bubble melt hash" or "bubble hash."	- **Smoked** (either alone or mixed in with dried cannabis or tobacco) - **Vaped** - **Dabbed**	THC: 40–80% CBD: less than 5%
Kief			
	Kief refers to the collection of trichomes that accumulate when sifted from dried cannabis, often using a three-chamber grinder.	- **Smoked** (either alone or mixed in with dried cannabis or tobacco)	THC: 40–50% CBD: less than 5%
Wax (crumble, budder)			
	Wax is a solvent-based (e.g., butane[3]) extract that is named after its appearance and consistency. Wax varies in level of THC depending on quality, but can contain well over 50% THC. **Crumble** is the drier and more crumbly form of wax, whereas **budder** contains a higher moisture content.	- **Vaped** - **Dabbed**	THC: 26–70% CBD: --
Shatter			
	Shatter is amber and glass-like in appearance and consistency. It is generally high in THC and low in CBD. Compression following the extraction process turns shatter into a substance called "cookie crumble" or "honeycomb."	- **Vaped** - **Dabbed**	THC: ~ 70% CBD: --
Live Resin			
	Live resin is made the same way as wax, but with fresh cannabis plant material that has been immediately frozen after harvest. This is the reason for the term "live." This process gives live resin a "more intense and complex" smell and taste, so it is more expensive than typical wax and budder products. The moisture in this extract gives it a slightly different appearance from wax and budder.	- **Vaped** - **Dabbed**	THC: 40–50% CBD: --
Rosin			
	Rosin refers to cannabis extracts that were made using "rosin tech," which is essentially the application of heat and compression to the resinous sap from cannabis plant matter, most often flower (or bud), kief or hash. This extraction method results in a sappy and translucent cannabis extract that is similar in appearance and composition to **shatter.** It is believed that rosin can reach comparable THC concentrations to that in solvent-based extracts, but this has yet to be scientifically tested.	- **Vaped** - **Dabbed**	THC: ~ 70% CBD: --

[2] Canadian *Cannabis Regulations* state that a "cannabis concentrate means a substance that has a concentration of greater than 3% [weight per weight] of THC, taking into account the potential to convert THCA into THC" (Government of Canada, 2018).

[3] Cannabis extracts using butane are often called butane hash oils (BHOs). BHOs appear to be common in the United States, particularly in illicit and unregulated markets (Al-Zouabi, Stogner, Miller, & Lane, 2018). It is currently unclear whether butane is a commonly used solvent on the Canadian illicit market or whether other solvents (e.g., CO_2) and extraction processes (e.g., distillation) are being used.

Product	Description	Method of Use	Average Levels of THC and CBD[1]
Tinctures and Oil Sprays			
	Tinctures and oil sprays are products consisting of a cannabis extract, a carrier liquid, such as coconut-derived MCT (medium-chain triglycerides) oil, and sometimes terpenes. These products vary widely in their THC and CBD levels and reasons for use. Tinctures come in plastic or glass bottles with droppers and are administered under the tongue (sublingually). Oil sprays are similarly intended to be sprayed under the tongue.	- **Sublingual** - **Ingested**	**High THC:** THC: 20–30 mg/ml CBD: 0–1 mg/ml **High CBD:** THC: 0.7–2 mg/ml CBD: 15–55 mg/ml **Balanced:** THC: 1–12.5 mg/ml CBD: 1–12.5 mg/ml
Softgels and Capsules			
	Softgels and capsules are comprised of similar ingredients to that of tinctures and oil sprays: a cannabis extract, a carrier liquid (e.g., MCT) and, sometimes, terpenes. These products vary widely in their THC and CBD levels.	- **Ingested**	**High THC:** THC: 2.5–10 mg/capsule CBD: 0–1 mg/capsule Capsules on the illicit market appear to contain up to 100 mg of THC. **High CBD:** THC: O–1 mg/capsule CBD: 9–25 mg/capsule **Balanced:** THC: 2–3 mg/capsule CBD: 2–3 mg/capsule
Vape Cartridges and Disposable Pens			
	Vape cartridges and pens contain high concentrated cannabis extracts and varying terpene (flavour) profiles. High THC vape products are the most commonly sold. However, it appears that high CBD and "balanced" vape products are becoming increasingly available.	- **Vaped**	**High THC:** THC: 70–95% CBD: 0–10% **High CBD:** THC: 0–5% CBD: 60–70% **Balanced:** THC: 40–60% CBD: 20–40%

Prevalence and Reasons for Use

Presently, there is no complete picture of the type and frequency of cannabis extracts being used by Canadians. However, several nationally representative surveys have begun to assess the prevalence of use of cannabis concentrates by Canadians. Data from the 2019 Canadian Cannabis Survey indicate that, among individuals who had used cannabis in the past 12 months, 23% said they had used hash or kief, 26% had used a cannabis oil cartridge or disposable vape pen and 17% had used a solid concentrate (shatter, budder, etc.) (Health Canada, 2019). The use of these cannabis products was more common among males and those aged 16 to 24 (Health Canada, 2019). Similarly, data from a large international survey showed that, among Canadians who reported using cannabis in the past 12 months, 25.1% said they had used hash or kief, 22.2% had used a cannabis oil for ingestion, 20.9% had used a cannabis oil for vaping, 16.8% had used a concentrate and 6.6% had used a tincture (Goodman, Wadsworth, Leos-Toro, Hammond, & International Cannabis Policy Study Team, 2020).

