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The Nose Knows: Aroma, but Not THC Mediates the Subjective Effects of Smoked and Vaporized Cannabis Flower

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Abstract: Previous studies have shown that cannabis consumers are willing to pay more money for higher-quality products; however, the definition of "quality" cannabis has not been defined. Despite the known health risks of THC overuse, THC potency has been adopted as the primary market-driving feature of cannabis products. The purpose of this study was to objectively identify features of cannabis that contribute to its appealing subjective effects. In the course of conducting cannabis competitions, commercially available cannabis inflorescences were distributed to healthy volunteers ("judges") in a randomized, double-blind fashion. Anonymous online survey data about the subjective effects of each cannabis sample were analyzed independently, by researchers not involved with the competitions. Pleasant subjective aroma (but not terpene expression, THC potency, or THC dose) was positively correlated with pleasant subjective effects. There was also a moderate but significant negative association between the amount of cannabis consumed and subjective appeal. These results suggest that, unlike THC potency, pleasant aroma is predictive of pleasant subjective effects. Similar to other agricultural commodities such as coffee and tea, aroma appears to be a robust indicator of the quality of cannabis inflorescence. These findings have wide-reaching public health implications, given the well-established health risks of THC overuse.

Keywords: cannabis; aroma; THC; potency; flower; vapor; smoke; inhalation; quality; terpenes

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1. Introduction

Until 2021, the National Institute on Drug Abuse (NIDA) was the exclusive source of cannabis for human research in the United States [1]. Thus, the vast majority of published studies about the subjective effects of cannabis rely on NIDA-supplied cannabis. However, recent studies have demonstrated that NIDA cannabis is not only genetically distinct from commercially available cannabis [2], but it also bears little chemical resemblance to the extensive variety of cannabis chemotypes sold in state-legal U.S. markets [3].

Cannabis sativa L. produces more than 500 phytochemicals, many of which have anti-inflammatory, analgesic, anti-oxidative, and psychoactive properties [4]. The psychomotor impairment and subjective mood-altering properties of cannabis are largely attributed to delta-9 tetrahydrocannabinol (THC, [5]), binding at the CB1 receptor [6]. Although the therapeutic properties of THC have been well demonstrated, particularly for analgesia [7,8], there are also well-established risks from excessive use. Of particular public health concern are the risks for impaired driving, cannabinoid hyperemesis, psychotomimetic episodes, and cannabis use disorder (CUD, [9–14]). Potency inflation in commercially available cannabis products in recent years is of great concern, given the robust link between adverse outcomes and high doses of THC [10,15–18]. Indeed, the use of high-potency cannabis, compared to lower-potency cannabis, is linked with an increased risk of psychosis and CUD [18].

The public health concerns about excessive THC use have been further fueled by both regulated cannabis market dynamics as well as carryover behavioral economic forces from the illicit legacy market: namely, the potency effect of prohibition [19]. Illicit substances, including cannabis, are purchased based on the consumer's perception of the substance's quality, and consumers often perceive that better drugs cost more money [20]. In the context of legalization, consumers are also willing to pay more money for higher-quality products; however, previous studies have failed to define the characteristics of "low- mid- and high-grade" cannabis [21,22]. In the absence of other metrics to characterize cannabis flower in terms of desirability and quality, THC potency appears to have been widely adopted as the primary indicator of quality. There is overwhelming demand for high-THC cannabis, and potency is a leading factor in purchasing decisions [23,24]. Because there is a direct correlation between THC potency and retail price per gram, consumer demand further incentivizes cannabis producers to bring ever more potent products to market in a risky feed-forward cycle [25].

Recent studies demonstrate that consumer demand is also increasing for other plant-derived molecules such as cannabidiol [23]. Interestingly, the effects of THC appear to be modulated by the presence of CBD [26]. This drug interaction has important implications for public health and safety, given CBD's potential to reduce THC-induced cognitive deficits, psychotomimetic effects, and other negative side effects [27–29].

Some reports suggest that other cannabis compounds, such as terpenes and terpenoids, could also modulate the subjective effects of THC [30], and that terpenes may potentiate the benefits of cannabis [31–33]. However, preclinical studies have largely failed to support the hypothesis that terpenes modulate the CB1 receptor-mediated effects of cannabinoids such as THC [34–36]. Although terpenes may be anecdotally ascribed to medical and subjective benefits based upon limited evidence, terpenes and other aromatic molecules such as esters, aldehydes, and ketones may still be important THC-independent indicators of quality, given their contribution to the aroma and flavor of cannabis [37,38]. Indeed, terpene content is increasingly being considered an indicator of high-quality cannabis products [39,40]. Although the quantification and reporting of terpenes is becoming a standardized practice in some regulated markets [41], it remains rare elsewhere.

The goal of this study was to characterize the subjective effects of phytochemically-rich commercially available cannabis cultivars in blinded, healthy adults. This unbiased evaluation of the subjective effects of cannabis inflorescence allowed us to examine the relative contributions of chemotype and aroma to subjective desirability. Historically, this type of analysis has not been possible, given the phytochemical paucity of NIDA-supplied cannabis. The current study relies on cannabis inflorescence produced by a diverse group of craft-scale organic cultivators in Oregon, all of whom participated in an annual cannabis competition (Cultivation Classic). The results of this study suggest that, unlike THC potency, pleasant aroma is predictive of pleasant subjective effects. Thus, there is a strong rationale to use aroma as the primary criterion in assessments of product quality. These findings have wide-reaching public health implications, given the well-established health risks of THC overuse.

