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Medicinal cannabis tea contains variable doses of cannabinoids and no terpenes

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Abstract

Tea is a recommended way of administration of prescribed cannabis plant products in Denmark. We aimed to investigate the cannabinoid and terpene doses contained in different teas. We analysed tetrahydrocannabinol (THC), tetrahydrocannabinolic acid (THCA), cannabidiol (CBD), cannabidiolic acid (CBDA), and terpene concentrations in three repeated preparations of each type of tea, and in plant material.

In standard tea, concentrations of THC were [median (min-max)] 9.5 (2.3–15), 19 (13–34), and 36 (26–57) μg/mL for products with a labelled content of 6.3%, 14%, and 22% total THC (THC + THCA), respectively. The CBD concentration in tea from a product labelled with 8% total CBD (CBD + CBDA) was 7.5 (1.9–10) μg/mL. Based on this, the recommended starting amount of 0.2 L of the different teas would contain between 0.46 and 11.3 mg THC, and 0.38 to 2.0 mg CBD. Adding creamer before, but not after boiling, increased the THC and CBD concentration 2.3–4.4 and 2.1-fold, respectively. Terpenes were detected in plant material, but not in tea.

The study elucidates THC and CBD doses in different teas, which may assist the clinician's choice of cannabis product. Moreover, it underscores the need for caution as administration as tea can result in exposure to different doses, even when the same cannabis product is used.

KEYWORDS
cannabinoids, terpenes, cannabis tea, drug formulation, medicinal cannabis

Plain English Summary

We aimed to investigate the content of cannabis tea, as tea is a recommended way of administrating medicinal cannabis in Denmark. Our results suggest that the recommended starting amount of 0.2 L of tea contains variable doses of cannabinoids and no terpenes. The doses of cannabinoids varied dependent on cannabis product and preparation method, and even when the same cannabis product and preparation method was used. The results may assist the clinician's choice of cannabis product, and it underscores the need for caution as administration as tea can result in exposure to different doses of cannabinoids.

1 | INTRODUCTION

Medical and recreational use of cannabis dates back approximately 5000 years,[1] and today cannabis is the most commonly used illicit drug worldwide as well as in Europe and Denmark, where 16% of young adults have used cannabis within the last year.[2–4] In the last decades, a renewed interest in medical purposes of cannabis has resulted in changes in legislation.[3,5] Cannabis legislation is heterogeneous worldwide, and the availability of medical cannabis products (MCPs) and the regulation of these differ extensively between countries, though a growing part of countries has provisions/guidelines for use of medicinal cannabis.[3] In Denmark, a medicinal cannabis pilot programme was implemented on the 1st of January 2018. This allowed physicians to prescribe certain MCPs for their patients.[5] The pilot programme was implemented for a 4-year period, which has later been extended with additional 4 years by a new political decision.[6]

The MCPs in the pilot programme are not authorised medicine, and no summary of product characteristics is available. Hence, the comprehensive knowledge, which is available for authorised medicine, does not exist for MCPs, and there are no clinical studies of efficacy or safety. Besides the MCPs encompassed within the pilot programme, physicians in Denmark can prescribe authorised medicine containing cannabinoids, including Sativex and Epidyolex, or magistral products containing cannabinoids. Finally, in special circumstances, a compassionate use permit can be issued for cannabis-based medicine authorised in other countries e.g. Marinol.[7]

A guideline from the Danish Medicines Agency on medicinal cannabis in the pilot programme outlines potentially relevant indications for treatment with MCPs. The indications include neuropathic pain, nausea and vomiting associated with chemotherapy, multiple sclerosis, and spinal cord injury.[8] Guidance regarding dosing or choosing between the different MCPs is not included in the official guideline.

Some of the first MCPs comprised in the Danish pilot programme were the three plant products: Bedrocan "CannGros,"[9] Bediol "CannGros,"[10] and Bedica "CannGros,"[11] which are declared to contain approximately 63/80, 140/<10, and 220/<10 mg/g total tetrahydrocannabinol (THC) (THC + tetrahydrocannabinolic acid (THCA))/total cannabidiol (CBD) (CBD + cannabidiolic acid (CBDA)). The MCP's vary in their content of terpenes as well.[12] Administration routes recommended in the product sheets for the products are consumption as tea (Figure 1) or by vaporisation.[9–11] No information regarding content of cannabinoids or terpenes in the final prepared cannabis tea is available in the product sheets, and neither is information on the variation in content of cannabinoids in tea prepared from the different plant products.

