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Optimization of Trimming Techniques for Enhancing Cannabinoid and Terpene Content in Medical Cannabis Inflorescences

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Keywords
Cannabis sativa L. · Trimming · Controlled atmosphere drying · Cannabinoids · Terpenes

Abstract
Introduction: *Cannabis sativa* L. inflorescences are widely used in the medicinal field as treatments for a variety of symptoms and illnesses due to their unique phytochemicals such as cannabinoids and terpenes. Common postharvest procedures for cannabis inflorescence include trimming, followed by drying, curing, and subsequent storage. The postharvest trimming step, particularly its timing (pre- or post-drying) and the extent of trimming, is not optimally refined in terms of its impact on the cannabinoid and terpene content. In this study, our objective was to identify the optimal trimming conditions for a commercially available medicinal cannabis hybrid chemovar, with the goal of maximizing its cannabinoid and terpene content. ***Methods:*** To achieve this, we investigated the effects of pre- versus post-drying trimming and evaluated the impact of mild versus aggressive trimming prior to drying on the cannabinoid and terpene profiles using liquid and gas chromatography. ***Results:*** Our results indicated that pre-drying mild trimming yielded the highest cannabinoid concentration, possibly due to optimal balance between stress signals and precursor influx from the sugar leaves to the inflorescence. On the other, post-drying trimming yielded the highest terpene content. ***Conclusion:*** Identifying the optimal trimming conditions that maximize both cannabinoid and terpene levels in cannabis is challenging. Therefore, growers face a decision in their trimming practices: to prioritize either enhanced cannabinoid content or increased aromatic terpene concentrations, as optimizing for both simultaneously appears to be difficult.

Introduction

Cannabis sativa L. is an annual, flowering herb in the family Cannabaceae. Inflorescences of medicinal cannabis are used worldwide for their medicinal properties for various medical conditions such as cancer, pain management, and rheumatic diseases [1–3]. The pharmacological activity of cannabis is mainly attributed to the phytochemicals cannabinoids and terpenes [1–3].

Cannabinoids, synthesized and sequestered within the glandular trichomes of the cannabis plant, play a pivotal role in modulating a range of physiological processes in

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humans, including appetite regulation and pain perception [4]. Among the diverse types of cannabinoids, the most prominent are the pharmacologically active neutral cannabinoids (-)-Δ9-trans-tetrahydrocannabinol (THC), cannabidiol (CBD), and cannabigerol (CBG) [5, 6]. THC, the primary psychoactive constituent of cannabis, is chiefly responsible for the "high" associated with cannabis consumption [7]. Conversely, CBD and CBG, devoid of psychoactive properties, are noted for their anti-inflammatory, analgesic, antioxidative, and anxiolytic effects [8]. The mono-carboxylated (acidic) forms of these cannabinoids, (-)-Δ9-trans-tetrahydrocannabinolic acid (THCA), cannabidiolic acid (CBDA), and cannabigerolic acid (CBGA), convert through heat-induced decarboxylation to their corresponding neutral cannabinoids [9]. Constituting over 95% of the cannabinoid content in cannabis inflorescences, the stability of these acidic cannabinoids is significantly influenced by external environmental factors, such as light intensity and temperature [10, 11].

