Available online at www.sciencedirect.com

ScienceDirect

Current Opinion in Food Science

The evolving landscape of cannabis edibles

Alexia Blake and Istok Nahtigal

Cannabis has become a global market as increasingly more jurisdictions legalize medical or recreational consumption. Canada and the United States have arguably pioneered this movement, being the first of the G7 countries to actively replace black markets with highly regulated, legal markets. Under this framework, advancements in extraction technology, production scalability, and accessibility to a wide variety of product forms have all been realized. In the United States, edibles and beverages continue to win over market share from dried flower, which is the traditional form of cannabis consumed through smoking or vaporizing. However, ingestible products such as edibles and beverages are notorious for delivering inconsistent effects, having short shelf-lives, and possessing an undesirable lingering cannabis taste. These shortcomings are due in part to challenges with analytical testing and a limited working knowledge of basic food science principles. Thus, there is an opportunity and need to leverage the expertise and best practices of the food industry to overcome these challenges to improve the taste, stability, consistency, and dose homogeneity of cannabis ingestibles.

Address
MedReleaf, PO Box 3040, Markham, ON L3R 6G4, Canada

Corresponding author: Blake, Alexia (alexia.ie.blake@gmail.com)

Current Opinion in Food Science 2019, **28**:25–31

This review comes from a themed issue on **Innovations in food science**

Edited by **Alejandro G Marangoni**

For a complete overview see the Issue and the Editorial

Available online 4th April 2019

https://doi.org/10.1016/j.cofs.2019.03.009

Introduction

The emergence of the global cannabis market is often compared to the dot-com boom of the mid 1990s. Marked by rapid growth, speculation, and volatility, the cannabis industry is reaching new heights as more jurisdictions move to legalize medical and even recreational consumption. Canada and the US have arguably been at the forefront of this movement. Canada became the first of the G7 countries to federally legalize cannabis cultivation and sale in 2013 under the *Marijuana for Medical Purposes Regulations* (MMPR), and legalized recreational use in 2018 under *The Cannabis Act*. In the United States, cannabis is regulated at the state-level, resulting in a highly fragmented industry defined by state-specific laws. Washington and Colorado were the first states to vote for recreational legalization in 2012, and in addition to California in 2016, have since shaped the development of the American cannabis market.

A wide variety of methods exist for consuming cannabis for both medical and recreational purposes. Dried cannabis flower, also known as bud, have historically been most popular when consumed through smoking or vaporization, but are slowly losing market share to other value-added product forms such as high-potency extracts, vape cartridges, topicals, edibles, and beverages [1]. Each product form and the method of administration offer a unique set of advantages and disadvantages, allowing the consumer to tailor their experience to their individual needs, preference, and experience with cannabis. As the cannabis industry continues to migrate from a black market to a legal market, resulting in an increasing accessibility of new product forms such as edibles and beverages, it is essential that best practices from the food industry are adopted to ensure that product quality and consumer safety are achieved.

Defining the edibles landscape

In a medical context, a cannabis edible is a product containing cannabis that is ingested. Examples include oils, tinctures, and oil-filled capsules. In a recreational context, edibles more commonly refer to cannabis-infused food products, such as baked goods, chocolates, gummies, and hard candies. Cannabis beverages are also popular among recreational consumers, but remain less popular compared to edibles due to product quality issues, such as creaming or sedimentation, that are in essence hindered by a limited knowledge of emulsion science.

The use of extract in edibles

Generally speaking, cannabis edibles are made with cannabis extract. An extract is any solid or oil-like substance that concentrates the trichomes or the chemical compounds found within them. Trichomes are found on the plant epidermal layer as glandular surface outgrowth, and are known to contain a complex chemical secretion, including cannabinoids and terpenes. Cannabinoids are the primary active ingredients in cannabis, while terpenes contribute to the aromatic properties and taste.