2. Materials and Methods

2.1. *Cannabis sativa* L. *Inflorescence*

All cannabis (n = 278 samples, 144 in 2019, 134 in 2020) was compliantly produced and routed through the Oregon Liquor and Cannabis Commission's (OLCC) regulated supply chain. As part of the routing process, all cannabis was tested by accredited independent laboratories. The battery of tests included pesticide residues, water activity, moisture content, and cannabinoid potency. All samples were shown to meet safety testing requirements (OLCC compliance testing was verified) prior to inclusion in the Cultivation Classic cannabis competitions in 2019 and 2020. The Cultivation Classic is an annual awards ceremony and event in Portland, Oregon, first founded in 2015. Conceived as a means of establishing rigorous evaluation of inhalable cannabis flower, it is also a community forum to support knowledge of ecological crop production methods and advance research and scientific insight in the nascent adult use cannabis market. Competing producers (cultivators) self-reported the exclusive use of organic crop production methods. In addition to comprehensive phytochemistry and qualitative effects, the competition organizers also conducted an agronomic quality assessment and an independent analysis of energy and water efficiency (Power Score, Resource Innovation Institute, Portland, OR, USA).

2.2. Analytical Chemistry Testing

In addition to the OLCC compliance testing, further cannabinoid potency and terpene potency testing was performed by a single independent laboratory. A single laboratory was used each year to mitigate previously observed variations between testing laboratories [42]. The laboratory varied between the two years of the study (Cascadia Labs, Tigard, OR, USA in 2019; Lightscale Labs, Portland, OR, USA in 2020). Both laboratories held accreditation from the Oregon Environmental Laboratory Accreditation Program (ORELAP), the state-run laboratory audit program within the Oregon Health Authority (OHA), at the time of testing.

An extended panel of both cannabinoid and terpene analytes was tested (n = 36 analytes in 2019, n = 55 analytes in 2020), along with moisture content. A liquid chromatograph with a diode array detector was employed as the primary instrumentation for analysis of cannabinoid potency. Moisture content was determined using the loss on drying technique via a thermogravimetric apparatus. The analytes tetrahydrocannabinolic acid (THCA) and delta-9-tetrahydrocannbinol (Δ9THC) were resolved and determined separately during the analysis. All reported cannabinoid potency results were adjusted for moisture content in the sample. The "Total THC" (THC) was calculated using the widely accepted decarboxylation equation below [43,44].

$$\text{THC} = (\text{THCA} \times 0.887) + \Delta 9\text{THC} \quad (1)$$

2.3. Volunteers

Competition "judges" (n = 276) were recruited to be representative of the Portland, OR, metropolitan region, based on U.S. Census demographic data [45]. In some cases, historically marginalized racial and gender minorities were intentionally overrepresented for the purpose of enhancing inclusivity. The diversity of volunteers was intended to mirror the real-world marketplace of diverse cannabis consumers. Recruitment strategies included outreach to both the general public (social media posts, advertisements in weekly newspapers, and email newsletters) and allied industry affiliates in the cannabis, beverage, and food industries (email). Exclusion criteria included individuals without recent (previous 6 months) use of cannabis, non-residents of Oregon, individuals younger than 21, anyone with a self-identified significant medical condition, and pregnant or breastfeeding parents. Of the total 276 volunteers, n = 157 participated in 2019. Seventy-seven (77) volunteers from 2019 also participated in 2020, in addition to n = 119 new volunteers in 2020, for a total of n = 196 volunteers in 2020.

2.4. Sample Kit Preparation

Each volunteer randomly received a sample kit containing 8–10 random samples of cannabis inflorescence (~1 g each) in sealed glass jars (Sana Packaging, Wheat Ridge, CO, USA). To facilitate data collection, each sample kit was associated with a unique set of login and password credentials to a purpose-built web-based application (Smart Analytics, LLC, Portland, OR, USA, see Section 2.6, below). The issuance of login credentials facilitated anonymous data collection: no personally identifying information, email addresses, IP addresses, or geolocation data were collected via the web application.

2.5. Experiential Evaluation

Cannabis consumption experiential data collection took place between 2 March–1 April 2019 and 1 March–12 April 2020. Upon receipt of their sample kits, volunteers received both web app credentials and printed versions of the online survey in order to facilitate offline notetaking for subsequent data entry. Volunteers were given 30+ days to consume the samples in their kit in order to minimize any carryover acute effects from the consumption of previous samples and to minimize the development of tolerance [46]. Volunteers were also encouraged to abstain from any cannabis use for 48 h prior to consuming any of the samples in their kit (i.e., take a tolerance break) in order to normalize baseline sensitivity to cannabis' subjective effects [47]. Volunteers were also encouraged to consume samples mindfully by conducting a mental and physical "body scan" to enhance awareness of their baseline physical and mood states prior to consuming any sample [48]. Repeated measures were accepted; that is, volunteers were not discouraged from consuming and completing a survey about the same cannabis sample more than once.

2.6. Measures

Upon first login to the web application, volunteers were prompted to answer demographic questions, including the frequency with which they typically consume cannabis. Volunteers were also asked an expectancy anchoring question about their preference for the intensity of cannabis' effects: "What do you typically consider a "good" or desirable effect from cannabis consumption?" with six ordinal answers ranging from "feeling totally normal, not impaired" to "on the verge of feeling uncomfortable". Volunteers answered a 15-item questionnaire about the subjective effects and desirability of each cannabis sample. The preference questions read: "Overall, the effects of this flower were appealing" and "The aroma of this flower was appealing" with 7-point Likert scales ranging from "strongly disagree" to "strongly agree". Subjective impact on mood effects was quantified using a semantic differential scale question, with the following adjectives at each end of a 7-point slider rating scale: "Sad-Happy". Volunteers were also asked to report the method (smoked, smoked with water filtration, or vaporized) and amount of cannabis consumed in a single session, using a visual dosing guide from the Daily Sessions, Frequency, Age of Onset, and Quantity of Cannabis Use Inventory (DFAQ-CU, [49]). Volunteers were also asked to report whether cannabis samples produced any of the following effects: dry mouth, dry eyes, tunnel vision, dizziness, headache, munchies, coughing or trouble breathing, trouble sleeping, racing heart, and psychedelic-like effects on the senses.