It is unclear how these patterns of use will change as new cannabis extracts become legally available in Canada. Research from the United States, particularly in states where these products are legal, might provide insight into what Canada can expect. A 2016 web-based survey of people living in the United States who use cannabis found that the use of cannabis concentrates was associated with greater odds of living in states with less restrictive recreational and medical cannabis policies (Daniulaityte et al., 2017). Consistent with the Canadian data, this study also found

that the use of cannabis concentrates, especially daily use, was associated with being male, being younger and using dried cannabis daily, and lower perceived risks associated with use of these concentrates (Daniulaityte et al., 2017). In line with these findings, an online survey conducted on people living in California, Colorado, Nevada, Oregon and Washington state found that, relative to those who never or occasionally used concentrates, individuals who frequently used these products experienced more symptoms of cannabis use disorder and used higher-strength cannabis even when not using concentrates. Interestingly, these individuals did not differ in self-reported physical and mental health or life satisfaction (Cinnamon Bidwell, YorkWilliams, Mueller, Bryan, & Hutchison, 2018).

In contrast to these later findings, more frequent use of butane hash oils was associated with higher levels of physical dependence, impaired control, cannabis-related academic or occupational problems, poor self-care and cannabis-related risk behaviour. After accounting for sociodemographic factors, age of onset of cannabis use, sensation seeking, overall frequency of cannabis use and frequency of other substance use, butane hash oil use was only associated with higher levels of physical dependence (Meier, 2017). In a large online survey conducted in over 20 countries (181,870 people), frequent use of concentrates was associated with a lifetime diagnosis of depression, anxiety and a greater number of substances used (Chan et al., 2017).

Collectively, these findings suggest that the use of concentrates is associated with problematic substance use and mental health disorders. However, it is unclear whether the use of high THC extracts and concentrates leads to diminished mental health and cannabis-related problems, whether these mental health outcomes predate the use of concentrates, or whether another factor accounts for both.

There has been little research investigating reasons why some individuals use cannabis extracts and concentrates over dried cannabis, or why they might prefer certain products over others. Qualities inherent to cannabis extracts and concentrates (e.g., cannabinoid profile) and the way in which they can be consumed, might predict preferences for particular products. For example, vaporizing or "vaping" is one of the more common ways of consuming cannabis extracts and concentrates. Because vaping is thought to minimize harmful effects to the lungs, this method of inhalation might become an increasingly popular way to consume cannabis, and one that facilitates the use of extracts and concentrates (e.g., vape pens) (e.g., Kowitt et al., 2019). However, as described in a recent brief from CCSA, *Vaping Linked with Severe Lung Illnesses*, vaping cannabis products has risks (Canadian Centre on Substance Use and Addiction, 2019).

Vaping does not produce the smell associated with smoking cannabis, making it a more discrete and versatile way of consuming it. An online survey conducted in the United States found that individuals were more likely to have vaped cannabis in locations other than a private residence, including in a motor vehicle, and more frequent vaping was associated with driving while impaired (Jones, Meier, & Pardini, 2018). These findings have implications for impaired driving and workplace health and safety.

Reasons for the use of certain cannabis extracts and concentrates might also vary by the cannabinoid profile (e.g., THC:CBD ratio) of the product. Concentrates, which are high in THC, are more commonly used by individuals who are experienced with cannabis and who generally consume cannabis more regularly (Cinnamon Bidwell et al., 2018; Daniulaityte et al., 2017). A recent online survey found that individuals who used concentrates said they did so for experimentation and out of curiosity (Sagar et al., 2018), but these products also appear to be more commonly used by individuals using cannabis for therapeutic purposes (Daniulaityte et al., 2017). However, 2019 data from the Canadian Cannabis Survey seems to show that the use of concentrates (e.g., shatter, budder) is less common among individuals using for medical purposes (13.1% said they used a cannabis concentrate or extract in the past 12 months), relative to those using for non-medical reasons (17.3% said they used a cannabis concentrate or extract in the past 12 months) (Health Canada, 2019). It is worth mentioning, however, that the line between medical and non-medical cannabis use is becoming increasingly blurred (Morean & Lederman, 2019).

CBD is steadily gaining a possibly premature reputation for having a variety of health and medical benefits. There is promising research supporting some benefits of CBD, THC and other cannabinoids for certain health conditions, including relief of chronic pain, anxiety and insomnia (Babson, Sottile, & Morabito, 2017; Bonaccorso, Ricciardi, Zangani, Chiappini, & Schifano, 2019; Lee, Bertoglio, Guimarães, & Stevenson, 2017; Lee, Grovey, Furnish, & Wallace, 2018; Jensen, Chen, Furnish, & Wallace, 2015; MacCallum & Russo, 2018). However, except for a few specific research programs (e.g., use of CBD for the treatment of seizures associated with rare forms of epilepsy in young children [Friedman, French, & Maccarrone, 2019]), there is little high-quality research assessing the efficiency of CBD in treating any health condition and the

safety of long-term use of CBD is unknown. CBD can also facilitate or inhibit the actions of a number of different drugs, especially those metabolized by CYP450 enzymes (e.g., opioids, benzodiazepines and antidepressants), and research assessing potential drug interactions is generally lacking (Brown & Winterstein, 2019). Despite the lack of evidence, there is a considerable amount of interest in CBD among Canadians. Moreover, as indicated in the 2019 Canadian Cannabis Survey, products higher in CBD and lower in THC are the most common types of products used among individuals for medical purposes, especially females. Parenthetically, only 33.5% of those reporting medical use had medical documentation for this purpose (Health Canada, 2019).