Cannabinoids are the main active compounds in cannabis. Delta-9-tetrahydrocannabinol (THC) and cannabidiol (CBD) are two of the most prevalent cannabinoids

consumed for medical or recreational purposes. THC is psychoactive, and is often used to manage pain, anxiety, nausea, and insomnia [2–4]. CBD is non-psychoactive, and is often consumed for its anxiolytic, antiseizure, and anti-inflammatory properties [2,4–6]. Either the plant material before extraction, or the recovered extract, must be heat treated to decarboxylate the cannabinoids from their acidic precursors, THCa and CBDa, into the neutral forms that are considered therapeutically active.

Numerous extraction processes have been developed with the purpose of recovering and concentrating cannabis trichomes. Extraction methods can be classified as solvent-based or solvent-less. Yield, terpene retention for enhanced taste or aroma, and product purity in the absence of solvent contaminants are some factors that often dictate the selection of one extraction method over another. For instance, solvent-less methods are considered to be simpler and deemed natural, but they do not offer the same mass yields and concentration factors compared to a solvent approach.

In Canada, due to restrictive federal regulations, commercial production of extract is achieved through one of two ways: solvent extraction using ethanol, or supercritical fluid extraction using carbon dioxide (CO_2). In the United States, butane extractions are a more popular option due to their high yields. A review of various extraction processes is provided below.

Solvent-based extraction

Solvent extraction is by no means a new technology. Alcohols and liquid esters have been employed to extract compounds from plant matrices, the latter being one of the first processes to decaffeinate coffee. Further advancements in science and technology have enabled the industrialization of numerous solvents, including water, air, hydrocarbons, and supercritical fluids.

Hydrocarbon extractions

Butane extractions have a long history of use in the food and perfume industries, and have recently been repurposed and made famous (or infamous) for cannabis extractions due to their speed, selectivity for cannabinoids, and excellent terpene retention. Thus, butane extractions have gained widespread popularity in North America, starting in the US black market, for producing high potency extracts, such as shatter, waxes, crumbles, and oils. However, BHO has also garnered negative publicity due to the presence of toxic residues from fuel additives present in commercially available butane and numerous explosions caused by 'kitchen improvised' processes.

In butane extraction (or BHO extraction), fuel-grade butane is sprayed through a column containing cannabis. A filter prevents plant material from passing into a secondary collection column that captures the cannabinoid-rich butane mixture. The mixture is placed in a vacuum oven to purge the solvent residue, leaving behind a golden coloured oil that typically contains 80% THC [7]. BHO is slowly regaining its good name as safer, closed-loop properly engineered extraction units become available.

Liquid hetero-hydrocarbons

Hetero-hydrocarbon solvents are hydrocarbons that contain chemical elements other than carbon and hydrogen. Contrary to pure hydrocarbons which have a strong aversion to water, the oxygenates show hydrophilicity, meaning these solvents can extract both hydrophobic and hydrophilic compounds, thereby producing extracts that are more chemically diverse. For cannabis extraction, downstream refinement is required to remove additional compounds and render refined resins.

While the solvents falling in this classification are vast, ethanol is by far the most popular in the cannabis industry owing to its familiarity, cost, and manageability. Ethanol extraction involves soaking dried cannabis flower in the solvent. The solvent dissolves the trichomes from the plant material and other components that have an affinity for the solvent. The plant material is removed by filtration or centrifugation to yield a clarified concentrated liquid. The solvent is removed using evaporation, reduced pressure distillation or molecular sieves. The resulting extract is typically dark in color, sap-like in consistency, and bitter in taste. Further processing to remove waxes and chlorophyll is almost always required to improve extract quality.

Inert gas extraction

Carbon dioxide is regarded as one of the safest, non-toxic, reusable, and environmentally friendly solvent extraction methods. Supercritical CO_2 has been used in many industries including decaffeination of coffee and tea, extracts of vanilla, fruits, omega-3 oils, and perfumes. Extraction with CO_2 can be done in two states: liquid or supercritical. The latter affords more flexibility to tune the selectivity of the solvent. A typical extraction process involves heating the liquid CO_2 to raise its pressure into the supercritical regime before passing through the plant material to extract the cannabinoids and terpenes. The saturated supercritical CO_2 enters a separator which lowers the pressure, thereby lowering the density of the fluid to cause precipitation of solubilized compounds.