The cannabis plant contains hundreds of different compounds, among these cannabinoids and terpenes. THC, which is regarded as the main euphoric component in cannabis, and CBD are the most studied cannabinoids. They primarily exist as the acidic precursors THCA and CBDA in the cannabis plant. These precursors are decarboxylated to THC and CBD by light or heat,[13] for which reason the heating process is a significant step for the final content of the cannabis tea. Boiling temperature (98–100°C) for 5 min have shown minor effect on the decarboxylation process, whereas baking in an oven for 30 min at 145°C have resulted in complete decarboxylation of THCA into THC and CBDA into CBD.[14,15] A boiling time of 15 or 20 min has been shown to give the highest cannabinoid content in water decoction, whereas longer boiling time has shown a tendency to plateau or even lower the content of cannabinoids.[15,16]

THC and CBD are lipophilic molecules; hence, the recovery in water decoction is low compared to fatty decoctions such as milk decoction or oil.[15,17–19] The recovery of cannabinoids in milk decoction and oil varies between 60 and 80%,[17,18] whereas the recovery in water decoctions is much lower[15,17] and possibly with a tendency to saturate,[16] meaning a higher amount of total THC (THCA + THC) in the plant product used, may not result in a higher THC content in the final cannabis tea. In general, the cannabinoid content of cannabis tea has showed high variability depending on method of preparing, as well as under standardised settings.[15–24] A range of different terpenes, which gives cannabis the distinctive smell, have been identified in cannabis. It has been suggested that terpenes could have a synergistic effect with

1) Boil 500 ml. of water in a pot with a lid on
2) Add 0.5 g of cannabis product
3) Leave it to simmer over low heat for 15 minutes with the lid on
4) Take it off the heat and sieve the tea

Put the tea in a thermos if consumed the same day

If tea for more days is made, coffee creamer should be added

FIGURE 1 The recipe for preparation of standard tea.[9–11]

cannabinoids; however, this synergy known as the "entourage effect" is controversial and scientific evidence is lacking.[25,26] Terpenes are volatile compounds, and boiling temperature for 5 min decreased the amount of terpenes drastically whereas baking for 30 min at 145°C almost completely erased the content of terpenes in cannabis plant material.[14]

Based on the current knowledge, we hypothesised that cannabis tea from the different products would contain different doses of THC and CBD and that terpenes would evaporate from the tea. Thus, the aim of this study was to elucidate the doses of cannabinoids and terpenes in tea prepared from three different MCPs and to clarify the variability of the exposure under standard settings to inform choosing between the cannabis products in the Danish medicinal cannabis pilot programme, which all have identical recommended starting doses of 0.2 L pr. day. Furthermore, we wanted to elucidate the impact of different preparation methods such as addition of creamer and baking of the MCP.

2 | MATERIALS AND METHODS

The study was conducted in accordance with the Basic and Clinical Pharmacology and Toxicology policy for experimental and clinical studies.[27]

2.1 | Plant products

The MCPs used for preparation of cannabis tea were[28,29]:

- Bedrocan "CannGros," 22% total THC (THC + THCA) (*Cannabis sativa L.* ssp. sativa "Afina," flos (cannabis flower), total THC (THC + THCA) 220 mg/g, total CBD (CBD + CBDA) < 10 mg/g),[30] batch nr.: 011061 and expiry date 31.12.2020.
- Bediol "CannGros," 6.3% total THC (THC + THCA) and 8.0% total CBD (CBD + CBDA) (*C. sativa L.* ssp. sativa "Elida," flos (cannabis flower, granulated), total THC (THC + THCA) 63 mg/g, total CBD (CBD + CBDA) 80 mg/g),[31] batch nr.: 011062 and expiry date 30.09.2020.
- Bedica "CannGros," 14% total THC (THC + THCA) (*C. sativa L.* ssp. indica "Talea," flos (cannabis flower, granulated), total THC (THC + THCA) 140 mg/g, total CBD (CBD + CBDA) < 10 mg/g),[32] batch nr.: 933663 and expiry date 31.07.2020.

The company CannGros was informed about the study.