Taken together, the available research suggests that reasons for using cannabis extracts and concentrates might vary by product type, method of use and context. A more in-depth understanding of these topics could be gained through the use of qualitative research methods, which should also encompass diverse groups of individuals, including those of varying age, sex, gender, culture and ethnicity.

Health and Safety Risks

The health and safety risks associated with the use of cannabis extracts and concentrates have not been well characterized. The available evidence suggests that the risks vary depending on the type of product (including the ingredients in the product) and method of use and are proportional to the amount of THC in the product. Individuals who indicated they used a variety of high-strength cannabis product reported that they had experienced stronger negative effects and less positive effects when using butane hash oils relative to high-potency dried cannabis (Chan et al., 2017). Similarly, a case series from the United States found that dabbing, an increasingly popular method of vaping concentrates, led to significant adverse health effects, including psychosis, neurotoxicity and cardiotoxicity (Alzghari, Fung, Rickner, Chacko, & Fleming, 2017). Although limited, this evidence suggests that concentrates, because of their high THC levels, carry with them an increased risk of over-intoxication, beyond that which is attributable to dried cannabis use (Allen et al., 2017).

In the United States, as of January 21, 2020, 2,711 individuals have been hospitalized or have died of lung injury associated with using e-cigarettes or vaping products (Centers for Disease Control and Prevention, 2020, Feb. 4). In Canada, as of January 28, 2020, 17 cases of lung illness associated with vaping but no deaths have been reported to the Public Health Agency of Canada (Government of Canada, 2020). An additive (or contaminant) called vitamin E acetate in illegal and unregulated cannabis vape liquids is currently suspected as the chemical responsible for the cases of lung injury. However, other chemicals cannot be ruled out at this time. In fact, vape oils, especially those on the illicit market, can contain an array of chemicals (e.g., flavourings, carrier liquids, particulates of the vape device or cartridge) that when heated and inhaled can be harmful to lung tissue. Research on the respiratory effects of repeated exposure to many of these chemicals has not been conducted. The injuries from vaping underscore the importance of being well informed of the health and safety risks associated with cannabis vaping products and all cannabis products before considering their use. An equally important message is for individuals to purchase cannabis products, including vape oils, from legal and regulated retailers and producers as products from these sources are strictly regulated and assessed for quality and the presence of contaminants. For a more comprehensive account of vaping-related lung illness, see *Vaping Linked with Severe Lung Illnesses*.

Edible cannabis products have received most of the attention around concerns of unintentional ingestion by children and pets. This concern also applies to cannabis extracts and concentrates. A 2017 systematic review found that the most common cannabis product ingested by children was a resin, followed by cookies and joints (Richards, Smith, & Moulin, 2017). Indeed, public education on proper labelling (e.g., amounts of THC, CBD and other ingredients), storage and disposal of all types of cannabis products will play an important role in mitigating the risk of unintentional ingestion. For a resource on how to safely store cannabis products, see CCSA's *How to Safely Store Your Cannabis*.

The health impacts associated with regular use (weekly or more frequent use for long periods of time) of cannabis extracts and concentrates are not known. It is likely that most of the health concerns that have been identified with regular use of dried cannabis, which are mostly attributed to THC, also apply to cannabis extracts and concentrates. Regular use of cannabis has been associated with difficulties in cognitive functioning (e.g., memory and concentration) (Scott et al., 2018) and an increased risk of developing certain mental illnesses, including psychosis and schizophrenia (Lowe, Sasiadek, Coles, & George, 2019). Regular use of cannabis during pregnancy has been related to increased risk of developmental disturbances (e.g., lower birth weight) in children of mothers who had smoked cannabis heavily (Corsi et al., 2019). Frequent exposure to cannabis smoke can lead to respiratory system harms, including bronchitis (Ribeiro & Ind, 2016). A comprehensive overview of the health impacts of cannabis use is provided in CCSA's Clearing the Smoke on Cannabis series.

A growing body of evidence suggests that the mental health impacts of cannabis use are not dependent only on frequency of use, but also on the amount or concentration of THC in the product. For example, in a study that examined the prevalence of first-episode psychosis across 11 sites in Europe and Brazil, daily cannabis use was associated with increased odds of psychotic disorder compared with those who do not use cannabis, increasing to nearly five times greater odds for daily use of high-potency types of cannabis. Statistical analyses indicated that if high-potency cannabis were no longer available, 12.2% of cases of first-episode psychosis could be prevented across the 11 sites (Di Forti et al., 2019). Further, supporting the notion that higher potency cannabis products carry greater risks to mental health, a large online survey conducted in over 20 countries found that frequent use of concentrates was associated with a lifetime diagnosis of depression, anxiety and a greater number of substances used (Chan et al., 2017). As well, individuals who dabbed reported that this method of vaping concentrates led to higher tolerance and withdrawal (as defined by the participants) (Loflin & Earleywine, 2014). More frequent use of butane hash oils was associated with higher levels of physical dependence, even after controlling for sociodemographic factors, age of onset of cannabis use, sensation seeking, overall frequency of cannabis use and frequency of other substance use (Meier, 2017). Consistent with these findings, a recent study found that, after accounting for the concurrent use of multiple cannabis products, the use of cannabis concentrates was strongly predictive of a progression from experimentation to persistent use over a 12-month period (Barrington-Trimis et al., 2020).

Collectively, the evidence suggests that the use of higher-potency cannabis products, especially concentrates, is associated with mental illness and symptoms of dependence. The causal direction of these associations and whether the relationship between mental illness and regular use of concentrates is reciprocal remains to be determined.