Terpenes, the aromatic compounds in medicinal cannabis, are essential for enhancing its therapeutic efficacy and patient experience, aiding in treatment adherence and compliance [12–14]. These compounds contribute to the "entourage effect," a synergistic interaction with cannabinoids like THC and CBD, amplifying cannabis' analgesic, anti-inflammatory, and anxiolytic properties [13–15]. Specific terpenes, such as β-myrcene, D-limonene, and linalool, offer additional medicinal benefits, including anti-inflammatory and mood-enhancing effects [13]. Maintaining consistent terpene profiles through optimal postharvest processes is crucial for patient satisfaction and therapeutic consistency. The plant genotype and the growth conditions are known to highly affect the cannabinoid and terpene composition as well as the inflorescence age [16–18]. In addition, the cannabinoid and terpene profiles are significantly influenced by postharvest processes [19]. These processes commence with trimming, followed by a drying period of 2–3 weeks, during which temperature and humidity are critical factors, resulting in a substantial weight reduction of up to 75–80% [19–22]. Subsequent curing involves loosely sealing the inflorescences in containers with periodic ventilation to eliminate residual moisture prior to final packaging [23]. The initial postharvest trimming stage of cannabis inflorescence is currently underresearched, with a notable absence of peer-reviewed scientific literature examining the impact of different trimming techniques on cannabinoid and terpene profiles. Trimming refers to a procedure where extraneous plant material, such as leaves and stems, is removed from the cannabis flowers, primarily to enhance the concentration of cannabinoids and terpenes by leaving only the desired inflorescence parts [19]. This process is performed manually or mechanically and is crucial for improving the aesthetic appeal, potency, and overall quality of the final product [19]. Two primary methods of trimming can be distinguished in cannabis postharvest processing: "wet trimming" and "dry trimming" [19]. In wet trimming, the small leaves of the inflorescence are removed prior to the drying stage, while in dry trimming, these leaves are removed post-drying [23]. The impact of these two methods on cannabinoid and terpene composition has not been scientifically studied yet. The entirety of the postharvest process, including trimming, is often guided by anecdotal beliefs rather than scientific evidence [19, 23]. A prevalent industry practice is trimming the inflorescence before drying for maximum preservation of the trichomes, as fresh trichomes are less breakable than dried ones [12, 20]. The subsequent drying step is usually done by either placing the trimmed inflorescence on breathable trays in a well-ventilated area or by hanging the entire plant upside down in shaded areas, from which larger leaves and stems were removed prior to hanging [20]. The degree of trimming, specifically the extent of leaf and stem removal from the harvested inflorescence, is another aspect that remains unexplored in terms of its impact on cannabinoid and terpene composition.

The lack of knowledge regarding the influence of timing and thoroughness of trimming on the cannabinoid and terpene profiles presents a significant challenge in optimizing the postharvest process for cannabis inflorescence. Addressing this gap, the present study investigated the impact of pre- versus post-drying trimming and compared the effects of mild versus aggressive trimming techniques before drying on the cannabinoid and terpene content in the commercially available hybrid chemovar Gen12. The study employed optimal drying conditions identified in our recent research, specifically drying in controlled atmosphere chambers under atmospheric conditions.

Materials and Methods

Chemicals

Ethanol, acetonitrile, formic acid, and anhydrous ammonium formate were obtained from Sigma-Aldrich (HPLC grade, Saint Louis, MO, USA). The Milli-Q Plus system provided ultrapure water (Millipore Corp., Billerica, MA, USA). The following cannabinoid and terpene analytical standards were obtained from RESTEK (RESTEK, Bellefonte, PA, USA): cannabidivarinic acid,

Fig. 1. Photos taken of each trimming treatment before drying. **a** Mild wet trimming (MWT). **b** Aggressive wet trimming (AWT). **c** Wet inflorescence before dry trimming (DT). **d** Representative picture of a dry inflorescence that underwent any of the trimming treatments (final form of all treatments).

cannabigerovarinic acid, CBDA, CBGA, CBG, CBD, (-)-Δ9-trans-tetrahydrocannabivarin, (-)-Δ9-trans-tetrahydrocannabivarinic acid, cannabinol, cannabinolic acid, cannabichromevarinic acid, THC, (-)-Δ8-trans-tetrahydrocannabinol, cannabicyclol, cannabicyclolic acid, cannabichromene, THCA, and cannabichromenic acid. Each of those standards was obtained at a stock concentration of 1,000 μg/mL except cannabicyclolic acid which was obtained at a stock concentration of 500 μg/mL. α-Pinene, camphene, β-pinene, β-myrcene, δ-3-carene, α-terpinene, p-cymene, D-limonene, ocimene, γ-terpinene, terpinolene, linalool, (−)-isopulegol, geraniol, β-caryophyllene, α-humulene, nerolidol, (−)-guaiol, and (−)-α-bisabolol were obtained as a standard mix at a stock concentration of 2,500 μg/mL each.

Plant Material

Fresh medicinal *Cannabis sativa* L. inflorescences from the commercially available hybrid chemovar – "Gen12" – were provided by the Bar-Lev farm in June 2023 (Bar-Lev Agricultural Crops, Kfar Hess, Israel, 32°15′21.2″N 34°57′01.0″E). The samples were analyzed for their cannabinoid and terpene content at the Agricultural Research Organization, the Department of Food Science, Israel. Only the inflorescence from the top of the main stem was sampled.