The content of cannabinoids was determined in plant material, and total THC (THC + THCA) and total CBD (CBD + CBDA) content in mg/g were calculated taking the differences in molar mass into account, with the formulas[28]:

$$\text{Total CBD (CBD + CBDA)} = \text{CBD} + 0.877 \cdot \text{CBDA}$$

$$\text{Total THC (THC + THCA)} = \text{THC} + 0.877 \cdot \text{THCA}$$

2.2 | Preparation of cannabis tea

Cannabis teas were prepared on the 5th of June 2020 according to Table 1, where three repetitions were made of each preparation. The creamer contained 35 g fat pr. 100 g. The Bedica product was baked in an oven for 30 min at 145°C (±10°C depending on place of temperature measurement in the oven) before preparation of tea with baked Bedica product. Preparations were transferred to brown glass vials, cooled at room temperature (up to 7 h) and stored at −80°C until analysis. Cannabis plant products were frozen (−80°C) in brown glass vials at the day of tea preparation and until analysis.

2.3 | Analysis of cannabinoids

Quantification of cannabinoids were performed in duplicates by ultra-performance liquid chromatography

TABLE 1 Methods for preparation of cannabis tea.

	Bedica	Bediol	Bedrocan
Standard recipe (Figure 1)	3 repetitions	3 repetitions	3 repetitions
Standard recipe with addition of 3 g of creamer after the 15 min of boiling	3 repetitions	3 repetitions	3 repetitions
Standard recipe with addition of 3 g of creamer prior to the 15 min of boiling	3 repetitions	3 repetitions	3 repetitions
Standard recipe, but prepared with baked cannabis product (145°C for 30 min)	3 repetitions		

coupled to a tandem mass spectrometer (UPLC-MS/MS) using a modified version of the previously published method.[33] In short, the modification consisted of addition of CBDA to the method (quantifier transition: 357.3 -> 245.0 and qualifier transition: 357.3 -> 311.2 monitored in negative mode) and quantification was done using stable isotope labelled CBD (CBD-D3) as internal standard.

Plant material (Bediol, Bedica, Bedrocan, baked Bedica) was homogenised using a standard blender and 1000 mg of the homogenised plant material was mixed with 20 mL methanol containing 1 mg/mL ibuprofen used for dilution control. The solution was mixed for 2 h and then centrifuged. The subsequent analysis consisted of diluting 100 μL supernatant 1000 times with 70% methanol and transferring 250 μL diluted sample or tea to a vial containing 15 μL 10% formic acid and 100 μL internal standard solution (0.002 mg/mL THC-D3, THCA-D3 and CBD-D3). Ten microlitres of the final diluted sample was injected on to the UPLC-MS/MS system. The measurement range was from 0.50 to 1000 mg/g in plant material and from 0.0005 to 500 μg/mL in tea and both precision and bias were below 15% for all compounds.

2.4 | Analysis of terpenes

The sample preparation for the terpene analysis was as follows: the cannabis flowers were grinded under liquid nitrogen and extracted with n-hexane (HPLC grade) where 300 mg cannabis flower were extracted with 3 mL n-hexane in the dark for 24 h while shaken. The samples were then centrifuged for 10 min at 3000 RPM, and the n-hexane was removed and ready for analysis. For the cannabis tea preparations, the tea was extracted with n-hexane the same way as the flowers with a volume ratio of 1:0.1 tea: n-hexane. All extract samples were stored at −18°C until analysis. Quantification of terpenes was performed by gas chromatography coupled to flame ionisation detector (GC-FID). The method used was as follows: A GC Agilent 7820A is equipped with an FID detector and a DP5 column. Injection volume was 1 μL, injector temperature 240°C, split ratio 10:1, flowrate 1.2 mL/min, and the carrier gas was helium. The temperature programme started at 60°C and increased at a rate of 3°C/min until 240°C with a hold time of 5 min, with a total run time of 66 min/analysis. Triplicate determinations were performed, and a deviation higher than 10% led to reanalysis. Quantifications were made in cannabis plant products (Bediol, Bedica, Bedrocan, baked Bedica) and tea preparations. 1-Octanol was used as internal standard.

2.5 | Data analysis

Cannabinoid concentrations in tea are presented as the median of the three repetitions of tea preparation (each quantified in duplicates) for each recipe along with the minimum and maximum concentration. Calculations were made in Microsoft® Excel® for Microsoft 365. Differences between concentrations in teas prepared with the same product but with different recipes were analysed by Kruskal-Wallis test followed by Dunn's test corrected for multiple comparisons. Standard tea was used as control and compared to the two other recipes, respectively.