If depressurized in a controlled manner, it is possible to collect fractions with a unique ratio of compounds. The collected fractions do not require any special post-extraction solvent removal techniques. Upon precipitation, the low-density CO_2 gas is condensed and recycled back into the system, and may be cycled through the plant material several times in a closed-loop extractor. While CO_2 extraction does require more advanced equipment,

several fabricators have designed small scale extraction units which have become very popular in the industry due to their affordability (Table 1).

Extract quality and composition

Extract quality and composition is highly dependent on the selected extraction process. Different solvents have varying affinities for the many compounds present in cannabis trichomes. For instance, dry-sieve or water extraction will recover the entire trichome. Hydrocarbon extraction will avoid water and pigments such as chlorophyll, while ethanol under certain conditions will extract pigments and aromatics like flavonoids. Carbon dioxide can extract a wide range of compounds depending on the specific conditions. These differences should be taken into account when considering the end product (e.g. terpene-rich or terpene-devoid extract) and to minimize the need for downstream refinement.

Terpenes and waxes are two of the most prominent compounds that define extract quality and composition. Terpenes and terpenoids are essential oil components that form the largest group of plant chemicals [8,9]. These compounds are responsible for the characteristic smell and flavor of cannabis, which may contain over 200 unique terpenoids in the plant [10–13]. The terpene profile is unique to each cannabis cultivar and a function of cultivation conditions, and generally comprises between 0.5–2% w/w of the trichomes. Monoterpenes are the predominate group and due to their volatility are lost at a rate of about 5% before processing and storage. Consequently, a higher relative proportion of the sesquiterpenoids (especially caryophyllene) is characteristic to extracts [11,14]. In general, a higher terpene concentration will render a less viscous and more aromatic oil, which will impart a stronger taste to an ingestible product.

Cannabis wax can be characterized by two specific groups of lipid substances, insoluble cutins, and epicuticular waxes (EPW) [15]. Depending on the extraction method employed, varying amounts of these compounds end up in the extract. Waxes increase extract viscosity and cloudiness, and are thus regarded as impurities and tend to be removed to enhance product quality.

Downstream refinement of extracts

The correct choice of the primary extraction process can significantly simplify refinement. Winterization, short-path distillation, and wiped film molecular distillation (WFMD) are commonly applied refinement processes. In essence, dewaxing is achieved through winterization using ethanol. Short path distillation is commonly applied to separate temperature and oxidation sensitive, high boiling point compounds from each other, such as the cannabinoids from the sesquiterpenes, triterpenoids, and pigments. The resulting cannabinoids fractions possess

Table 1

Summary of solvent-less extraction methods

Extraction method	Process description	Final product	Process advantages	Process limitations
Dry-sieve extraction	Dried cannabis is beaten against a mesh screen causing the trichomes to fall off Alternatively, dry ice can used to prevent trichome caking	Powdered-like product known as Kief with a potency of 35–50% THC Kief can be mixed with dried flower or be further pressed into hashish	Simple process	Time consuming Difficult to scale
Water extraction	Cannabis in sieve-like bags is submerged in freezing cold water Cold temperatures and stirring causes the trichomes to fall off Trichomes are filtered through a series of collection screens before settling Settled trichomes are collected and dried	A resin known as water hash or bubble hash, often reaching 35–50% THC depending on the potency of starting material	Simple process	Difficult to scale Limited concentration factor
Rosin press extraction	Wet or dried cannabis material, hash or kief, is placed between heat-resistant material, such as parchment paper or thin mylar Pressure is applied to the cannabis placed between two heated pressure plates The heat melts the trichomes, while the pressure squeezes the liquified trichome resin between the plates for collection	A sap-like extract with a high potency ranging between 40–70% THC	Simple process High potency compared to other solvent-less methods Considered high-quality and artisanal	Low mass extraction yields given that waxes and trichome cell walls are left behind in the press cake Difficult to scale and maintain consistency due to artisanal nature

high potency, and are referred to as 'distillates'. Wiped Film Molecular Distillation (WFMD) is similar to short path distillation (SPD), but allowing for greater refinement levels.