Edible Cannabis Products

Edible cannabis products, popularly known as “edibles,” are food and beverage products that have been infused with a typically oil- or alcohol-based cannabis extract. Edibles can take many different forms, including chocolates, cookies, brownies, candies and various types of beverages (Barrus et al., 2016). Essentially, anything you can add a cannabis extract to can be considered an edible and making these products is a relatively easy process. The main step in the process is to ensure that the cannabis product (e.g., dried cannabis or extract) has been sufficiently “decarboxylated” prior to combining with food ingredients. Edible cannabis products vary considerably in their concentrations of THC and other cannabinoids, particularly in the illegal and unregulated markets. In Canada, the legal limit of THC per package of edible cannabis is 10 mg, although it is recommended that individuals who are new to cannabis start with no more than 2.5 mg of THC.

> ***What is decarboxylation?***
> *Eating or drinking raw cannabis will not produce intoxicating or impairing effects because the main cannabinoid that produces these effects (THC) is in a different form. In the living cannabis plant, THC has a carboxyl group attached to it, making it tetrahydrocannabinolic acid or THCA. Decarboxylation is the process of removing the carboxyl group, which is achieved through heat and time (Casiraghi et al., 2018). Smoking and vaping are the fastest ways to decarboxylate cannabinoids, although drying or curing raw cannabis material also leads to decarboxylation.*

Prevalence and Reasons for Use

Data from the 2019 Canadian Cannabis Survey indicated that, among individuals who used cannabis in the past 12 months, 44% said that they had eaten cannabis in food, which was an increase from 41% in 2018 and 34% in 2017 (Health Canada, 2019). This survey further indicated that, while a greater percentage of males reported using dried flower, hash and concentrates or extracts, higher percentage of females reported using edible food products (48%) compared to males (42%). These data suggest that males prefer dried flower and concentrates, while females prefer edible cannabis products.

There has yet to be any published research exploring why Canadians consume edible cannabis. A qualitative study conducted in the United States indicated that individuals prefer edible cannabis to smoked cannabis because with no smoke there is no smell and no second-hand smoke. Participants in the study also liked the convenience, discreetness, longer-lasting highs and less-intense highs associated with edibles, and the perceived ability of these cannabis products to aid in relaxation and reduce anxiety more so than smoking cannabis. On the other hand, participants disliked the delayed effects, unexpected highs and the unpredictability of the high, and were concerned about the inconsistent distribution of cannabis in the products (Giombi, Kosa, Rains, & Cates, 2018).

A study conducted in San Francisco examined gender differences in perceptions of edible cannabis among 15 to 19 year olds. This study found that young men and women used edibles mainly to reduce the likelihood of getting

caught at school, to avoid smelling like cannabis and to reduce the respiratory harms associated with smoking. Interestingly, some young women said that edibles could be a way to avoid publicly presenting themselves as "cannabis users." Both those who used edibles and those who did not reported being aware of the potentially negative consequences related to edible use. This awareness included hearing (perhaps inaccurately) of individuals who died from edibles and several youth reported being concerned about the high produced by edibles. Females who did not use edibles appeared to be more concerned than males about these cannabis products and compared them to drinks that could be spiked with drugs. By contrast, some young men said that "if you can't handle edibles you shouldn't be using them" (Friese, Slater, Annechino, & Battle, 2016). These findings identify attitudes and beliefs among young men and women that might be useful in prevention and harm reduction messaging.

Health and Safety Risks

Over-intoxication (or "unexpected high") as a result of over-consumption is arguably the main health risk that accompanies edible cannabis products (Allen et al., 2017). Since it can take up to four hours for effects to peak, people new to cannabis can grow impatient or think that the product is ineffective and consume another portion. Some individuals might simply not know how much THC to consume in an edible cannabis product in the first place, resulting in them ingesting a larger amount of THC than they can handle. For instance, in March 2014, a young man living in Colorado ate a single portion (10 mg of THC) of a cookie that contained 65 mg of THC in total. Approximately 30–60 minutes later, not feeling any effects, he consumed the remainder of the cookie. During the next two hours, he reportedly exhibited erratic speech and hostile behaviours. Approximately three and a half hours after initial ingestion and two and a half hours after consuming the remainder of the cookie, he jumped off a fourth floor balcony and died from trauma (Hancock-Allen, Barker, VanDyke, & Holmes, 2015). This event led Colorado authorities to change the regulations around the labelling and packaging of cannabis products, and highlighted the importance of education. To minimize the risk, Health Canada has limited the amount of THC to 10 mg per package in total, regardless of the number of units of edible cannabis in a package, and has enforced strict regulations around packaging and labelling.

Over-consumption can lead to the development of psychosis (Favrat et al., 2005; Hudak, Severn, & Nordstrom, 2015) and can result in serious injury or death. For some individuals, over-consumption might also result in cardiovascular events (Monte et al., 2019) and stroke (Atchaneeyasakul, Torres, & Malik, 2017), although the relative risk of these events is currently not known. Public education on the distinct pharmacological properties of edible cannabis, including dosing, and the delayed onset and longer duration of effects can help reduce the risk of over-consumption and over-intoxication or cannabis poisoning.