Differences between concentrations in teas prepared with the same recipe but with different products were analysed by Kruskal-Wallis test followed by Dunn's test corrected for multiple comparisons. Bediol was used as control and compared to Bedica and Bedrocan, respectively.

The statistical analysis was performed with GraphPad Prism version 10.2.1.

Terpene concentrations in all samples are presented as mean of the three repetitions for each sample ± SD. Calculations were made in Microsoft® Excel® for Microsoft 365.

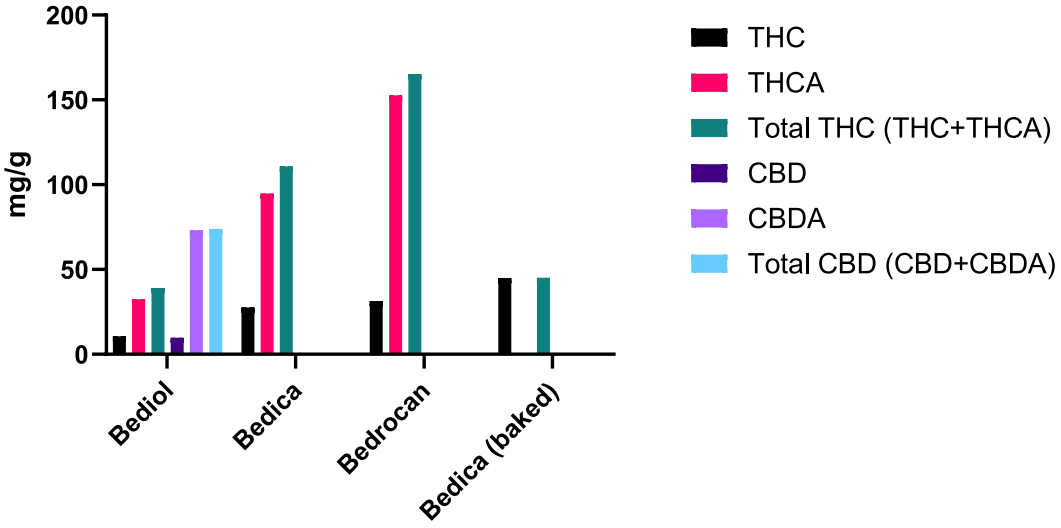

FIGURE 2 Content of cannabinoids in cannabis plant material. CBD, cannabidiol; CBDA, cannabidiolic acid; THC, tetrahydrocannabinol; THCA, tetrahydrocannabinolic acid.

The span of doses of THC, CBD, THCA, and CBDA contained in 0.2 L of each tea was calculated from the measured min-max concentration values, as 0.2 L is the recommended starting dose for all of the products when prepared as standard tea.[9–11]

3 | RESULTS

3.1 | Cannabis plant material

The results of quantification of cannabinoids in cannabis plant material are presented in Figure 2. The measured total THC (THC + THCA, THC + 0.877·THCA) contents were 39, 111, and 165 mg/g corresponding to 62%, 79%, and 75% of the labelled total THC (THC + THCA) in Bediol, Bedica, and Bedrocan, respectively. The main part of the total THC (THC + THCA) content originated from THCA, where the content was 32, 95, and 153 mg/g for Bediol, Bedica, and Bedrocan, respectively. The baked Bedica product differed substantially from the other plant products with a content of THCA which was close to zero and a THC content of 45 mg/g.

The total CBD (CBD + CBDA, CBD + 0.877·CBDA) content in Bediol was 74 mg/g, and the main part originated from CBDA where the content was 73 mg/g. The measured total CBD (CBD + CBDA) content in Bediol corresponded to 92% of the labelled total CBD (CBD + CBDA).

The results of quantification of terpenes in cannabis plant material are presented in Table 2. Twenty-two different terpenes were quantified in the different plant material analysed.

3.2 | Cannabis standard tea

Figures 3 and4 show the individual concentrations of cannabinoids in cannabis tea according to cannabis plant product and preparation method. After standard preparation, the concentrations of THC (Figure 3A) were 9.5 (min 2.3, max 15), 19 (min 13, max 34), and 36 (min 26, max 57) μg/mL in tea prepared from Bediol, Bedica, and Bedrocan, respectively. The concentrations of THCA were higher than THC in all preparations and were 14 (min 8.9, max 16), 35 (min 35, max 40), and 45 (min 35, max 48) μg/mL, respectively (Figure 3B). CBD and CBDA were only present in considerable amounts in tea prepared from Bediol, where the concentrations were 7.5 (min 1.9, max 10) and 51 (min 50, max 58) μg/mL, respectively (Figure 4).