Edibles as an alternative method of cannabis consumption

In Canada, the federal government has proposed regulations for introducing cannabis edibles and beverages to the legal market. This legislation is being finalized, with the intention of legalizing these new product forms by October 2019. In the United States, market data have revealed that cannabis edibles have rapidly gained popularity with both medical and recreational consumers. While smoking may be the traditional method of consuming cannabis, edible sales in California and Colorado state reached a cumulative $625M USD in 2018, while beverage sales reached $35 million within the same jurisdictions (Table 2).

There are several reasons why consumer preferences are changing. First, consumers perceive edibles to be a safer and healthier means of consuming cannabis compared to smoking or vaporization. Similarly, some physicians prescribing medical cannabis to Canadian patients have advocated that patients consider capsules and oils as an alternative to smoking.

Secondly, edibles are a convenient and discrete method of consuming cannabis, and unlike smoking, there is no preparation required to consume the product. Their portability makes it easy for consumers to use these products outside their homes, which may be appealing to individuals looking to consume at social gatherings or outdoor events. Finally, ingesting edibles containing THC offers a noticeably different psychoactive experience compared to inhalation that some individuals may prefer.

The pharmacokinetics of edibles

The psychoactive effects of THC are felt within minutes after smoking, with peak effects reportedly occurring within 10–15 min [3,16,17]. In comparison, it may take 30–90 min after consuming an edible for the effects of THC to be experienced. Peak effects occur over a wide range of 2–6 hours, and can be delayed if the edible is taken after eating a meal. The duration of effects after smoking are reportedly 2 hour, while the psychoactive effects experienced after consuming a THC edible can last up to 8 hours depending on factors such food and dose.

This difference in onset and duration is primarily due to differences in drug metabolism, which are known to be dependent on the route of administration. With smoking, cannabinoids such as THC enter systemic circulation via lung alveoli [18]. With oral administration, as is the case with edibles, cannabinoids must travel from the stomach to the liver through the portal vein before reaching systemic circulation.

During a process known as first-pass metabolism, THC is metabolized by CYP450 enzymes in the liver into various metabolites, most noticeably 11-OH-THC [3,19]. Interestingly, this predominant metabolite also possesses its own psychoactive effects, which are thought to be more potent than THC [2,18, 20]. Following metabolism, both THC and 11-OH-THC enter systemic circulation before crossing the blood–brain barrier. Pharmacokinetic studies have revealed that almost 50% THC is metabolised into 11-OH-THC following oral administration [2,3,16]. In comparison, plasma levels of 11-OH-THC are much lower following smoking as inhalation avoids first-pass metabolism (Figure 1).

The time required for first-pass effects and metabolism of THC into 11-OH-THC are two factors that contribute to the delayed onset and low oral bioavailability of THC. More generally but outside the scope of this discussion, the bioavailability of THC is also limited by its poor water solubility, as outlined by the FDA's drug classification scheme known as the Biopharmaceutics Classification System (BCS) [22]. Similar trends are observed for other cannabinoids, such as CBD. Pharmacokinetic studies have reported that the oral bioavailability of THC and CBD has been reported as 6–10% and 4–10%, respectively [2,3,16].