2.7. Data Analyses

Experiential analyses were completed by independent, blinded researchers who were not affiliated with the Cultivation Classic cannabis competition. The analyses included a total of 3063 individual cannabis consumption sessions (n = 1692 surveys in 2019 and n = 1371 in 2020). Each cannabis sample had a median of 10 individual survey responses (range: 5–23). Scores on the Likert and semantic differential scales were converted to numerical points, in order to calculate a composite appeal score. Specifically, subjective preference scores (out of 7 points) were summed with mood scores ("Sad-Happy" out of 7 points). Statistical analyses were performed using R ([50], version 4.2.1 accessed on 25 June 2022). When dealing with clustered data, for example multiple ratings of the same sample by the same individual, general estimating equations (GEE) were used to account for the clustering [51]. A total of 13 statistical comparisons (including post-hoc comparisons) were performed in this manuscript, and raw, unadjusted p values are reported throughout.

3. Results

3.1. Volunteer, Consumption, and Inflorescence Characteristics

A total of n = 278 commercially available organic cannabis inflorescences were examined in this study (see chemotype distribution in Figure 1). Seventy-seven percent of samples entered into the competition were Type I flowers (THC-predominant, as previously defined in [52,53], Table 1). A total of 276 volunteers provided anonymous survey responses (51.3% female, 46.2% male, and 2.5% non-binary).

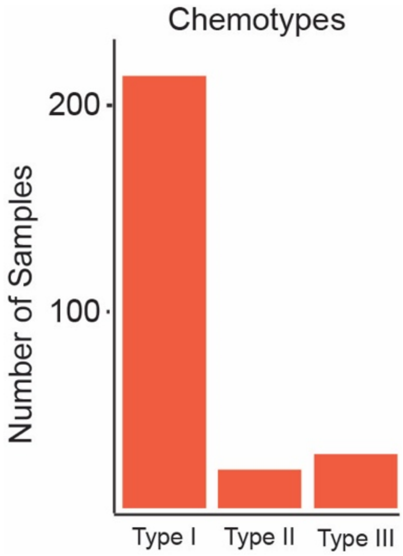

Figure 1. Chemotype distribution of evaluated cannabis inflorescence. n = 278 samples were evaluated in this study. Most competition entries were high-THC Type I flowers with less than 0.5% CBD (n = 215). There were n = 28 Type II and n = 35 Type III samples.

Table 1. Cannabis chemotype designations, as previously defined in [52,53].

Chemotype Designation	THC	CBD	Descriptor
Type I	>0.3%	<0.5%	Predominantly THC
Type II	>0.3%	>0.5%	Mixed THC & CBD
Type III	<0.3%	>0.5%	Predominantly CBD

Volunteer characteristics can be found in Figure 2. Most volunteers were aged 30–39 and were daily cannabis consumers at the time they volunteered to participate as judges for the competition (Figure 2a,b). Time-stamped surveys revealed that twelve percent of volunteers (n = 32) did not adhere to the guidance about taking a 48 h tolerance break prior to consuming the samples in their kit. Of these volunteers, 53% (n = 17) were individuals who typically consume cannabis multiple times daily, and an additional 38% (n = 12) were once-daily consumers. When asked an anchoring question about their preference for the intensity of cannabis' effects ("What do you typically consider a "good" or desirable effect from cannabis consumption?"), most volunteers reported a "prominent shift in perception" (Figure 2c). Most volunteers consumed samples via unfiltered smoke inhalation (50.0% of all sessions). Vaporizing was the least common method of consumption (17.7% of sessions).

3.2. Data Analyses

The factors that contribute to experiential appeal have not previously been defined in the context of commercial cannabis use by healthy adults. Thus, we sought to operationalize "appeal" by incorporating two domains: raw enjoyment ("Overall, the effects of this flower were appealing") and positive mood ("Sad-Happy"). Because scores on these domains were collected using somewhat limited 7-point scales, a composite subjective appeal score was calculated by summing these scores (a total of 14 possible points). This composite analysis strategy doubled the granularity of the subjective appeal data, allowing for a higher degree of precision in the analysis.