3.3 | Tea with creamer

Adding creamer to the standard recipe prior to boiling resulted in a 2.3–4.4-fold increase in median THC and a 0.8–1.7-fold change in median THCA concentrations in the different teas, which was significant for tea prepared with Bedica, but not Bediol and Bedrocan (Figure 3). Adding creamer prior to boiling increased the median CBD concentration 2.1-fold for tea prepared with Bediol. The changes were not statistically significant for CBD ($p = 0.54$), nor for CBDA ($p = 0.63$) (Figure 4). Adding creamer to the standard tea after boiling did not significantly change the cannabinoid concentrations (Figures 3 and4).

TABLE 2 Content of terpenes in cannabis plant material presented as mean ± SD.

Terpene (μg/g)	Bediol	Bedica	Bedrocan	Bedica (baked)
α-Pinene	2230 ± 90	2517 ± 50	1550 ± 62	0.025 ± 0.0003
γ-Terpinene	0.318 ± 0.02	0.233 ± 0.01	0.916 ± 0.02	N/D
Linalool	0.409 ± 0.02	5167 ± 155	2383 ± 95	0.332 ± 0.003
β-Pinene	0.803 ± 0.04	0.497 ± 0.01	2310 ± 69	0.001 ± 0.00001
Limonene	0.646 ± 0.03	0.321 ± 0.01	7011 ± 280	0.049 ± 0.001
Myrcene	15 965 ± 479	6002 ± 240	13 212 ± 528	0.168 ± 0.003
Trans-caryophullene	5727 ± 229	7621 ± 304	10 404 ± 416	0.368 ± 0.004
Geraniol	5127 ± 154	4502 ± 135	5770 ± 807	0.510 ± 0.01
Camphene	0.0426 ± 0.002	0.028 ± 0.0005	0.041 ± 0.0008	N/D
Humulene	2472 ± 99	2972 ± 89	4536 ± 181	0.185 ± 0.004
3-Carene	0.314 ± 0.006	0.145 ± 0.003	0.859 ± 0.02	N/D
α-Terpinene	0.556 ± 0.01	0.434 ± 0.009	1666 ± 67	N/D
Fenchone	6074 ± 243	0.056 ± 0,0007	N/D	N/D
Fenchol	N/D	0.081 ± 0.002	0.252 ± 0.003	N/D
Camphor	0.600 ± 0.007	0.125 ± 0.001	0.718 ± 0.007	N/D
Isoborneol	0.152 ± 0.006	N/D	0.162 ± 0.003	0.049 ± 0.0005
Borneol	N/D	0.111 ± 0.001	0.206 ± 0.006	0.077 ± 0.002
α-Terpineol	0.677 ± 0.02	0.258 ± 0.005	3109 ± 93	N/D
Pulegone	0.172 ± 0.003	0.153 ± 0.003	0.172 ± 0.002	0.165 ± 0.003
Cedrene	0.871 ± 0.02	N/D	0.165 ± 0.002	N/D
Cedrol	N/D	9619 ± 289	1038 ± 31	N/D
Nerolidol	0.592 ± 0.02	4814 ± 192	1298 ± 65	N/D

Abbreviations: N/D, not detected; SD, standard deviation.