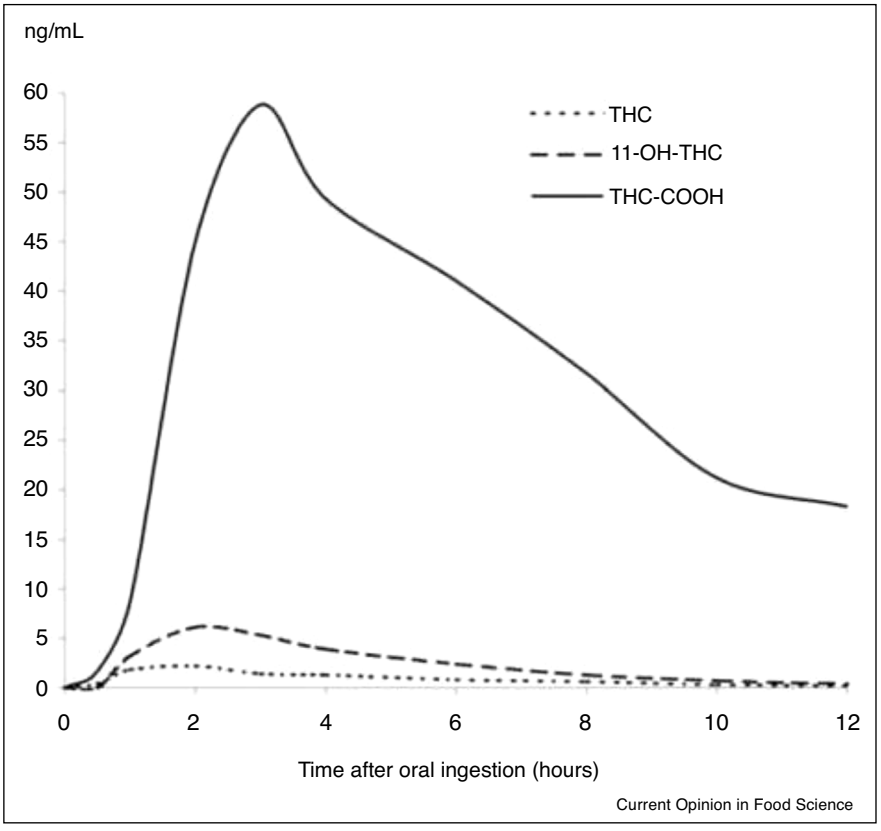
Delayed onset and prolonged drug action have desirable applications within a medical setting. For example, patients with chronic pain, epilepsy, or anxiety may benefit from a product that provides sustained relief for 8 hours. In a recreational setting, however, the variable onset and extensive duration of effects can be overwhelming to consumers. As thus, edibles have developed

Table 2

2018 market data for California and Colorado states provided by BDS Analytics. Ingestibles include candy, chocolates, infused foods, pills, and tinctures. Financial figures are reported in USD. Accessed 12 February 2019

Product category	Sales in 2018	Units sold	Average retail price/unit
Dried flower	$1.6 billion	250.87 million grams	$6.38
Ingestible	$625.99 million	31.96 million	$19.59
Beverages	$35.79 million	2 million	$14.90

Figure 1



Mean plasma concentrations (ng/L) of Δ9-THC (THC), 11-hydroxy-THC (11-OH-THC) and 11-nor-9-carboxy-THC (THC-COOH) of six patients after ingestion of a single oral dose of 15 mg THC [21].

a notorious reputation of being difficult to dose properly and delivering an inconsistent experience. Paranoia and anxiety are two of the most common adverse reactions experienced by both medical patients and recreational consumers after ingesting THC. However, tolerance to the effects of cannabis and its side effects have been reported to develop with continued use [2].

Compliance, quality, and safety concerns

As is the case with food, cannabis product quality is an issue of public health and safety. Despite best efforts and existing regulations in both the United States and Canada, challenges with analytical testing, quality-controlled manufacturing, and a lack of basic food science principles present obstacles to the advancement of this industry and endanger both product quality and consumer safety.

Testing and reporting requirements

In the United States, testing and reporting requirements are mandated at the state level, and often differ between states. Moreover, product cannot be moved across state borders, meaning that product cultivated in a state can be commercially sold only in that state. The result of this segregation is that each state operates as its own entity with its own rules and regulations for testing, packaging, and labelling.

In Canada, licensed cannabis producers are required to comply with stringent federal requirements for the production, storage, packaging, and testing of all medical and recreational products. For example, licensed producers are required to test each batch of product at an accredited laboratory before releasing the product for sale. Certificates of analysis and retention samples of each batch must be inventoried for two years. Release testing must cover potency testing (THC, CBD, and their acidic precursors), microbial contamination, heavy metals, aflatoxins, pesticides, moisture content, residual solvent in the case of extracts, and disintegration time for capsules. Specifications for methodology, analytical results or reporting nomenclature are provided for each test.

Batch consistency and dose homogeneity

It is not uncommon for recreational THC edibles to contain 10, 20, or even 100 mg. In most cases, the

product is divided by the consumer into smaller servings based on the dose they desire to ingest. Therefore, inhomogeneous distribution would mean that each piece contains a different and unknown dose, thereby introducing uncertainty and variability into the consumer's experience. As mentioned, THC edibles and beverages are notorious amongst consumers for delivering inconsistent effects between doses. As mentioned, there is inherently great variability in both the onset and duration of effects, as well as the intensity of psychoactive effects for edibles. Inhomogeneous distribution of THC in the product may further contribute to this inconsistency.