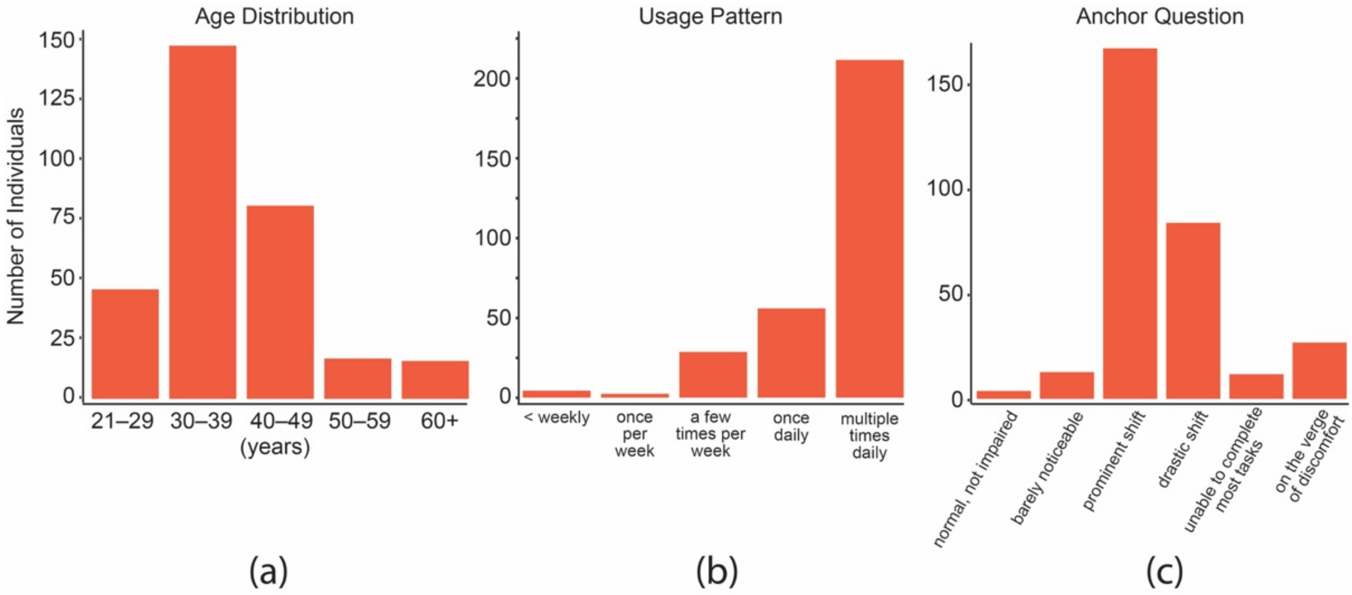

Figure 2. Volunteer characteristics. (**a**) Age distribution of volunteers: most individuals who completed anonymous surveys were aged 30–39. The overall age distribution reflected the Portland metropolitan area, according to US Census data. (**b**) Cannabis use patterns: prior to volunteering to judge samples at the competition, most individuals used cannabis multiple times per day. (**c**) Expectancy characteristics: When asked about their preference for the intensity of cannabis' effects ("What do you typically consider a "good" or desirable effect from cannabis consumption?"), most volunteers reported a preference for a "prominent shift in perception."

The most commonly used amount of cannabis in a single session was 0.25 g (44.6% of all recorded sessions, Figure 3a). Generalized estimating equations (GEE) first revealed that there was a mild but statistically significant negative correlation between the amount of cannabis consumed (grams) and subjective appeal. That is, smaller amounts of cannabis consumed were associated with the greatest subjective appeal (Figure 3a, GEE, $p = 0.021$). There was also a moderate but significant negative relationship between consumption frequency and subjective appeal (GEE, $p = 0.038$). Specifically, volunteers who typically consumed cannabis less than once per week reported higher subjective enjoyment than volunteers who consumed multiple times daily. We also analyzed whether consumption method (smoked, smoked with water filtration, or vaporized) impacted subjective appeal. Although the GEE model revealed that consumption method significantly contributed to subjective appeal ($p = 0.026$), the mean appeal score was very similar for water-filtered smoking, unfiltered smoking, and vaporized sessions (mean appeal scores of 8.33, 8.45, and 8.58, respectively, Figure 3b). Post-hoc analysis revealed a significant difference between water-filtered and vaporized consumption methods: other pair-wise comparisons were not significant (Tukey's all-pair comparison, $p = 0.020$). We also found age-dependent effects on subjective appeal, with older volunteers reporting more subjective appeal than younger volunteers. People aged 40 and older reported significantly higher subjective enjoyment scores than those under 40 (GEE, $p = 0.038$). Volunteers aged 60 and older reported higher subjective appeal scores than any other age group ($p < 0.001$, 60+ vs. 21–30 years).

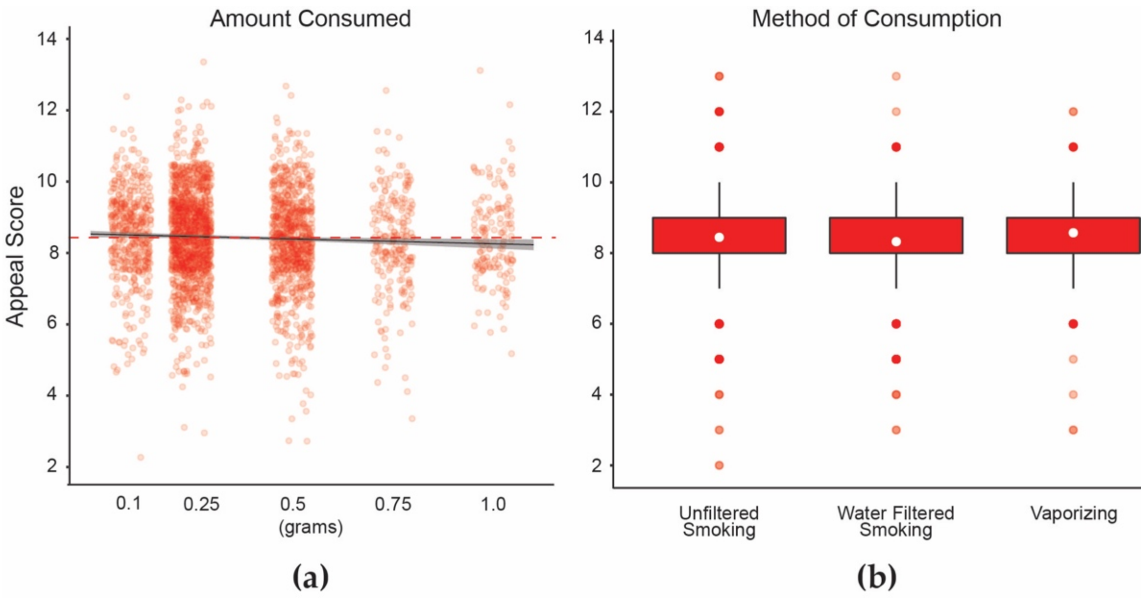

Figure 3. Cannabis consumption and subjective appeal. (**a**) Subjective appeal based on amount of cannabis consumed: Volunteers were given a visual reference guide to estimate the amount of cannabis they consumed in a single session (adapted with permission from DFAQ-CU, [49]). The most commonly reported amount of cannabis consumed in a single session was 0.25 g (44.6% of all sessions). There was a moderate but significant negative correlation between the amount of cannabis consumed and subjective appeal (black line, $p = 0.021$). (**b**) Subjective appeal based on consumption method: GEE modeling revealed a significant effect of consumption method on appeal ($p = 0.026$); however, mean appeal scores were very similar for unfiltered smoking, water-filtered smoking, and vaporizing (8.45, 8.33, and 8.58 respectively). Tukey's post-hoc analysis revealed a significant difference between water-filtered and vaporized consumption methods: ($p = 0.020$).

