Study report

The Volcano® *Medic* cannabis vaporizer: Optimal temperature for single-dose administration of 100 mg cannabis or 10 mg Dronabinol

LabAssistent Phytochemical Services
Utrechtse Veer 12b
Leiden, The Netherlands

Partner of PRISNA BV
Product Isolation from Nature

Performed this study for:
Storz&Bickel GmbH
Tuttlingen
Germany

LabAssistent project #:
2010-003c

Study period:
February-March 2010

This report has 13 pages, including this first page

Introduction

The Volcano Medic®, by Storz & Bickel, has been developed for the medical administration of cannabinoids present in herbal cannabis (flos) or in ethanolic solution (Dronabinol, THC). Previous studies showed that a single load of the filling chamber can be used several times before the load is exhausted. Although this approach may reduce costs, it is not common practice for patients to use the same medicine more than once. Although consecutive balloon fillings (up to 4-6 fillings) all contain significant amounts of cannabinoids, the relative composition of each balloon is different, even more so when the volatile terpenoids present in cannabis flos are considered. As a result, the repeated use of a single load can not result in a reproducible administration of medicinal compounds from cannabis.

Another approach to reduce the cost of cannabinoid medication administered by means of the Volcano Medic, is to determine the lowest loading dose of cannabis or Dronabinol that still has a significant medicinal effect (minimizing costs). When that specific load is used, and only a single balloon can be filled with it, the loss of cannabinoids in the residue should be reduced to a minimum (efficient use). At the same time, the amount of THC maximally released into the vapor should not be so high that accidental overdosing can occur (safety). All this should be achieved by determination of the right temperature setting in combination with a minimal amount of loaded sample.

At first glance, the highest temperature setting seems to be the obvious choice because the highest amount of cannabinoids will evaporate (high efficacy). A low content of cannabinoids in left-over material has the added effect that materials, once used, have no significant abuse potential, for example when a child accidentally opens up a used filling chamber, or a sample is improperly exposed of (safety concerns). However, a higher temperature results in a harsher taste of the vapor, leading to irritation of the throat and coughing in many users. For that specific reason, the evaporation temperature should be as low as possible, as 185°C is preferred by many users (user-friendly). For optimal use of the Volcano vaporizer, a balance has to be found between all these requirements.

Based on previous study reports it was concluded that 100 mg of Bedrocan cannabis material is the optimal amount that fits these requirements. With a THC content of ca. 20% this is equivalent to 20 mg of THC present in the loaded sample. At the highest temperature setting of 230°C it was previously determined that 56% of THC is evaporated into the balloon This amounts to about 11 mg of THC, which is close to the range of 2.5 – 10 mg that is considered as relatively safe for a single dose administration of THC by most researchers (see clinical trials). At lower temperature settings (190-220°C) the amount of THC should drop within the 2.5 – 10 mg range.

The goal of this study is to determine the optimal temperature for the single dose administration of 100 mg of Bedrocan cannabis flos, varieties *Bedrocan* and *Bediol*. First, a quick 'scan' of temperature settings (190 - 200 - 210 - 220 - 230°C) was performed with a single experiment at each setting. Based on the results, the two most promising

temperature settings were tested in more detail by performing experiments in three-fold. At the same two temperatures, the evaporation of 10 mg Dronabinol was evaluated. During each experiment, a second balloon was filled with the same load of the filling chamber, in order to determine the abuse potential of left-over material. Finally, the used material (cannabis flos or liquid pad) was extracted to quantify non-evaporated cannabinoids. The final goal of the study is to find a single temperature setting that can be used for the administration of herbal cannabis material, as well as Dronabinol solution, is a safe, cost-effective, efficient, and user-friendly way.

Experimental

Solvents

All organic solvents were analytical grade and obtained from Merck Biosolve Ltd. Valkenswaard, The Netherlands.

Cannabis plant material

Variety *Bedrocan*: Batch number *(A1)01.87.011208*; harvest date March 2, 2009.
Variety *Bediol*: Batch number *(A1)05.23.080908*; harvest date December 1, 2008

Cannabis plant material (female flowertops) was medical grade and obtained from Bedrocan BV (Veendam, The Netherlands). Plants were cultivated under standardized conditions according to the requirements of Good Agricultural Practice (GAP). After harvest, the plant material was air-dried in the dark under constant temperature and humidity for 1 week. Materials were stored in a freezer (-20°C) until used in our study. The same cannabis material is officially dispensed through Dutch pharmacies under the Dutch medicinal cannabis program, supervised by the Office of Medicinal Cannabis (OMC).