Trimming Process

On harvest day (day 0), freshly harvested cannabis inflorescences were divided into three distinct treatment groups: mild wet trimming (MWT), aggressive wet trimming (AWT), and dry trimming (DT), with each group comprising 30 inflorescences of the hybrid cannabis chemovar Gen12. In the MWT group, only the stems were completely removed and the small sugar leaves near the inflorescence were trimmed halfway (only the top half of each sugar leaf was removed) prior to drying (Fig. 1a). For the AWT group, both the stems and sugar leaves were fully manually removed before drying (Fig. 1b). Additionally, 30 inflorescences were analyzed on the day of harvest (day 0) without prior drying to establish baseline levels of cannabinoids and terpenes. This initial analysis allows for subsequent comparisons of cannabinoid and terpene levels following various treatments. For this purpose, all sugar leaves and stems were removed, ensuring that the analyzed levels of cannabinoids and terpenes reflected only the composition of the inflorescences.

The DT group underwent trimming after a 6-day drying period, employing the AWT method (Fig. 1c). To ensure uniform trimming at the conclusion of the drying period across all treatments, the inflorescences in the MWT group were further subjected to aggressive trimming after drying completion to completely remove any remaining sugar leaves. At the conclusion of the drying process and prior to extraction for chemical analysis, all inflorescences subjected to any of the trimming treatments exhibited uniform trimming and, consequently, presented a consistent appearance (Fig. 1d).

Drying Process

The inflorescence was weighted and placed in breathable trays inside controlled-atmosphere drying chambers under controlled atmospheric conditions at 15°C for drying and curing. To attain a relative humidity of less than 10%, we used gases with humidity levels below 0.1%. Additionally, within the controlled atmosphere drying chambers, we inserted 500 g of dried silica gel pearls in each chamber (Drying Pearls Orange, Merck, Germany) to absorb the moisture during the drying process. The controlled-atmosphere drying chambers restored the desired drying and curing conditions within the chambers every 30 min. After 6 days, the inflorescences were completely dry, since no additional inflorescence weight loss was observed (the weight change was within the error range of the water content), and therefore no additional curing step was needed. The final water content of the dried inflorescence was 10% ± 1%. For calculating the cannabinoid and terpene content, the fresh (wet) inflorescence weight at harvest day was normalized to dry weight using the average weight loss of 75 ± 2.6%.

Sample Preparation

Fresh or dried cannabis inflorescences from Gen12 chemovar were ground homogenously with a mortar and pestle in the presence of liquid nitrogen, providing 5 replicates from each treatment group. The homogenously ground cannabis samples (500 ± 0.5 mg for fresh inflorescences and 100 ± 0.1 mg for dried inflorescences) were extracted with 4 mL of ethanol in 15-mL Falcon tubes and shaken (Digital Orbital Shaker, MRC, Israel) in the dark for 15 min at 500 rpm. One mL of the extract was transferred to an Eppendorf tube and centrifuged for 4 min at 12,000 rpm. For the determination of cannabinoid levels, a dilution of 1:11 of the supernatant with ethanol was carried out, and 1 mL aliquot was transferred to an HPLC vial and subjected to high-pressure liquid-chromatography-photodiode array (HPLC-PDA) analysis. For the determination of terpene levels, 0.25 mL of the supernatant was inserted into a vial and analyzed via gas chromatography-mass spectroscopy (GC/MS).

Quantification of Cannabinoids by HPLC-PDA and Terpenes by GC/MS

The ethanolic cannabis extracts were analyzed as described in Birenboim et al. [24], utilizing HPLC-PDA (Acquity Arc FTN-R; Model PDA-2998, Waters Corp., Milford, MA, USA) equipped with Kinetex® 1.7 µm XB-C18 100A LC column (150 × 2.1 mm i.d. and 1.7 µm particle size; Phenomenex, Torrance, CA, USA) for the cannabinoid analysis. Cannabinoids were quantified by comparing the integrated peak area with the corresponding cannabinoid calibration curve ranging from 1 to 1,000 µg/mL.

The terpene analysis was carried out by GC/MS (Agilent, Santa Clara, CA, USA) as recently reported by Birenboim et al. [24] utilizing DB-5 capillary column (5% phenyl, 95% dimethylpolysiloxane, 30 m × 0.250 mm, 0.25 m; Agilent, Santa Clara, CA, USA) for analyte separation. Terpenes were quantified by comparing the integrated peak area with the corresponding terpene calibration curve ranging from 0.5 to 250 µg/mL. The methods' analytical validation parameters (i.e., R^2, limit of detection, limit of quantification, repeatability, and accuracy) were recently published in Birenboim et al. [24].