In line with previous reports [54,55] we found that THC potency was not correlated with subjective appeal ($p = 0.170$, Figure 4a). However, we found a small but statistically significant interaction between biological sex and THC potency, with males reporting slightly more enjoyment of high-THC samples (GEE, $p = 0.012$, non-binary individuals were excluded from this model). We next examined the dose-response relationship between THC and subjective appeal by estimating the milligrams of THC consumed in a single session (THC potency $\times$ grams consumed = THC dose). Contrary to widely held public opinions, the dose of THC consumed in a single session was not correlated with subjective appeal ($p = 0.270$, Figure 4b). We also assessed the relationship between THC potency and unwanted subjective effects. There was no relationship between THC potency and dry eyes, dry mouth, appetite stimulation ("munchies"), or trouble sleeping. There was a small relationship between THC potency and tachycardia, with high-THC inflorescence more likely to produce racing hearts (logistic GEE, $p = 0.060$).

The strongest contribution to subjective appeal that we observed was pleasant subjective aroma (Figure 5a). That is, cannabis flowers with the most appealing aromas were the most likely to have the greatest subjective appeal (GEE, $p < 0.001$). Because terpenes and terpenoids are known to contribute to the aroma of cannabis, we also assessed the relationship between total terpene expression and subjective appeal. Similar to total THC potency, we found no association between total terpene expression and experiential appeal (GEE, $p = 0.444$, Figure 5b). Inflorescences with higher total terpene content were not more subjectively appealing. We also assessed the degree of interpersonal variability in the reported aroma scores. We found a significant negative relationship between a cultivar's mean aroma score and the standard deviation of that aroma score (linear regression, $p < 0.001$). That is, there was a high degree of interpersonal consensus when a cultivar had a high aroma score, and low consensus when a cultivar had a low aroma score (Figure 6).

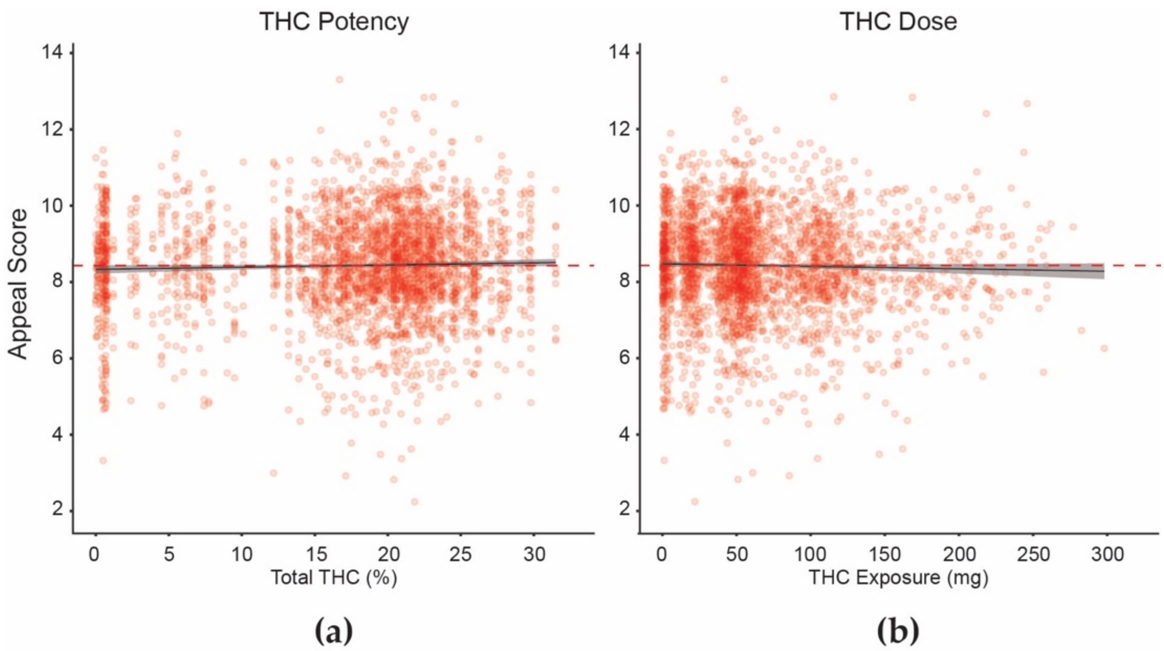

Figure 4. No relationship between THC and subjective appeal. (**a**) THC Potency: Subjective appeal was not associated with the THC potency of cannabis inflorescence samples. (**b**) THC Dose: The estimated maximal exposure to THC (amount consumed x THC potency) was also not associated with subjective appeal.