Cannabis used in the study was grinded with the Storz&Bickel Grinder, as delivered with the Volcano device, and homogenized by mixing with a spoon. Material was used immediately without storage.

THC solution

Pure THC was isolated from herbal cannabis material, obtained through Bedrocan BV, the Neherlands. The methods for isolation and quality control have been published, and are available from LabAssistent. The final THC solution had a concentration of 25 mg/ml (2.5%) in ethanol, and had a purity of ≥98%. Batch number was THC#580. A full Certificate of Analysis is available from LabAssistant. No significant amounts of the THC degradation products delta-8-THC or CBN were present.

Overview of Vaporizing Conditions

The following settings and conditions were used for the experiments:

- Volcano type: Medic (Digit for 220-230°C)
- Filling chamber type: Easy valve
- Valve type: Easy valve
- Mouthpiece type: Medic
- Temperature setting:
  - *Bedrocan*, *Bediol* 190-200-210-220-230°C
  - THC 200-210°C
- Amount of filling:
  - Bedrocan, Bediol: 100 mg
  - THC 10 mg
- Balloon: standard balloon

Filling of the balloons

Cannabis material

For each experimental condition an exact amount of grinded material was accurately (+/-0.5 mg) weighed on a calibrated analytical balance and placed in the standard filling chamber of the Volcano. The filling chamber was placed onto a Volcano apparatus set at the desired temperature (range 190-230°C) and the balloon was filled according to the instructions of the manufacturer. The balloon was then removed from the filling chamber and the vapor was extracted within two minutes. The filling chamber was allowed to cool down to room temperature (ca. 10 min) before filling the second balloon.

After filling two consecutive balloons, the cannabis was removed from the filling chamber and extracted with ethanol. In this way, the amount of residual (non-vaporized) cannabinoids in the plant material could be determined.

N.B.: for the experiments performed at 220°C and 230 °C a Volcano Digit was used, as the temperature setting of the Volcano Medic is limited to 210°C.

THC solution

The ethanolic THC solution was accurately placed onto the liquid pad present in the filling chamber, by using a precision pipette. Alcohol was evaporated on the Volcano vaporizer at 100°C for 1 minute without a balloon attached to the filling chamber. THC does not evaporate under these conditions. The filling chamber was placed onto a Volcano apparatus set at the proper temperature (200 or 210°C) and the balloon was filled according to the instructions of the manufacturer. The balloon was then removed from the filling chamber and the vapor was extracted within two minutes. The filling chamber was allowed to cool down to room temperature (≥ 10 min) before filling the second balloon.

After filling two consecutive balloons, the liquid pad was removed from the filling chamber and extracted with ethanol. In this way, the amount of residual (non-vaporized) THC present on the liquid pad could be determined.

Preparation of vapor extracts

Cannabinoids were recovered from the vapor inside the balloon by condensation onto glass fiber filters, designed to capture particles ≥ 0.1 microns. Glass fiber filters (Cambridge type, borosilicate glass, 44 mm diameter) and tightly fitting filter holders for vapor extraction were obtained from Borgwaldt Technik GmbH (Hamburg, Germany). The Volcano Medic mouthpiece was connected to the filled balloon. With the use of a vacuumpump, the vapor was aspired through the glass-fiber filter with a constant flow of 30L/min. The filter was then placed in a 50ml plastic tube and extracted with ethanol (15ml, 10 min, under constant agitation). Extraction was repeated three times and extracts were combined. Ethanol was added to a final volume of exactly 50ml. These final vapor extracts were stored at -20°C until analysis.