Statistical Analysis

For each compound analyzed, one-way ANOVA followed by Tukey's post hoc test was used to determine the differences in cannabinoid and terpene concentrations between the different trimming groups at $\alpha = 0.05$ using GraphPad PRISM 10 (San Diego, CA, USA).

Results

Impact of Trimming Timing and Extent on the Cannabinoid Content

In this section, we explored the impact of two apparently opposing processes, namely, trimming before drying and trimming after drying, on the cannabinoid and terpene content. Trimming before drying constitutes mechanical stress that could potentially induce the synthesis of cannabinoids and terpenes as a protective measure by the plant [25]. On the other hand, removal of the sugar leaves possibly reduces the availability of precursors for the synthesis of the aforementioned secondary metabolites. The present study aimed at resolving the question of optimal timing of trimming and the extent of it.

The MWT group exhibited a notably higher total cannabinoid content compared to both the DT group (by 4%) and the AWT group (by 3.5%; Fig. 2). Notably, MWT led to significantly higher levels of acidic cannabinoids (THCA, CBDA, and CBGA) and neutral cannabinoids (THC and CBG) than those observed in the post-drying DT group and at harvest day (Fig. 2). In terms of trimming extent and its effect on specific cannabinoid concentrations, only THCA and CBGA showed significantly increased levels with MWT compared to AWT (Fig. 2). For other cannabinoids, no notable differences were observed (Fig. 2). Remarkably, the MWT technique emerged as the sole treatment group to significantly elevate levels of all acidic cannabinoids, as well as the neutral cannabinoids THC and CBG, when compared to the initial levels (Fig. 2). This finding serves as evidence that significant metabolic activity continues during the drying process and can be influenced by external factors to enhance cannabinoid yield.

Impact of Trimming Timing and Extent on the Terpene Content

The impact of different trimming methods on terpene composition contrasted markedly with their effects on cannabinoids (Fig. 3). For the majority (over 80%) of the mono- and sesqui-terpenes analyzed, specifically β-caryophyllene, α-pinene, β-pinene, α-humulene, and γ-elemene, only the post-DT technique significantly enhanced these terpene levels compared to both the baseline and other trimming methods. No notable differences were observed between harvest day and the pre-drying trimming techniques (MWT and AWT), for these terpenes (Fig. 3). Subsequently, the highest terpene content was observed after DT (Fig. 3).

Exceptions to this pattern were observed for β-eudesmol, which did not show significant variations among the different trimming techniques, yet its concentration significantly exceeded the initial level (Fig. 3). In contrast, β-myrcene was found in significantly higher concentrations in the MWT group, followed by the DT group (Fig. 3). These results indicate that each terpene may react differently to the different trimming procedures.