Cannabis in most forms and through most methods of use impairs the cognitive and psychomotor abilities needed to operate a motor vehicle. Such impairment includes the use of edible cannabis. Unlike cannabis products that are inhaled, however, the onset and the duration of intoxication and impairment after ingesting cannabis is significantly delayed (30 minutes to two hours) and persists for up to 12 hours. It is difficult to predict when the psychoactive effects will emerge and when they will subside. This difficulty makes it hard to determine when it will be safe for an individual to drive a motor vehicle. There are currently no evidence-based recommendations as to when, after consuming edible cannabis, it is safe to drive. More scientific research is needed, but in the meantime, as some residual effects (e.g., drowsiness) can persist for up to 24 hours, driving during this timeframe should be avoided. For more information on cannabis and driving, see *Clearing the Smoke on Cannabis: Cannabis Use and Driving — An Update*.

Legalization of edible cannabis products introduces the risk of unintentional ingestion, especially by children (Berger, 2014; Potera, 2015). As an example, Colorado Regional Poison Control observed a significant increase in pediatric cannabis ingestion cases over the two years following cannabis legalization in the state (Wang, Roosevelt, & Heard, 2016). Children who ingest cannabis vary in the symptoms they present, with cardiovascular and respiratory difficulties being some of the more severe symptoms (Richards et al., 2017; Vo et al., 2018). Education around proper storage and disposal of cannabis products can reduce the risk of unintentional ingestion.

Food-borne disease is an underappreciated health risk associated with edible cannabis. In Europe and the United States, the cannabis industry has experienced a number of outbreaks and product recalls linked to food-borne pathogens, moulds, unsanitary conditions, temperature abuse and the presence of pesticides in edible cannabis products (Diplock, Leatherdale, & Majowicz, 2017). The probability of these risks in Canada, especially within the regulated cannabis market, is likely low. However, the same cannot be said for edible cannabis products that have been produced and sold by illegal and unregulated sources. This concern extends to homemade cannabis edible products, especially for people who may not be experienced with proper food handling and who are selling[4] or sharing their

[4] In Canada, it is illegal to sell any form of cannabis product without the appropriate licence.

"baked goods." Moreover, homemade cannabis products also increase the risk of over-intoxication because the individual is unable to predict how much THC they are actually consuming. For example, even if the individual knows exactly how much THC was in the cannabis extract that was used in the brownie recipe and did their best to evenly distribute the extract across the entire brownie, without the proper lab equipment it is impossible to tell how much THC is in one square of brownie versus another square. Purchasing regulated products from a licensed retailer is an important way for consumers to ensure consistent distribution of THC and therefore a more predictable "high."

Over-intoxication, unintended ingestion, impaired driving and food safety are the immediate health and safety concerns that accompany edible cannabis products. By contrast, little is known about the long-term health consequences of regular use of edible cannabis. Most of the risks associated with frequently inhaling THC-containing products, such as increased risk of psychosis, likely apply to ingesting THC products. The unique harms associated with edible cannabis, however, might be difficult to identify given that individuals who regularly use cannabis typically use a variety of other cannabis products, including those that are inhaled and ingested. It might, therefore, be useful to measure an individual's "total cannabis (or cannabinoid) exposure," across multiple cannabis products and methods, when predicting health outcomes.

Cannabis Topicals

Cannabis topicals are cannabinoid-infused oils, creams and lotions intended for application directly to the skin, hair or nails.

Prevalence and Reasons for Use

The 2019 Canadian Cannabis Survey indicated that 17% of Canadians used topical ointments for medical purposes, which did not change from 2018. Topical ointments are more common used by Canadian women (11%) than men (6%) (Health Canada, 2018). CBD appears to be a popular cannabinoid in illicit topical cannabis products, largely because this cannabinoid is believed to have anti-inflammatory and anti-oxidant properties (Milando & Friedman, 2019). There is some early research supporting the use of topical CBD agents for localized pain and for some skin conditions, including psoriasis dermatitis and lupus (Dhadwal & Kirchhof, 2018; Maida & Corban, 2017; Palmieri, Laurino, & Vadalà, 2019; Sheriff, Lin, Dubin, & Khorasani, 2019; Wilkinson & Williamson, 2007). In fact, dermatologists are interested in authorizing the use of cannabinoids and patients are speaking about cannabinoids with their dermatologists (Robinson, Murphy, & Friedman, 2018). However, few clinical trials have assessed the efficacy of topical cannabis products, and the health impacts associated with regular and long-term use of these products are not known.

Cannabis topicals are also used for a variety of cosmetic purposes, including general skincare and haircare, as massage oils and for sexual enhancement (e.g., condoms comprising cannabis-derived compositions). These appear to be fast growing markets in the United States, but it is uncertain what these products will ultimately look like in Canada. It is worth mentioning, however, that several large cosmetic companies have taken advantage of the "cannabis hype" following its legalization and released a variety of products containing cannabis sativa seed oil. Cannabis sativa seed oil is derived from the seeds of the hemp plant, which contain no THC and negligible levels of CBD, but is marketed as having other ingredients that are good for the skin and hair.

Health and Safety Risks

Since there has been little research on cannabis topicals, the health and safety risks associated with the use of these products is largely unknown. It appears that applying these products to the skin does not elicit psychoactive effects, partly because of the low levels of cannabinoids in these products and the difficulty of THC penetrating the skin barrier. As previously mentioned, permeability enhancers can facilitate the transport of cannabinoids into the bloodstream. Although unlikely, it is also possible that the application of topicals with high levels of THC over large areas of broken or damaged skin could deliver amounts of this cannabinoid significant enough to produce psychoactive effects. Cannabis topicals might also produce allergic reactions, including itchiness, swelling and hives, in some individuals (Decuyper et al., 2018; Dhadwal & Kirchhof, 2018), and there are concerns that topical creams, especially those in the unregulated market, could have traces of pesticides, fungus or contaminants.