Dose homogeneity and batch consistency can be addressed by implementing basic food science principles pertaining to formulation development, and by introducing quality control checks into the manufacturing process. With respect to the formulation, challenges often arise when trying to integrate hydrophobic cannabis extract into aqueous-based formulations, such as beverages or candies. The result is an inhomogeneous product with limited shelf-stability that is prone to phase-separation, and further characterized by a poor sensory profile marred by the botanical taste of terpenes. Proper emulsification could address these issues, and also regulate the onset time of THC.

With respect to manufacturing, quality control checks and chemical analysis are helpful for achieving dose homogeneity and consistency. These checks should be applied to starting material, such as cannabis extract, in order to identify the starting concentration and mass of active material. Analysis should also be conducted on in-process mixes and on the final product to ensure homogeneity, consistency, and that target potency have been achieved. Unfortunately, conducting such analysis using high pressure liquid chromatography (HPLC) or gas chromatography mass spectrometry (GCMS) may be outside the scope of knowledge of a small business, in which case outsourcing to a third-party lab is a remaining (albeit expensive) option.

Analytical testing

Another contributing factor to the variability associated with THC edibles is that the label claim may be inaccurate. Several studies have reported that many products being tested do not comply with their potency label claim [21,22]. Of even more concern is the observation that different labs, despite their accreditations, return different analytical results after testing the same product [23–26].

One reason for these discrepancies is that there is no harmonized compendial method for cannabinoid testing. Differences arise in sample preparation, which may involve a range of organic solvents. Furthermore, assaying is often conducted using liquid or gas chromatography. The development and implementation of standardized analytical procedures is a huge obstacle for the industry that must be addressed in order to promote safe cannabis consumption among both recreational and medical consumers. Not only must these methods be reproducible, but they must also have low limits of quantification so that they can be applied to different product matrices containing as low as 10 ppm THC, CBD, or the plethora of other cannabinoids that, while outside the scope of this discussion, are nevertheless gaining more attention, such as CBN, CBG, and THCV.

The future of edibles

The cannabis industry has made great stride in recent years, following the global movement to advance the medical, and in some cases the recreational use of cannabis in its various product forms. As a nascent industry, this progress can be further advanced by applying knowledge from other established disciplines, such as food or pharmaceuticals. Today's perception of cannabis edibles and beverages is that they deliver inconsistent effects. Erratic absorption yields a variable onset and unknown duration that make for a unique experience with each dose. Collaborating with the food industry could render the necessary advancements in analytical testing, formulation development, and manufacturing that are required to improve the quality of edibles and beverages as they pertain to taste, dose consistency, and dose homogeneity.

In addition to accessing formulation expertise, cannabis producers would further benefit from working with food manufacturers who are well versed in food safety and sanitation practices. Established practices for preventing cross-contaminating between CBD and THC products, scalable manufacturing, packaging processes, recall programs, and shelf-life studies are only a few examples of how the food industry could mentor the rapidly growing cannabis sector while advancing public safety.

Conflict of interest statement

Nothing declared.

References

1. **Flower, where have you gone?** *BDS Analytics*. 2019 . [Online]. Available: *https://bdsanalytics.com/flower-where-have-you-gone/* .

2. Health Canada: *Information for Health Care Professionals: Cannabis (Marihuana, Marijuana) and the Cannabinoids*. 2018.

3. Huestis MA: **Human cannabinoid pharmacokinetics**. *Chem Biodivers* 2007, **4**:1770-1804.

4. McPartland JM, Duncan M, Di Marzo V, Pertwee RG: **Are cannabidiol and Δ9-tetrahydrocannabivarin negative**

modulators of the endocannabinoid system? A systematic review. *Br J Pharmacol* 2015, **172**:737-753.