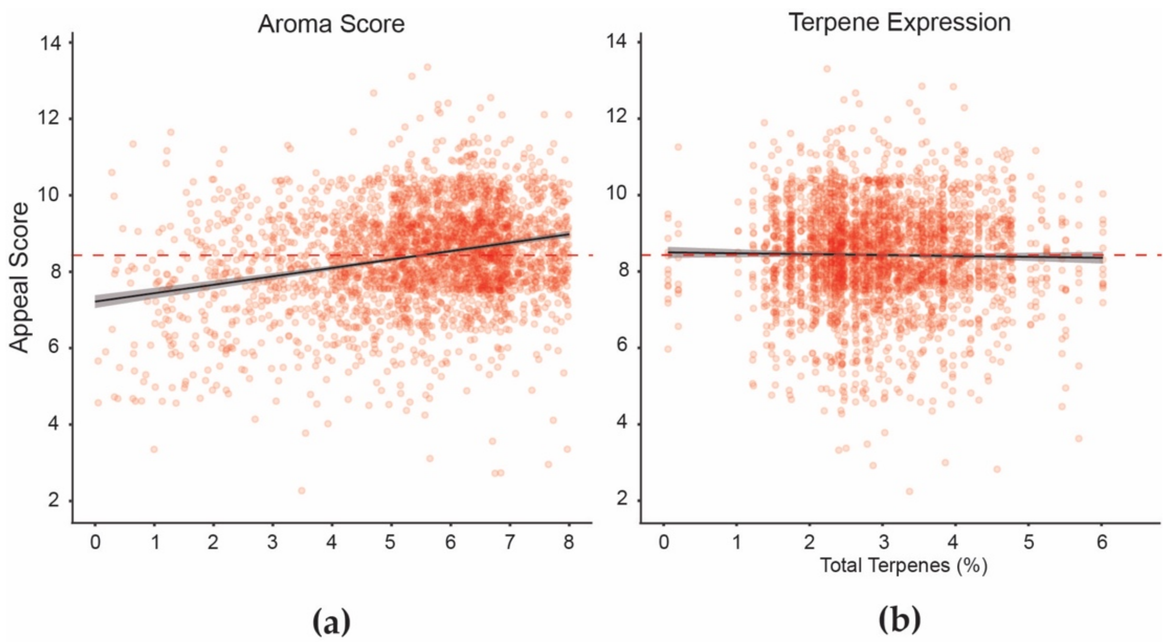

Figure 5. Aromatic features and subjective appeal. (**a**) Pleasant subjective aroma is correlated with subjective appeal: cannabis flowers with the most appealing aromas were the most likely to have the greatest subjective appeal (black line, $p < 0.001$). Visual jitter has been introduced in this figure so that the distribution of the data is clearer; however, statistics were performed on the raw data. (**b**) There was no relationship between terpenoid expression and appeal: terpene expression (total %) was not correlated with subjective appeal.

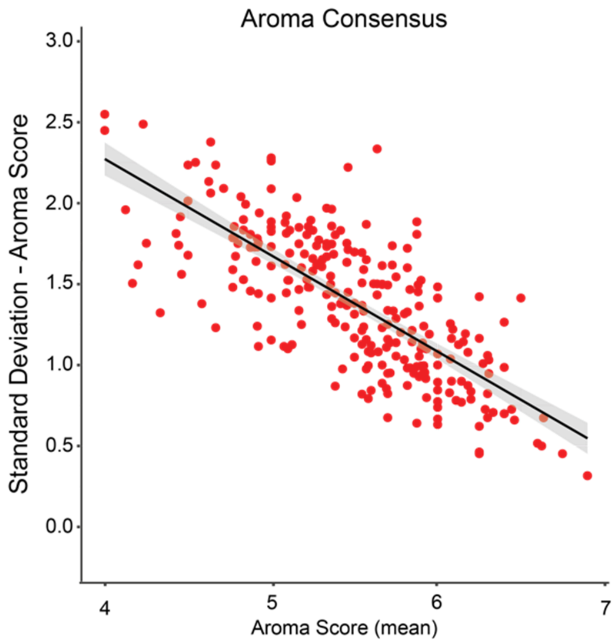

Figure 6. Interpersonal consensus regarding the appeal of cannabis aroma. Each point represents the mean aroma score for each flower, plotted against the standard deviation (SD) in reported aroma scores for the same flower. Mean and SD were negatively associated, with SD decreasing as aroma scores increased (black line, $p < 0.001$).

4. Discussion

This is the first study to examine the subjective effects of a large number of phytochemically diverse, commercially available cannabis inflorescences in blinded, healthy adults. The results of this randomized, objective assessment demonstrate that pleasant subjective aroma, but not terpene expression, THC potency, or THC dose, is positively associated with pleasant subjective effects (appeal and positive mood). There was a negative association between mean aroma ratings and the variability of aroma ratings, with variability in interpersonal subjective aroma ratings decreasing as mean aroma scores increased. There was also a negative association between the amount of cannabis consumed and overall appeal, with smaller amounts producing greater appeal. Interestingly, people who reported a typical cannabis consumption frequency of once per week or less were the most likely to report higher subjective appeal scores. Although tolerance to THC's subjective effects (in frequent consumers) may have contributed to this finding, the vast majority of judges (88%) adhered to the guidance about taking a 48 h tolerance break prior to consuming the samples in their kit. Thus, the mechanisms underlying the relationship between consumption frequency and subjective appeal are unclear. We also observed a small interaction between sex and THC potency, with males being more likely to report appealing effects of high-THC inflorescence samples. In this study, THC potency was not associated with unwanted effects such as dry eye, dry mouth, or increased appetite; however, it was modestly associated with tachycardia. Compared to all other age groups, volunteers aged 60 and older reported the greatest overall appeal of inhaled cannabis inflorescence.

The results of this study have important harm reduction and public health implications. Experimental, observational, and population-level studies have consistently demonstrated the dose-dependent risks of THC [10,15–17]. The frequent use of potent THC products enhances the risk for negative outcomes such as psychosis, cannabinoid hyperemesis, and CUD [9–12,18]. Decades of research are at odds with the free market dynamics in regulated cannabis markets, where high-THC inflorescences have a much higher market share compared to moderate- and low-THC products [56]. At least partially contributing to this phenomenon is the wholesale buying "floor" (often arbitrarily set at 20% THC), whereby retailers refuse to stock dispensary shelves with low-THC inflorescence [57].

Undoubtedly, the potency floor is driven by economics, given that THC potency is the leading characteristic for determining the wholesale value of cannabis inflorescence [25,58]. Acutely aware of the higher monetary value of high-THC flower, cannabis producers and breeders have an intrinsic pressure to selectively breed and intensively cultivate for THC potency, above all other agricultural or phytochemical features [59]. The result of these pressures is a narrowing of consumer purchase choices to ever more potent products. Thus, the high market value of high-THC cannabis not only puts public health at risk via overexposure to THC, but it also negatively impacts medical patients, who tend to prefer lower-THC products [60].