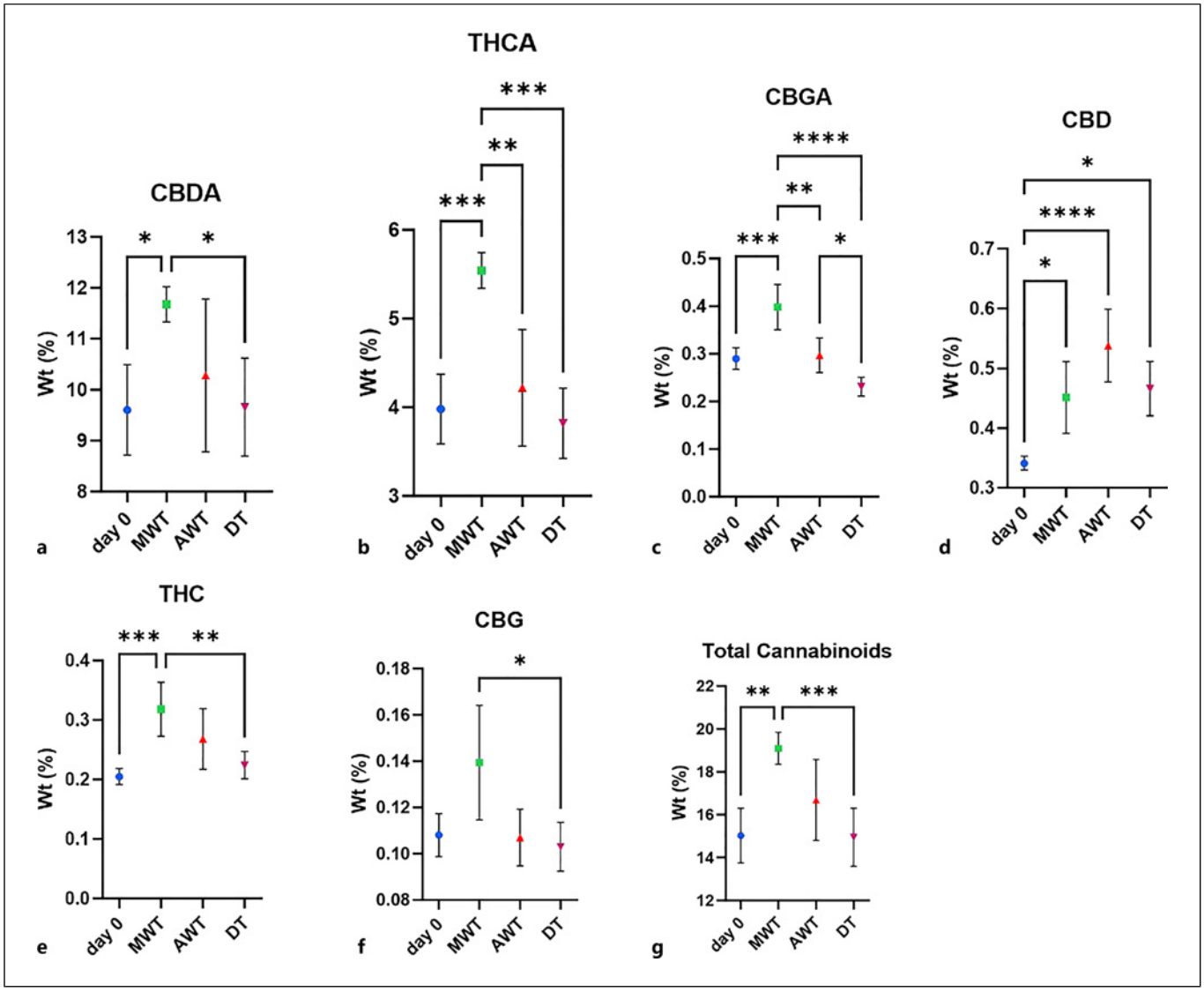

Fig. 2. a–g Mean cannabinoid concentrations (± SD) in the "Gen12" chemovar (in DW%, y-axis, $n = 5$) determined under one of three different trimming procedures: mild wet trimming (MWT), aggressive wet trimming (AWT), and dry trimming (DT) by HPLC-PDA. Statistical significance between the different trimming procedures and harvest day for each cannabinoid was determined using one-way ANOVA followed by Tukey's post hoc test (p value <0.0332 [*], $p < 0.0021$ [**], $p < 0.0002$ [***], $p < 0.0001$ [****]). Day 0 refers to baseline levels of cannabinoids determined on harvest day.

Discussion

Regarding cannabinoid content preservation, our findings indicate that pre-drying MWT is more effective compared to other trimming methods. This technique, by not entirely removing the sugar leaves, possibly allows for the increased flow of precursors necessary for enhanced cannabinoid synthesis while simultaneously providing an adequate stress signal to boost cannabinoid production. Notably, with the exception of CBGA, which was present in relatively low concentrations (0.3–0.4%) across all treatments, no significant differences were observed in the majority of cannabinoid concentrations or total cannabinoid content between the pre-drying AWT and post-drying DT. This suggests that completely removing sugar leaves before drying impedes the influx of precursors for cannabinoid synthesis, thus negating any potential increase in cannabinoid synthesis that might be triggered by a stress signal.