Pharmacokinetics and Pharmacodynamics of Cannabis and Cannabinoids

Pharmacokinetics refers to the way a drug is absorbed, distributed, metabolized and eliminated from the body. **Pharmacodynamics** refers to the effects a drug has on the brain and body, including the psychoactive — intoxicating and impairing — effects associated with cannabis. The absorption and metabolism of cannabinoids by the body varies by method of administration and this, in turn, influences the onset and duration of psychoactive effects (Grotenhermen, 2003; Huestis, 2007).

Smoking and Vaping

As of the publication date of this document, no published scientific studies have examined the pharmacokinetics or pharmacodynamics of vaping cannabis extracts. It is likely that the time course of psychoactive effects is comparable to that of smoked or vaped dried cannabis, and the magnitude of psychoactive effects is proportional to the amount of THC in the cannabis product. Accordingly, the pharmacokinetics and pharmacodynamics of smoked and vaped dried cannabis might provide insight into how inhaling extracts and concentrates affect the mind and body.

THC is detectible in an individual's blood during and immediately following the smoking of dried cannabis, followed soon after by the presence of THC metabolites, including 11-OH-THC and THCCOOH (Grotenhermen, 2003; Huestis, 2007). 11-OH-THC is the psychoactive metabolite of THC, whereas THCCOOH seems to have no psychoactive properties. Blood concentrations of THC peak within 10 minutes from the onset of smoking and sharply decrease afterwards, returning to baseline within one to four hours (Newmeyer et al., 2016; Spindle et al., 2018). The concentrations and duration of blood THC varies considerably across individuals and this is partly related to an individual's past exposure to cannabis. For example, individuals who used cannabis occasionally had THC detectible in their blood for 12 minutes to 44 hours after inhalation, whereas THC was detectible among individuals who frequently used cannabis for more than 72 hours after use (Newmeyer et al., 2016). THC is lipophilic (combines with or dissolves in lipids or fats) and can be stored in fat tissue (Huestis, 2007). This means that regular and heavy cannabis use can result in detectible levels of THC and its metabolites as much as 30 days after an individual has abstained (Bergamaschi et al., 2013). The time course of blood CBD levels following inhalation of cannabis smoke appears to parallel that of THC (Millar, Stone, Yates, & O'Sullivan, 2018).

Self-reported drug effects typically emerge within 10 minutes of inhalation, peak within the first hour and return to baseline in about three to four hours (Spindle et al., 2018; 2019). Importantly, while THC concentrations of five ng/ml are related to noticeable intoxication or impairment, levels of THC or metabolites do not consistently predict cognitive and behavioural outcomes (Spindle et al., 2018; 2019). Moreover, self-reported drug effects as well as cognitive and psychomotor impairment often persist for several hours after systemic THC concentrations returned to basal levels (Spindle et al., 2018; 2019). These findings have important health and safety implications in the workplace and with respect to impaired driving.

Blood THC concentrations, levels of intoxication and impairment are to some extent proportional to the dose of THC inhaled (Newmeyer et al., 2016; Spindle et al., 2019). Bioavailability[5] of THC following inhalation of dried cannabis is about 25% to 30%, which is greater than that of ingested cannabis (Ashton, 2001; Grotenhermen, 2003). There is, however, considerable variation across individuals, which have been noted to range from 2% to 56% (Huestis, 2007). Individual differences in smoking behaviours, including depth of inhalation, puff duration and length of breath holding, partly influence the bioavailability of THC (Grotenhermen, 2003; Huestis, 2007). Sex differences, including differences in body mass, can also influence the pharmacokinetics of THC. In a recent study, it was shown that females exhibited higher levels of blood THC and metabolites following equivalent doses of inhaled cannabis relative to their male counterparts (Spindle et al., 2019). Similar to these findings, it was recently shown that females experienced the same acute effects of smoked cannabis as males at a lower observed dose (Matheson et al., 2019). These findings highlight the need for more research on sex differences in the pharmacology of THC, especially when it is consumed by routes in which titrating to the desired effect is more difficult (e.g., cannabis edibles) (Matheson et al., 2019). The average bioavailability of inhaled CBD, which has been reported to be 31%, is similar to that of THC (Millar et al., 2018).

Vaping dried cannabis has been shown to have a comparable pharmacokinetic profile to that of smoking dried cannabis (Newmeyer et al., 2016; Newmeyer, Swortwood, Abulseoud, & Huestis, 2017). A recent study, however, reported greater blood concentrations of THC as well as greater subjective drug effects following vaping relative to an equal dose of smoked cannabis (Spindle et al., 2018). Indeed, during the smoking of dried cannabis, a significant amount of THC is lost to combustion and to side stream smoke (Grotenhermen, 2003), whereas these are minimized through the use of a vaporizer (Spindle et al., 2019). For these reasons, vaping might be a more effective and efficient method of cannabinoid delivery to the lungs and, ultimately, the bloodstream and the brain. Due to the greater efficacy of vaping, a lower THC product can be used to obtain a similar effect to that of comparatively higher THC dried cannabis.

As mentioned, there have not been any studies of the pharmacokinetics and pharmacodynamics of vaporized cannabis extracts. However, findings about the vaping of dried cannabis might be relevant to cannabis extracts and concentrates, given that many of these products

[5] Bioavailability in this context refers to the percentage of THC in the original cannabis product that ultimately makes it into blood circulation. The bioavailability of THC does not represent how much THC makes it to the brain. The percentage of THC that reaches the brain can be much lower (< 1%) (McGilveray, 2005).

are consumed through vaping methods (e.g., dabbing). In this respect, vaping and dabbing of cannabis extracts might produce greater psychoactive effects relative to an equivalent THC dose of smoked dried cannabis.