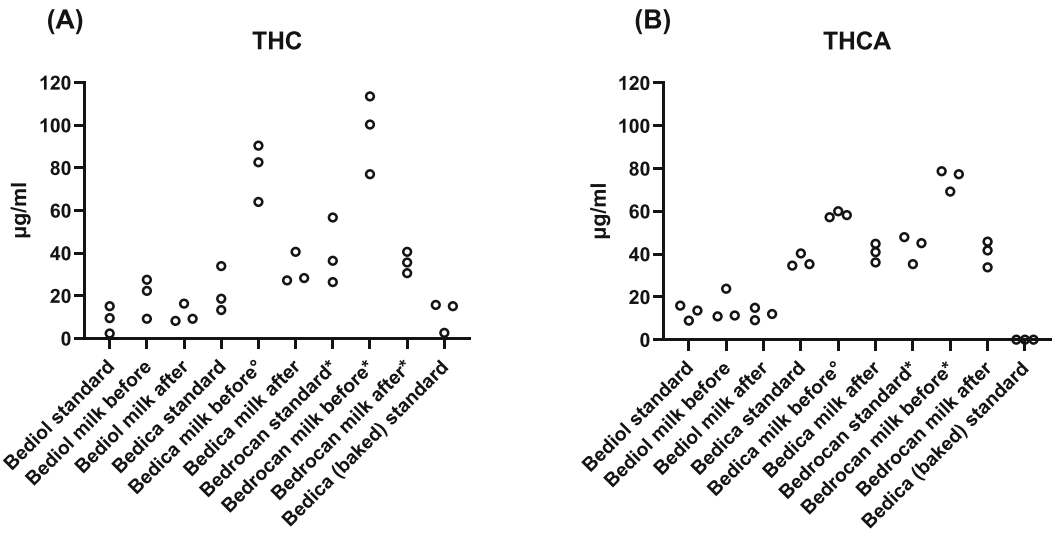

FIGURE 3 Content of THC and THCA in cannabis tea presented as individual measured concentrations. THC, tetrahydrocannabinol; THCA, tetrahydrocannabinolic acid. *significant difference in concentrations between tea prepared with this product and tea prepared with Bediol, when prepared with the same recipe. °significant difference in concentrations between tea prepared with this recipe and tea prepared with the standard recipe, when prepared with the same product.

3.4 | Comparison of tea from different products

The concentrations of THC and THCA were highest in cannabis tea prepared from Bedrocan, which had the highest content of total THC (THC + THCA), and lowest in tea prepared from Bediol, which had the lowest content of total THC (THC + THCA). Tea prepared with Bedrocan had significantly higher concentrations of both THC and THCA compared to tea prepared with Bediol, except for the THCA concentration in tea prepared with milk after boiling, when the same recipe was used (Figure 3).

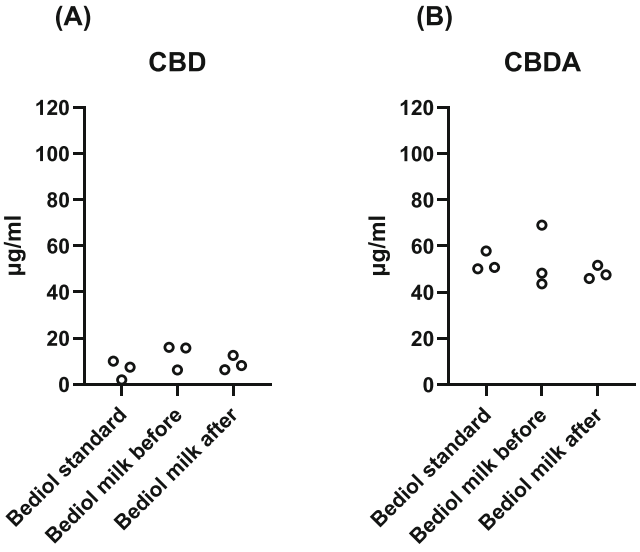

FIGURE 4 Content of CBD and CBDA in cannabis tea presented as individual measured concentrations. CBD, cannabidiol; CBDA, cannabidiolic acid.

Tea prepared according to the standard recipe with baked Bedica had a THC concentration of 15 (min 2.7, max 16) µg/mL (Figure 3A).

3.5 | Doses of THC, CBD, THCA, and CBDA in 0.2 L tea

THC dose in 0.2 L tea ranged from 0.46 mg in Bediol standard tea to 22.7 mg in Bedrocan tea with creamer added before boiling. CBD dose ranged from 0.38 mg in standard Bediol tea to 3.2 mg in Bediol tea with creamer added before boiling. For THCA and CBDA, the doses ranged from 1.8 to 15.7 mg and 8.7 to 13.8 mg, respectively (Table 3).

3.6 | Terpenes in cannabis tea

No terpenes were detected in any of the tea preparations.

4 | DISCUSSION

The main findings of the present study were that cannabis tea contained varying doses of cannabinoids, when the same tea preparations were repeated, and when different plant products and preparation methods were used, and that no terpenes were detected in any of the teas.