Sugars synthesized in leaves are transported to the inflorescence and are essential in the synthesis of secondary

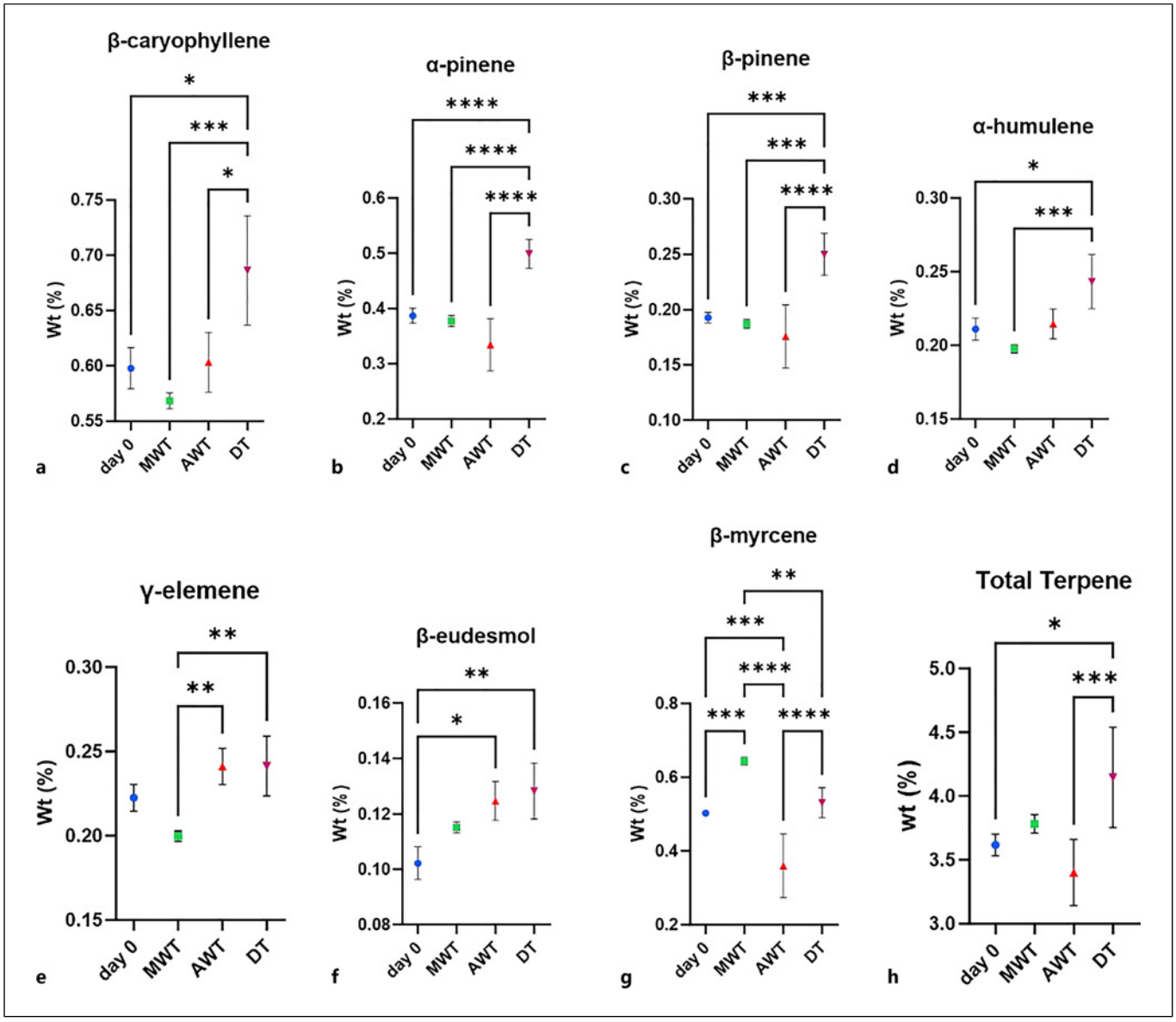

Fig. 3. a–h Mean terpene concentrations (± SD) of the "Gen12" chemovar (in DW%, y-axis, $n = 5$) determined under one of three different trimming procedures: mild wet trimming (MWT), aggressive wet trimming (AWT), and dry trimming (DT) by HPLC-PDA. Statistical significance between the different trimming procedures and harvest day for each terpene was calculated using one-way ANOVA followed by Tukey's post hoc test (p value <0.0332 [*], $p < 0.0021$ [**], $p < 0.0002$ [***], $p < 0.0001$ [****]). Day 0 refers to baseline levels of terpenes determined on harvest day.