Cannabinoid analysis by UPLC

Quantitative analysis was performed with a Waters Acquity Ultra Performance LC (UPLC) system. The UPLC method used for the quantitative analysis of cannabinoids present in the vapor extracts has been fully validated according to ICH guidelines. This method is part of the official Dutch Monography for the quality control of medicinal cannabis distributed through Dutch pharmacies. The ethanolic samples (vapor extracts) were diluted 10 times in the mobile phase of the UPLC method (acetonitrile/water 70:30, + 0.1% formic acid), and analyzed by UPLC to determine the cannabinoid composition.
The UPLC system consisted of a Solvent Delivery Pump (Serial number: J05UPB 162M), an Auto Sampler (Serial number: J05UPS 062M), and a Photodiode Array Detector (Serial number: J05UPD 449M). Equipment control, data acquisition and integration were performed with Water Empower 2 software. Chromatographic separation was achieved using a Waters C_{18} analytical column (1.7µm, 2.1x150 mm) protected by a Waters C_{18} guard column. The mobile phase consisted of acetonitrile and water, both acidified with 0.1% formic acid. The gradient elution is shown below:

t(min.)	% water	% acetonitrile
0.0	30	70
6.0	30	70
10.5	0	100
10.7	0	100
11.0	30	70
12.5	30	70

Total runtime was 12.5 minutes. Flow-rate was set to 0.3 ml/min, the injection volume was 10µL, and detection wavelength was 228 nm. For identification of cannabinoids,

full UV-spectra were recorded in the range of 200-400nm. All experiments were carried out at a column temperature of 30°C.

Processing of the data

Peaks were quantified at 228nm with the use of calibrated standards. All original data (chromatograms and integration data) is available from LabAssistent.

The following cannabinoids were quantitatively analyzed:

- THC delta-9-tetrahydrocannabinol
- THCA tetrahydrocannabinolic acid
- CBD cannabidiol
- CBDA cannabidiolic acid
- CBN cannabinol (degradation product of THC)
- D8-THC delta-8-tetrahydrocannabinol (degradation product of THC)
- CBG cannabigerol
- CBC cannabichromene

Other cannabinoids were below the threshold of UV-detection.

Results

Results of the quantitative UPLC analyses are presented in bar-diagrams in appendices 1-4. Values are expressed as milligrams of cannabinoid present in the balloon.

Bedrocan & Bediol

The quick scan of temperatures (appendix 1) indicated that the settings 200°C and 210°C were the two temperatures that fulfilled the requirements set out in the introduction of this report:

- THC content of the balloon is below the level of 10 mg (risk of overdosing)
- Temperature as low as possible, to reduce risk of irritation of the lungs (user comfort)
- High proportion of cannabinoids evaporated into the first balloon (efficacy)
- No significant abuse potential of the left-over material (safety)

Experiments at these temperature settings were repeated in three-fold in order to calculate mean values and standard error. Results for cannabis, variety *Bedrocan* are shown in appendix 2, for variety *Bediol* in appendix 3.

Dronabinol (THC) solution

The temperature settings 200°C and 210°C were also applied for the evaporation of Dronabinol (THC in ethanolic solution). Results are shown in appendix 4. No degradation products such as delta-8-THC or CBN could be detected.

Discussion & Conclusion

This study was performed to determine the optimal temperature setting for the administration of a 100 mg loading dose of cannabis, or a 10 mg loading dose of THC. A quick scan of temperature settings over the range of 190-230°C indicated that 200 and 210°C were the two settings most likely to yield the desired results. To confirm this, experiments at both settings were repeated in three-fold for more accurate mean values. Based on the final results, an evaporation temperature of 210°C was selected as most optimal. This setting combines a high delivery of cannabinoids, and acceptable taste, with a low residue of cannabinoids in the left-over material. At 210°C, the second balloon contains less than half the amount of cannabinoids present in the first balloon. This implies that a filling chamber left unattended after use, has only very limited abuse potential.

The setting of 210°C also seems to be ideal for the evaporation of pure THC; almost 60% of the loaded dose (10 mg) of THC was recovered from the vapor. The second balloon filled with the same load contained almost no more THC (< 0.5 mg), even further reducing the risk of abuse after administration.

Because the maximum temperature setting of the Volcano Medic has been set to 210°C, the patient using the Volcano at home can never accidentally overdose himself. In case of making a mistake, the temperature setting can only be lower than 210°C, resulting in a *lower* dose of cannabinoids, but never a higher one. As a result, the use of a pre-dosed amount of 100 mg *Bedrocan*/*Bediol* or 10 mg THC, in combination with the Volcano Medic, is a virtually 'idiot-proof' administration form for medicinal cannabinoids.