In cannabis plant material, we found a total THC (THC + THCA) and total CBD (CBD + CBDA) content, which were lower than labelled on the products. We found an apparently higher content of THC and a lower content of THCA in Bedrocan plant product compared to

TABLE 3 Doses of THC, THCA, CBD, and CBDA contained in 0.2 L of the different teas.

Tea	THC dose in 0.2 L (mg)	THCA dose in 0.2 L (mg)	CBD dose in 0.2 L (mg)	CBDA dose in 0.2 L (mg)
Bediol standard	0.46–3.0	1.8–3.2	0.38–2.0	10.0–11.6
Bediol creamer added before boiling	1.8–5.5	2.2–4.8	1.2–3.2	8.7–13.8
Bedica standard	2.7–6.8	6.9–8.1		
Bedica creamer added before boiling	12.8–18.1	11.5–12.0		
Bedrocan standard	5.3–11.3	7.1–9.6		
Bedrocan creamer added before boiling	15.4–22.7	13.9–15.7		

Note: Calculated based on the min–max concentrations measured in the present study. 0.2 L is the recommended starting dose for all cannabis plant products in the Danish medicinal cannabis pilot programme.
Abbreviations: CBD, cannabidiol; CBDA, cannabidiolic acid; THC, tetrahydrocannabinol; THCA, tetrahydrocannabinolic acid.

a study by Hazekamp et al.[16] They found a THC content of 6 mg/g and a THCA content of 191 mg/g, which correspond to a total THC (THC + THCA) of 174 mg/g. It could be expected that the cannabinoid content of plant material decreases over time, due to decarboxylation while in storage.[13] Reanalysis of the same cannabis plant material after 1 year has shown an increase in the content of THC and CBD, a decrease in THCA and CBDA, and an overall decrease in total THC (THC + THCA) and total CBD (CBD + CBDA).[19] Thus, our finding of a higher content of THC and a lower content of THCA may suggest that our product has been older. This supports that a shelf-life of 1 year has been added to the product sheets for Bedrocan, Bediol, and Bedica during the pilot programme.[9–11,30–32] The measured content of cannabinoids in plant material can in addition to decarboxylation while in storage be influenced by the analysis method, where adsorption to surfaces is an issue,[29,34] and by biological variance between different plants in a batch.

However, our results may suggest that the variability of THC and CBD doses in tea can be higher than observed in the present study, if products with different age are used.

In our study, the doses of THC and THCA contained in cannabis tea prepared according to the standard recipe, reflected the total THC (THC + THCA) content in the plant product. A higher content of total THC (THC + THCA) in the plant product resulted in higher doses of THC and THCA in the tea. However, a high variability of THC was seen between the three repetitions of each standard tea ranging from a factor 2.1 with tea prepared from Bedrocan to 6.5 with tea prepared from Bediol. "Standard recipes" of cannabis tea differ between studies, and different cannabis products are used. Therefore, a direct comparison between the different cannabis tea studies is difficult. However, one study has determined the concentration of THC in tea prepared with Bedrocan. The study found a mean THC concentration of 10 μg/mL, a mean THCA concentration of 43 μg/mL, and a variability of 15% and 12%.[16] The THC concentration is only 28% compared to our findings, whereas the THCA concentration is similar. Differences in the preparation methods, where a larger amount of tea was prepared, could influence the result even though the same study does not find that changing water volume and amount of cannabis plant product significantly changes the content.[16] Concentrations of cannabinoids in tea made from the Italian cannabis strain named FM2 have been investigated thoroughly in several studies.[15,19–24] FM2 contains 5–8% total THC (THC + THCA) and 7–12% total CBD (CBD + CBDA), which is similar to Bediol. In general, the cannabinoid concentrations found in these studies are consistent with our concentrations in tea prepared with Bediol, when the preparation method was comparable (Table 4). In the study by Baratta et al.,[19] 146 tea samples were made with different water volumes and different ratios between water and cannabis plant material. In samples where the ratio of cannabis plant material and water were similar to ours, their results were consistent with our findings (Table 4). As in our study, they found a high variability in the cannabinoid concentration between the same preparations with up to a factor 9.5 difference in the THC concentrations.

Adding creamer to the standard recipe after boiling is the recommended procedure if tea for more days is prepared at the same time.[9–11] This did not change the concentrations of cannabinoids, which has been shown in an earlier study as well.[16] However, deviating from the instruction by adding creamer to the standard recipe

TABLE 4 Concentrations of cannabinoids in tea prepared from the Italian cannabis strain FM2.