Underlying the systemic potency issues within regulated cannabis markets is consumer demand for THC. Despite the fact that the perceived value of potent products is a carryover from cannabis prohibition [19,20], THC potency remains a major factor in consumer purchase decisions [23,24]. Our analysis revealed that, contrary to both market dynamics and consumer perception, neither THC potency nor THC dose had an impact on subjective appeal. In the context of naturalistic recreational enjoyment, some hemp-like chemovars and Type II chemovars were just as appealing as chemovars with 20% THC or more. These findings are in alignment with previous reports, which demonstrate that the subjective and rewarding effects of THC-containing cannabis do not have a linear dose-response relationship [54,55]. Although controlled experiments have demonstrated a dose-dependent effect of THC on psychomotor impairment [61], the results of the current study suggest that impairment and enjoyment are unrelated phenomena. In other words, high-THC cannabis may cause people to feel high, but high-THC cannabis is not always enjoyable.

We also found a small but statistically significant interaction between biological sex and THC potency, with males reporting slightly more enjoyment of high-THC cannabis samples. This finding is in line with previous research, which suggests that females are more sensitive to the subjective effects of THC [62,63] and that women may experience less subjective appeal at higher THC doses [63,64].

Interestingly, despite the lack of effect of a THC dose, we observed a negative correlation between the amount of cannabis consumed and subjective appeal. Although the biphasic dose responses of cannabinoids have been observed in several studies [65–68], most of these studies rely on the isolated administration of cannabinoids, rather than the naturalistic consumption of scores of quantifiable analytes, as in the current work. With small amounts of cannabis (0.1–0.25 g), it is possible that THC's effects may have been modulated by the presence of other molecules, an effect that may have been occluded by THC's effects with larger amounts of cannabis. Various molecules produced by the cannabis plant are known to interact (either antagonistically, additively, or synergistically [30]). However, these poorly characterized interactions are often dependent upon the experimental species and methodology, and the results are difficult to replicate or generalize [34,36,69]. Alternatively, the observed greater appeal of small amounts of cannabis may have been an anomaly, given that routine cannabis users self-titrate to their desired levels of intoxication and impairment [17]. Because volunteers were consuming blinded cannabis samples of unknown potency, they may have conservatively started with smaller amounts (0.1–0.25 g), failing to titrate higher because pleasant subjective effects had already been achieved.

We also observed a negative relationship between subjective appeal and cannabis use frequency. That is, cannabis was most enjoyable for people who used it less often. These results suggest that, similar to analgesia and psychomotor impairment [70,71], tolerance develops to the appealing and mood-enhancing properties of THC. In alignment with harm reduction strategies, these results support the idea that maximal cannabis enjoyment can be achieved through the use of small amounts of low-THC cannabis once per week or less.

Although a recent survey suggests that 60% of cannabis consumers use aroma as a selection criterion when buying cannabis [72], the current study is the first to demonstrate that a pleasant subjective aroma is statistically associated with a pleasant consumption experience. Although we found some interpersonal consensus (low standard deviation) about the pleasantness of a cultivar's aroma, this finding was most prominent in cultivars with the highest subjective aroma scores. That is, for flowers with lower aroma ratings, there was a high degree of variability in reported aroma pleasantness. These results suggest that the hedonic tone of cannabis aroma is not entirely objective, and that third-party ratings of pleasant aroma may not generalize to other individuals.

Because aroma and experiential appeal were assessed by the same volunteers, it is possible that common method variance may explain the positive association between pleasant aroma and subjective appeal scores. However, a more parsimonious explanation (and one supported by the subjectivity data discussed above) is that the association between aroma and enjoyment was driven by expectancy. That is, a pleasant subjective sensory experience may have primed individuals for a pleasant consumption experience. This hypothesis is further supported by the observed relationship between subjective experiential appeal and consumption method: slightly higher subjective appeal scores were reported for sessions in which cannabis samples were vaporized, particularly compared to water-filtered smoking. One possible explanation for this is that aromatic molecules may be pyrolyzed at combustion temperatures and lost through water filtration, thus diminishing the overall sensory experience. Combined, these results provide a strong rationale for consumers to be able to smell flowers before purchasing them.

For centuries, humans have selectively bred and cultivated a wide variety of plants specifically for their aroma (both raw biomass as well as extracted essential oils [73–75]. This includes *Humulus lupulus* L. (hops), which is closely related to the *Cannabis sativa* L. plant and produces many of the same aromatic molecules [76–78]. For other consumer agricultural products such as tea and coffee, aroma is a critical indication of quality, consumer appeal, and therefore price differentiation [79,80]. For cannabis, aromatic characteristics have only recently started to be considered an indicator of quality [39,40], and these efforts are largely focused on terpenes and terpenoids. In this study, we found no relationship between total terpene content and subjective appeal. In other words, cannabis inflorescence with higher terpene content was not more enjoyable than inflorescence with lower terpene content. This suggests that although terpenes may partially contribute to aroma, the subjective aroma character and experiential appeal of cannabis are very likely to involve other aromatic compounds as well.

Indeed, molecules such as volatile sulfur compounds and aldehydes have also been recognized as important contributing factors in cannabis' aroma [38,81], and a single cannabis chemovar may contain dozens of aromatic analytes. However, the psychophysics of cannabis (the relationship between the aromatic components and the perceptions they produce in humans) is severely underdeveloped. In some respects, regulated cannabis markets currently utilize the Strongest Component Model (SCM) of aroma characterization, which has been well described by the flavors and fragrances industry [82,83]. The SCM posits that the simplest way to quantify the aroma of a multi-component mixture is to report the component with the highest odor value or intensity (for example, "earthy" or "citrus" cannabis aromas, as in [84]). However, given the known perceptual differences between synthesized aroma compositions and naturally-occurring aromas [85], it is unlikely that the SCM model for fragrances and perfumes generalizes to cannabis. For example, in controlled experiments using wine and apple juice, aromatic additives at sub-threshold levels of detection significantly impact the perceived character and intensity of the dominant aroma [85,86]. This could be partially explained by the high degree of peripheral modulation of aromas in the olfactory epithelium [87]. That is, multi-component mixtures do not elicit a simple sum of individual olfactory neuron responses: Instead, neuronal activity in response to a dominant odorant can either be antagonized or potentiated by the presence of even a single additional aromatic molecule [87]. Higher-order cognitive processing of sensory information is also highly likely to modulate the perceived aroma of cannabis [88]. Thus, the complex aromatic makeup of cannabis inflorescence presents a complex perceptual challenge, one that is likely prone to oversimplification in the commercial context of regulated cannabis markets.