5. Grotenhermen F: **Clinical pharmacodynamics of cannabinoids**. *J Cannabis Ther* 2004, **4**.

6. Mechoulam R, Gallily R: **Cannabidiol: an overview of some pharmacological aspects**. *J Clin Pharmacol* 2016, **42**.

7. Black S: **Concentrated cannabis, Pt. 1: extraction 101**. *High Times*. 2017 . [Online]. Available *https://hightimes.com/grow/concentrated-cannabis-part-i-extractions-101/*.

8. Schmidt E: **Production of essential oils**. In *Handbook of Essential Oils: Science, Technology, and Applications.* Edited by Baser K, Buchbauer G. Boca Raton: CRC Press; 2010:83-120.

9. Langenheim J: **Higher plant terpenoids: a phytocentric overview of their ecological roles**. *J Chem Ecol* 1994, **20**:1223-1279.

10. Hendriks H, Malingré M, Batterman S, Bos R: **Mono- and sesquiterpene hydrocarbons of the essential oil of cannabis sativa**. *Phytochemistry* 1975, **14**:814-815.

11. Ross S, Elsohly M: **The volatile oil composition of fresh and air-dried buds of cannabis sativa**. *J Nat Prod* 1996, **59**:49-51.

12. Mediavilla V, Steinemann S: **Essential oil of *Cannabis Sativa* L. strains**. *J Int Hemp Assoc* 1997, **4**:82-84.

13. Rothschild M, Bergstrom G, Wangberg S-A: **Cannabis sativa: volatile compounds from pollen and entire male and female plants of two variants, Northern Lights and Hawaian Indica**. *Bot J Linn Soc* 2005, **147**:387-397.

14. Gershenzon J: **Metabolic costs of terpenoid accumulation in higher plants**. *J Chem Ecol* 1994, **20**:1281-1328.

15. Zeisler-Diehl V, Müller Y, Schreiber L: **Epicuticular wax on leaf cuticles does not establish the transpiration barrier, which is essentially formed by intracuticular wax**. *J Plant Physiol* 2018, **227**:66-74.

16. Grotenhermen F: **Clinical pharmacokinetics of cannabinoids**. *J Cannabis Ther* 2003, **3**:3-51.

17. Abramovici H: **Information for health care professionals: cannabis (marihuana, marijuana) and the cannabinoids - Health Canada**. *Ethics* 2013, **9**:152.

18. Karschner EL, Darwin WD, Goodwin RS, Wright S, Huestis MA: **Plasma Cannabinoid pharmacokinetics following controlled oral Δ9-tetrahydrocannabinol and oromucosal cannabis extract administration**. *Clin Chem* 2011, **57**:66-75.

19. Watanabe K, Yamaori S, Funahashi T, Kimura T, Yamamoto I: **Cytochrome P450 enzymes involved in the metabolism of tetrahydrocannabinols and cannabinol by human hepatic microsomes**. *Life Sci* 2007, **80**:1415-1419.

20. Orens A, Light M, Rowberry J, Matsen J, Lewandowski B: *Marijuana Equivalency in Portion and Dosage - An Assessment of Physical and Pharmacokinetic Relationships in Marijuana Production and Consumption in Colorado*. 2015.

21. Frytak S, Moertel C, Rubin J: **Metabolic studies of delta-9-tetrahydrocannabinol in cancer patients**. *Cancer Treat Rep* 1984, **68**:1427-1431.

22. Kalepu S, Manthina M, Padavala V: **Oral lipid-based drug delivery systems – an overview**. *Acta Pharm Sin B* 2013, **3**:361-372.

23. Baca R: **Tests show THC content in marijuana edibles is inconsistent**. *The Denver Post*. 2014.

24. Vandrey R, Raber JC, Raber ME: **Cannabinoid dose and label accuracy in edible medical cannabis products**. *JAMA* 2015, **313**:2491-2493.

25. Jikomes N, Zoorob M: **The cannabinoid content of legal cannabis in Washington State varies systematically across testing facilities and popular consumer products**. *Nat Sci Rep* 2018, **8**:4519-4538.

26. Hazekamp A, Gieringer D: *California Ring Test: How Accurate is Potency Testing of Cannabis*. O'Shaughnessy's; 2011:17-20.