Reference	THC (μg/mL)	THCA (μg/mL)	CBD (μg/mL)	CBDA (μg/mL)	Comment
Pérez-Acevedo[23,24]	3	12	7	44	
Baratta 2019[19]	8.7	18.1	10.7	48.3	39 samples
	7.2	18.1	10.1	51.8	6 samples
	8.3	19.1	10.9	53.6	6 samples
Pacifici 2017[15]	7	8	9	38	
Pichini 2020[21]	3.6	16	4.2	40	
Pellesi 2018[20]	9.25	11.1	9.65	44.1	
Barco 2018[22]	22.4		19.2		Added milk
Our results (median):					
Bediol standard tea	9.5	14	7.5	51	
Bediol creamer added before boiling	22	11	16	48	

Abbreviations: CBD, cannabidiol; CBDA, cannabidiolic acid; THC, tetrahydrocannabinol; THCA, tetrahydrocannabinolic acid.

before boiling significantly increased the exposure to THC and THCA for tea prepared with Bedica. This was expected due to the lipophilic nature of the cannabinoids and findings in earlier studies. Surprisingly, the concentrations of CBD and CBDA were not statistically significantly increased by adding creamer before boiling, even though CBD and CBDA are lipophilic structures with a high extraction in oil[19] and a high partition coefficient (log P, CBDA > CBD > THCA > THC).[35]

The recommended starting dose of 0.2 L tea is equal for all three products analysed in the present study. However, the exposure to THC could be as low as less than 0.5 mg to more than 10 mg pr. 0.2 L of tea depending on which product is used for preparation of the standard tea. Violating the instruction by adding creamer before could increase the dose to more than 20 mg in Bedrocan tea. The recommended starting dose for Sativex, which contains both THC and CBD, is one spray containing 2.7 mg THC and 2.5 mg CBD.[36] Thus, initiating treatment with tea could probably result in both under and overdosing THC depending on which product is prescribed. With regard to CBD, initiating treatment with 0.2 L Bediol tea would most likely be subtherapeutic, and to reach maximum recommended doses of Sativex (32.4 mg THC and 30 mg CBD[36]), it would require intake of 3.0–15.6 L standard Bediol tea pr. day according to our measurements.

The acidic precursors THCA and CBDA were abundant in cannabis tea. Pre-clinical studies have suggested several pharmacodynamic effects of the acidic precursors,[35,37,38] but clinical evidence is lacking. Notably, CBDA was found in considerably higher concentrations than CBD in Bediol teas. We did not bake the Bediol plant product, but the total decarboxylation of THCA to THC in the baked Bedica product may suggest that baking of Bediol could increase the dose of CBD in tea prepared from this product. However, baking of the Bedica plant product before preparing tea did not numerically increase the dose of THC in the tea.

In cannabis plant material, a range of different terpenes were quantified. In the baked Bedica product, the content of terpenes was low compared to the non-baked, which is in agreement with the volatile nature of terpenes and earlier findings.[14] In tea preparations, no terpenes were detected, which again could be due to the volatile and lipophilic nature of terpenes.[25]

This study has some limitations. Only three repetitions were made of each preparation of cannabis tea. More repetitions could have given more robust data. We had no control with the boiling temperature, but this would also be the case, when patients prepare cannabis tea in their own kitchen.

5 | CONCLUSION

The present study elucidates THC, THCA, CBD, and CBDA doses in different teas, which may assist the clinician's choice of cannabis product. Initiating treatment with the recommended starting dose of 0.2 L tea made of the three products may result in underdosing using Bediol, and overdosing using Bedrocan, if starting doses of THC comparable to the starting dose of Sativex are aimed for. Moreover, the study underscores the need for caution using cannabis administrated as tea because of uncertainty about the actual dose contained in each preparation, even when the same cannabis product and recipe is used. Furthermore, adding creamer to the tea before boiling instead of after, as recommended, increases the median THC and CBD dose 2.1–4.4-fold. The study does not support an entourage effect of cannabis tea, as no terpenes were detected in tea.

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CONFLICT OF INTEREST STATEMENT

The authors declare no conflicts of interest.

DATA AVAILABILITY STATEMENT

The data that support the findings of this study are available from the corresponding author upon reasonable request.

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