Although quantitative methods for detecting aromatic biomarkers may prove to be helpful screening tools for cannabis breeders and cultivators [89], the pleasant hedonic tone of aroma is still best characterized subjectively by humans [90,91]. In other words, quantitative methods may be helpful for identifying the aromatic constituents of cannabis, but sensory analysis is likely required to effectively evaluate what is pleasant and therefore high-quality. Aromatic features (analytes) may not always confer experiential benefits. Taken together, previous findings and our results suggest that, compared to quantified THC and terpene content, subjective aroma is a superior indicator of the quality (and therefore wholesale value) of cannabis inflorescence. This evidence may have wide-reaching impacts on the field, given that previous studies have failed to define the characteristics of "low-mid- and high-grade" cannabis [21,22].

This study has several limitations. First, to minimize the risk of unpleasant side effects due to excessive THC consumption, the volunteer inclusion criteria were limited to individuals who had some recent experience using cannabis (within the previous 6 months). Thus, the results herein are subject to selection bias and may not be generalizable to cannabis naïve individuals. However, the overt strategy to recruit diverse volunteers (age, gender, and ethnicity) may have increased generalizability to some degree. Another limitation of this study was the inability to rule out carryover subjective effects from prior cannabis consumption sessions. In this naturalistic study, volunteers had the option to record their responses during or immediately following cannabis consumption via the web-based application. However, volunteers were also given the choice of recording their experiences manually (offline) for subsequent data entry. Thus, using time-stamped surveys, we were unable to verify that all volunteers consumed samples with sufficient time between consumption sessions to prevent carryover effects from previous samples. However, competition organizers went to great lengths to prevent carryover effects by: (1) giving volunteers sufficient time (30–45 days) to consume all 8–10 samples within their kit without having to consume more than 2–3 times per week; (2) explicitly educating volunteers about carryover effects at the time of random judge kit distribution; and (3) encouraging volunteers to avoid consuming more than one sample per day. This study exclusively analyzed the subjective effects of cannabis inflorescence. Therefore, the generalizability of these findings (particularly for manufactured goods that have no residual cannabis-like aroma) may be limited. Finally, the THC dose-response analysis herein relies on the key assumption that volunteers consumed the entire amount of cannabis recorded for that consumption session. Because the survey did not ask about the number of inhalations or whether or not the entire amount was consumed, it is possible that volunteers consumed less than what they recorded on the survey. Furthermore, due to the naturalistic nature of data collection, it was not possible to calculate the bioavailability or loss of THC through pyrolysis and side-stream smoke [92,93]. Thus, our dose-response analysis should be interpreted as an estimation of maximal exposure rather than the actual lung deposition dose, which was likely much lower [94].

5. Conclusions

With a constantly growing worldwide legal cannabis consumer base, there is a great need for consumer education about how to consume safely and responsibly. Aligned with harm reduction approaches, these blinded, unbiased results suggest that optimal recreational enjoyment may be achieved by the use of small amounts of low-potency cannabis with a pleasant aroma, particularly when used once per week or less. The results of this study may help support consumers in making evidence-based decisions that can support subjective enjoyment while decreasing health risks. The results clearly support (1) using aroma as the primary criterion in assessments of product quality, (2) regulating cannabis in a manner that allows consumers to smell flower before buying it (either in open or vented containers), (3) de-emphasizing the market value of high-THC products, and (4) diversifying regulated retail marketplaces to include a variety of inflorescence from 0.3–19% THC. These evidence-based practices would have important public health implications by minimizing THC as the primary driver of market demand and thus reducing the risks associated with THC overconsumption.

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Institutional Review Board Statement: The human experiential data were not collected specifically for the purposes of this study: Rather, data were collected for the purposes of industry-sponsored educational events (awards ceremonies to publicly recognize Oregon's best cannabis). Once the data collection and educational events were complete, the anonymous database was made available for research. Once the research team took custody of the anonymous data, there was no interaction with survey respondents, and no interventions were performed. The members of this research team did not have access to respondent identifiers. Given the non-research purpose for which the data was collected and the anonymous nature of the archival database upon which the research was based, this study was not considered human subjects research and thus exempt from IRB oversight.

Informed Consent Statement: The retrospective, anonymous dataset used allowed us to determine that this study was not Human Subjects Research and therefore did not require IRB oversight. Written informed consent was not obtained because participating volunteers were deidentified at the time of data collection. It was not possible to attempt to contact these individuals to tell them about the study retrospectively or obtain consent for publication because respondents could not be identified from the anonymous database.

Data Availability Statement: 3rd Party Data. Restrictions apply to the availability of these data. Data was obtained from Smart Analytics, LLC and are available from the corresponding author with the permission of Smart Analytics, LLC.

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Conflicts of Interest: J.P., J.L.S. and A.R.W.-P. have equity interests in Smart Analytics, LLC, the consulting firm hired to produce the Cultivation Classic. Smart Analytics was responsible for producing the data collection tools (software and SOPs), and collecting the data analyzed in this study. To mitigate any conflict of interest, all data were independently analyzed and interpreted by S.D., who has no relationship with Smart Analytics. Legacy Research Institute, a division of Legacy Health, conducts annual Conflict of Interest assessments, and determined that there is no conflict of interest between A.R.W.-P.'s research and consulting activities. This research received no funding from Smart Analytics or any other entity. Data was collected for the purposes of industry-sponsored educational events. Although these events had numerous corporate sponsors, none of these entities had any role in the role in the design of the study; in the collection, analyses, or interpretation of data; in the writing of the manuscript; or in the decision to publish the results.

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