Ingestion

The absorption of THC and CBD after ingesting a cannabis product such as a capsule is considerably slower and less predictable than that of inhaled cannabis. The unpredictability is because ingested cannabis, including the cannabinoids present, are degraded by the acid in the stomach and in the gut, and they undergo extensive first-pass metabolism by the liver (Grotenhermen, 2003; Huestis, 2007). Blood plasma THC concentrations peak about one to three hours after ingestion, although for some individuals the peak can occur four to six hours after consumption (Newmeyer et al., 2016; Vandrey et al., 2017), and some individuals might display more than one blood plasma peak (Huestis, 2007). The bioavailability is much lower (~6%) following ingestion and is more variable across individuals (4%–20%) relative to inhalation (Ashton, 2001; Grotenhermen, 2003; Huestis, 2007). However, while bioavailability of THC is low, a greater amount of THC is converted to the 11 OH THC metabolite when ingested (Newmeyer et al., 2016).

In line with the time course of blood cannabinoids, the onset of psychoactive effects has been shown to occur 30 to 60 minutes after ingestion, to peak at one and a half to three hours, and to last six to eight hours (Vandrey et al., 2017), although the effects can last longer for some individuals. When an edible cannabis product such as a brownie is ingested, blood levels of THC, 11-OH-THC and THCCOOH were shown to be moderately-to-highly correlated with the intensity of intoxication (i.e., subjective drug effects) and, to a lesser extent, cognitive impairment (Vandrey et al., 2017). It should, however, be underscored that blood levels of THC and other cannabinoids are significantly lower following ingestion relative to inhalation, and blood concentrations of three ng/ml can be associated with significant intoxication and impairment. Thus, absolute values of blood plasma THC, 11-OH-THC and THCCOOH following ingestion of a cannabis product might not be strongly predictive of the magnitude of intoxication and impairment, especially among individuals who are new to cannabis (Vandrey et al., 2017).

Sublingual and Buccal Administration

Sublingual administration is when a drug is applied and held under the tongue, whereas buccal administration is when a drug is applied inside the cheek. The pharmacokinetics and pharmacodynamics of these routes of administration of cannabis products have not been extensively studied. Since sublingual and buccal administration bypass the gut and first-pass metabolism by the liver, they are believed to be more efficient drug delivery methods than ingestion. Based on this reasoning, tinctures, which are administered sublingually, are thought to produce a quicker onset of psychoactive or therapeutic effects relative to an ingested cannabis product.

The available evidence is mixed and more complex. In an earlier study, the presence of THC, 11 OH THC and CBD were detectible in blood plasma within 30 minutes, regardless of method of administration. However, peak concentrations of THC and 11-OH-THC were highest following ingestion of a 10 mg THC and 10 mg CBD dose relative to an identical dose that was administered sublingually or buccally. Additionally, peak THC concentrations were reached the fastest following the ingestion method (63 minutes), followed by sublingual (98 minutes), then buccal (~170 minutes) administration (Guy & Robson, 2004b). A more recent study did not find significant differences in peak concentrations and in time to peak concentration, which occurred two to four hours after administration, following an oral dose of synthetic THC and a similar dose of Sativex®.[6] However, slightly greater bioavailability was noted after Sativex administration, whereas higher concentrations of 11-OH-THC were detected after ingestion of oral THC capsules (Karschner et al., 2011).

Studies examining the pharmacokinetics of sublingual and buccal administration commonly found a considerable degree of variability across individuals (Guy & Robson, 2004a, 2004b; Karschner et al., 2011). The variability is partly related to individuals swallowing some of the cannabis product. It has not been possible to distinguish between blood plasma cannabinoids attributable to sublingual or buccal absorption and those absorbed through ingestion (Karschner et al., 2011). Further, previous cannabis exposure seems also to play a role in this variability, where individuals who use cannabis more frequently display a more rapid increase in blood THC following dose administration, an effect suggested to be related to the saturation of fat stores with THC (Karschner et al., 2011).

[6] Sativex is a cannabis extract that is made up an almost 1:1 ratio of THC to CBD and is administered as sublingual or buccal spray. Sativex has been approved in Canada as an adjunctive treatment for symptom relief of spasticity in adult individuals with multiple sclerosis (Bayer, 2019).

The pharmacodynamics, including the onset, duration and magnitude of psychoactive effects, have not been well characterized following sublingual and buccal administration of a cannabis extract. For individuals who reported intoxication following the use of Sativex, they generally did so between 30 and 150 minutes after dose administration, but there was large variability among individuals (Guy & Robson, 2004a, 2004b). More research using larger sample sizes is needed to determine how different formulations (e.g., alcohol- versus oil-based) and cannabinoid profiles (e.g., THC:CBD ratios) influence the pharmacological properties of cannabis extracts when taken sublingually and buccally.