metabolites such as cannabinoids and terpenes [26]. The role of sugars in this process is not direct but rather through their participation in the primary metabolic pathways that provide the necessary energy and precursors for the active secondary metabolite synthesis [26]. The sugars contribute to the generation of the necessary energy in the form of adenosine triphosphate, the reducing power, and acetyl-coA needed for the biosynthesis of these compounds [26]. The cannabinoid synthesis in cannabis plants occurs solely in the trichomes, which are substantially more abundant in the inflorescence than in any other plant part, and involves a complex biosynthetic pathway where precursors are derived from primary metabolic processes [11]. The primary precursors for cannabinoids are hexanoyl-CoA, a product of the fatty acid synthesis pathway, and geranyl-pyrophosphate, produced through the methylerythritol phosphate pathway, a part of the more general terpenoid biosynthesis pathway [9, 10]. Numerous studies clearly demonstrated that stress factors

such as mechanical damage, insect herbivory, extreme heat, and drought induce the synthesis of cannabinoids and terpenes in the cannabis plant [25–28]. The primary role of cannabinoids is believed to be protective, acting as defense chemicals, deterring herbivores, and protecting the plant from UV radiation and environmental stress [29]. Consequently, a trimming methodology that would induce mechanical stress, but simultaneously enable the influx of cannabinoid precursors to the inflorescence, would be considered optimal for significantly elevating cannabinoid levels as was demonstrated by our MWT technique.

In contrast to the cannabinoids, DT trimming technique was found to be most effective in enhancing terpene yield, rendering the inflorescence more aromatic. Furthermore, while wet trimming seems to boost cannabinoid content, possibly due to the plant's defensive response to the physical damage of trimming, DT actually increases terpene levels, especially when the inflorescence is left intact during drying.

The unique response of β-eudesmol and β-myrcene to different cannabis trimming methods, as opposed to the majority of the terpenes, could be attributed to their distinct biochemical properties, their roles in the plant, chemical stability, volatility, and interaction with other plant constituents during the trimming process. However, without specific research focusing on the response of β-eudesmol and β-myrcene to trimming methods, it is challenging to provide a definitive explanation. Understanding the variability and behavior of terpenes like β-eudesmol and β-myrcene requires detailed chemical analysis and might vary depending on the cannabis strain and environmental conditions during cultivation and processing.

Furthermore, identifying the ideal trimming conditions to simultaneously maximize cannabinoid and terpene levels in cannabis presents a significant challenge. Hence, regarding trimming practices, growers must make a choice between prioritizing enhanced cannabinoid content or achieving higher aromatic terpene concentrations, as optimizing for both concurrently seems difficult.

Conclusions

In this study, we examined how timing and method of trimming affect cannabinoid and terpene profiles in the Gen12 medicinal cannabis chemovar. Our results show that a gentle pre-drying trim increases total cannabinoid content more effectively than other methods. By partially retaining sugar leaves, this approach possibly supports an enhanced flow of precursors necessary for cannabinoid synthesis and provides stress signals that elevate cannabinoid production. Conversely, for most mono- and sesqui-terpenes, only post-dry trimming significantly raised their levels. The variation in cannabinoid and terpene content across different trimming methods may be due to differing stress responses from mechanical injury before drying, influencing the plant's defensive system and thus affecting cannabinoid or terpene synthesis. Notwithstanding, optimal trimming and post-harvest practices might vary across different cannabis chemovars, necessitating individual optimization for each. To strengthen the applicability of our findings, future studies should expand the sample size and include various strains of *Cannabis sativa* L. to ensure broader generalizability. Additionally, incorporating feedback from industry professionals regarding practical implementation challenges and economic considerations of different trimming methods will be crucial. This collaborative effort will not only refine the effectiveness of the proposed methods but also enhance their economic viability and acceptance within the industry.

Statement of Ethics

An ethics statement was not required for this study type since no human or animal subjects or materials were used.

Conflict of Interest Statement

The authors have no conflicts of interest to declare.

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Author Contributions

Nimrod Brikenstein: conceptualization, data curation, investigation, methodology, and writing – original draft. Matan Birenboim: investigation. David Kenigsbuch: conceptualization, project administration, supervision, and writing – review and editing. Jakob Avi Shimshoni: conceptualization, project administration, formal analysis, supervision, and writing – review and editing.

Data Availability Statement

The data that support the findings of this study are not publicly available since they contain information that could compromise the privacy of the research participants but are available from the corresponding author (J.S.) upon request.

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