Topical and Transdermal Application

Since cannabinoids are highly hydrophobic — that is, they repel water — it is difficult to transport these molecules across the aqueous layer of the skin (Huestis, 2007). This fact is partly why cannabis topicals are thought to have no effect on the central nervous system and not be able to cause intoxication and impairment. However, this supposition has not been extensively tested in humans and over the range of possible cannabis topical formulations. Indeed, it appears that certain cannabinoids are more skin-permeable than others (e.g., Δ8-tetrahydrocannabinol), and that the use of transdermal patches with "permeation enhancers" can facilitate absorption through the skin (Bruni et al., 2018). Preclinical studies have shown that topical cannabinoid application, with and without enhancers, can result in notable blood concentrations of cannabinoids that can persist for long periods of time (e.g., more than 48 hours) (Health Canada, 2018). Once again, however, there have been no clinical studies examining the presence of systemic cannabinoid levels and the potential for psychoactive effects following the use of topical and transdermal cannabis products.

Conclusions and Implications

The recent legalization of edible cannabis products, cannabis extracts and cannabis topicals introduces Canadians to a wide array of cannabis products. As emphasized throughout this report, these new classes of cannabis products carry with them health and safety risks that are not part of using dried cannabis, and the health impacts associated with long-term use of these products are not known. The new products and methods of administration can facilitate cannabis use in locations that require discretion, and the increased availability of vaporizers and edible cannabis products could increase the risk of cannabis-related problems in settings such as the classroom or the highway. Public education, prompt dissemination of novel research findings and careful monitoring of policies around these products are central to mitigating the harms. CCSA has developed a number of resources that can be found at ccsa.ca/research-cannabis under the **New Cannabis Products** tab, including a two-page primer on the new cannabis products. For information on cannabis policy and regulations across provinces and territories, visit ccsa.ca/policy-and-regulations-cannabis.

The term cannabis extracts describes a vast number of products that differ considerably in their appearance, taste, smell and, most importantly, their THC:CBD ratio. While we do not understand the full scope of the health effects of cannabis extracts, it is reasonable to suspect that the risks are proportional to the concentrations of THC in a product.[7] Cannabis concentrates carry with them a higher risk of over-intoxication than dried cannabis and less potent cannabis products. Regular use of concentrates has been associated with cannabis dependence and mental health disorders, and the risk of developing a psychotic disorder seems to be related to levels of THC. While edible cannabis has received the most media attention around the legalization of new classes of cannabis, it is the high-potency concentrates that arguably carry the most risk of harm. Public education on how to read and understand package labelling should be a priority as these products come on the market. At the same time, research on the pharmacokinetics and pharmacodynamics of the range of cannabis extracts such as shatter and the new methods of use such as dabbing is needed to inform public education efforts. CCSA has developed *7 Things You Need to Know about Cannabis Extracts*, a list of tips to lower the risks associated with cannabis extracts and concentrates.

The main concern associated with edible cannabis products is over-consumption causing over-intoxication, especially among those new to cannabis. In most cases, this happens when someone is unaware that the onset of psychoactive effects is delayed up to four hours after ingesting cannabis. The delay can lead the individual to consume more cannabis and eventually become over-intoxicated. Even being aware of the delay in onset and the longer lasting effects, it can be difficult for an individual new to edible cannabis to determine what dose of THC to start with. The legal THC limit for a unit of edible cannabis product is 10 mg. For some, this amount of THC might produce a mild to moderate high, whereas for others 10 mg of THC could cause severe intoxication and impairment. While variability in the psychoactive effects and blood cannabinoid levels that result from ingesting edible cannabis products has often been reported, the causes of this variability are not well understood and research into them is ongoing. In the meantime, people are recommended to "**start low and go slow**," consuming no more than 2.5 mg of THC at one time

[7] Different cannabis extracts and the ways in which they are used might carry with them additional and unique risks. Dabbing, for example, involves the use of a torch that increases the risk of burns and fires.

in a food or drink product. For CCSA resources on edible cannabis, see *Edible Cannabis: Always Read the Label*, *7 Things You Need to Know about Edible Cannabis* and *Cannabis: Inhaling vs Ingesting*.

There is a limited amount of scientific evidence on cannabis topicals. There have not been any studies looking at the pharmacokinetics and pharmacodynamics on topical cannabis products in humans or their impact on health following long-term use. Cannabis topicals do not seem to produce intoxicating or impairing effects, partly because cannabinoids do not penetrate the skin well and so do not reach the bloodstream. This feature of topicals has not been tested across the range of possible topical formulations and methods of delivery (e.g., transdermal patches). Preclinical studies show that topical application of cannabinoids resulted in measureable blood concentrations that were present for long periods (Paudel, Hammell, Agu, Valiveti, & Stinchcomb, 2010; Valiveti, Hammell, Earles, & Stinchcomb, 2004). These findings from animal research might have implications for driving and in workplaces that conduct drug testing. Although cannabis topicals are being marketed for several medical purposes (e.g., arthritis and skin diseases), their effectiveness has not been well established.

The focus of this report has been on the potential harms or health impacts of the new classes of cannabis. This focus reflects the available but limited evidence on edible cannabis products, cannabis extracts and cannabis topicals. That this report has not touched on the medical or therapeutic role of the new classes of cannabis products and methods of use is not to say that they have none. In fact, certain methods of cannabinoid delivery such as ingestion and transdermal application might provide therapeutic value, while minimizing the negative health outcomes associated with other methods of use such as the harms to the respiratory system from smoking cannabis. Ingested and topical cannabis products provide longer lasting therapeutic effects, whereas inhaled products provide more immediate ones. *Clearing the Smoke of Cannabis: Medical Use of Cannabis and Cannabinoids — An Update* offers a more comprehensive discussion on these topics. Research and monitoring of edible cannabis products, cannabis extracts and cannabis topicals as well as sustained public education about them should continue. These initiatives could mitigate the health and safety concerns associated with the use of these new classes of cannabis products.

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