It is interesting to note that at the highest setting of 230°C, ca. 11 mg of THC was detected in the balloon, corresponding perfectly to the calculated amount as described in the introduction of this report (based on a delivery of 56%). This indicates once more the reproducibility of cannabinoid administration with the Volcano vaporizer.

DISCLAIMER: The results presented in this report have been obtained with two specific medicinal strains of Cannabis (Bedrocan variety *Bedrocan*, and *Bediol*), and may not apply to other types of herbal cannabis. Additional study should be performed before making any claims about the efficacy of vaporizing materials other than those specified in this report.

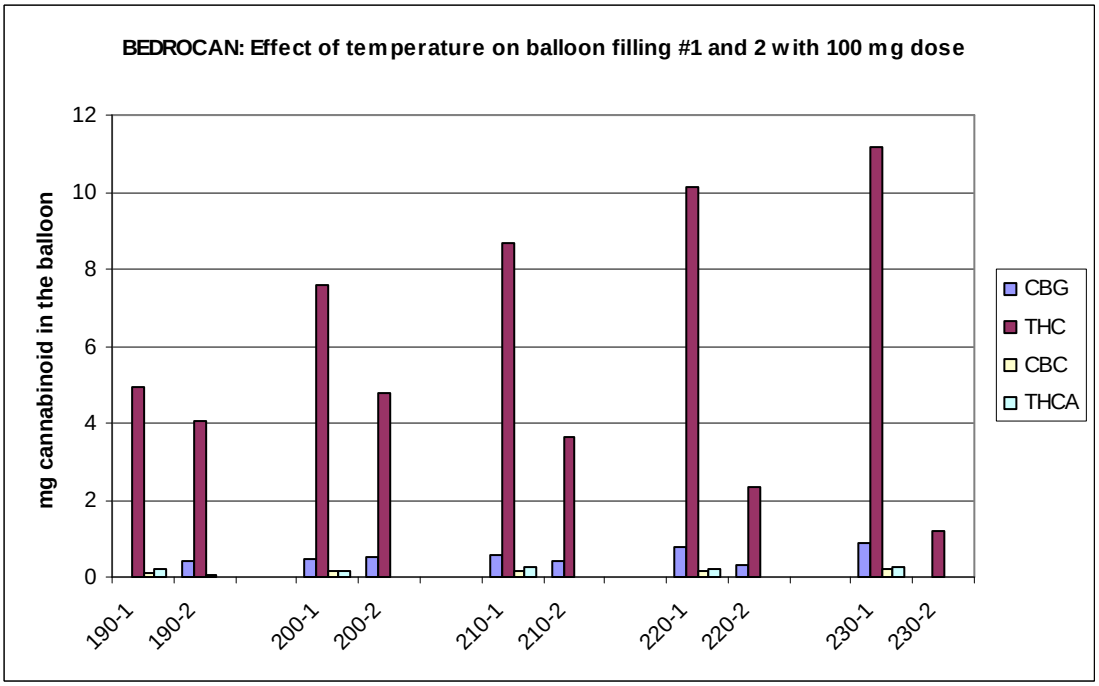
This report was prepared in Leiden, The Netherlands, by Arno Hazekamp:

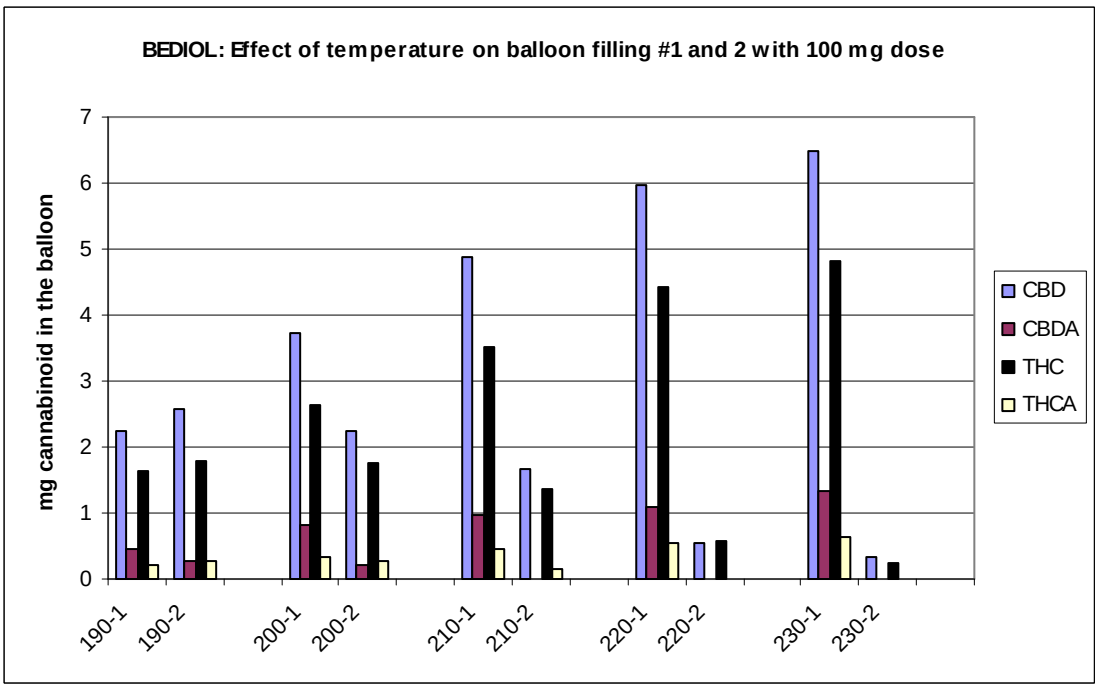
Signed:

Dr. Arno Hazekamp
Study director
LabAssistent

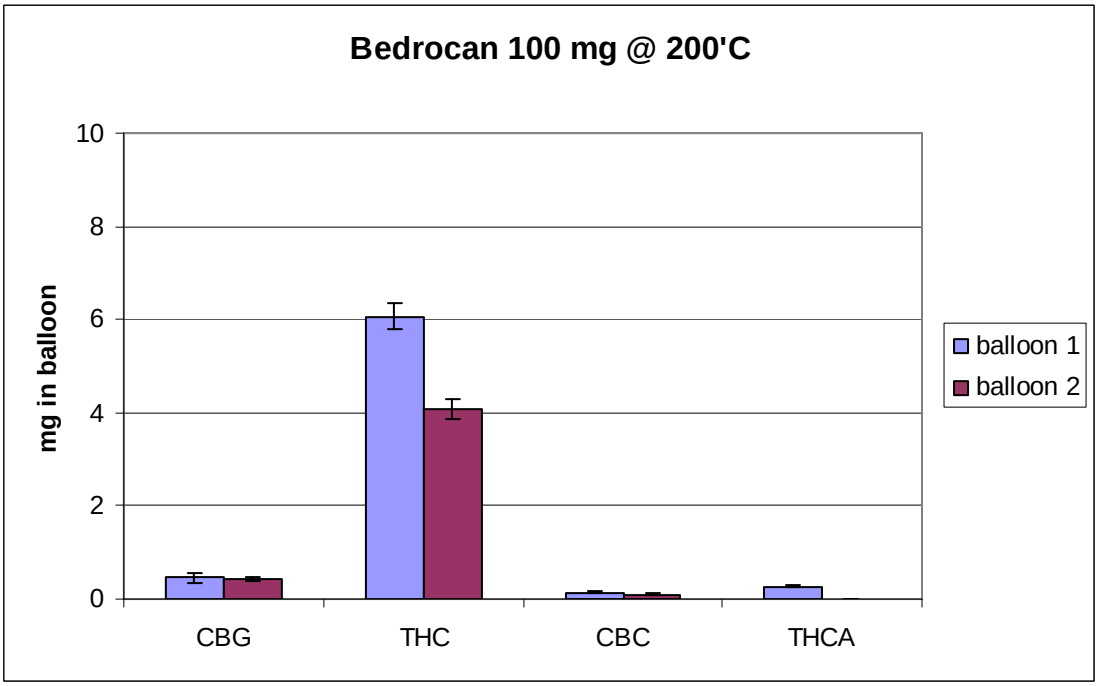
Leiden, 24 March 2010

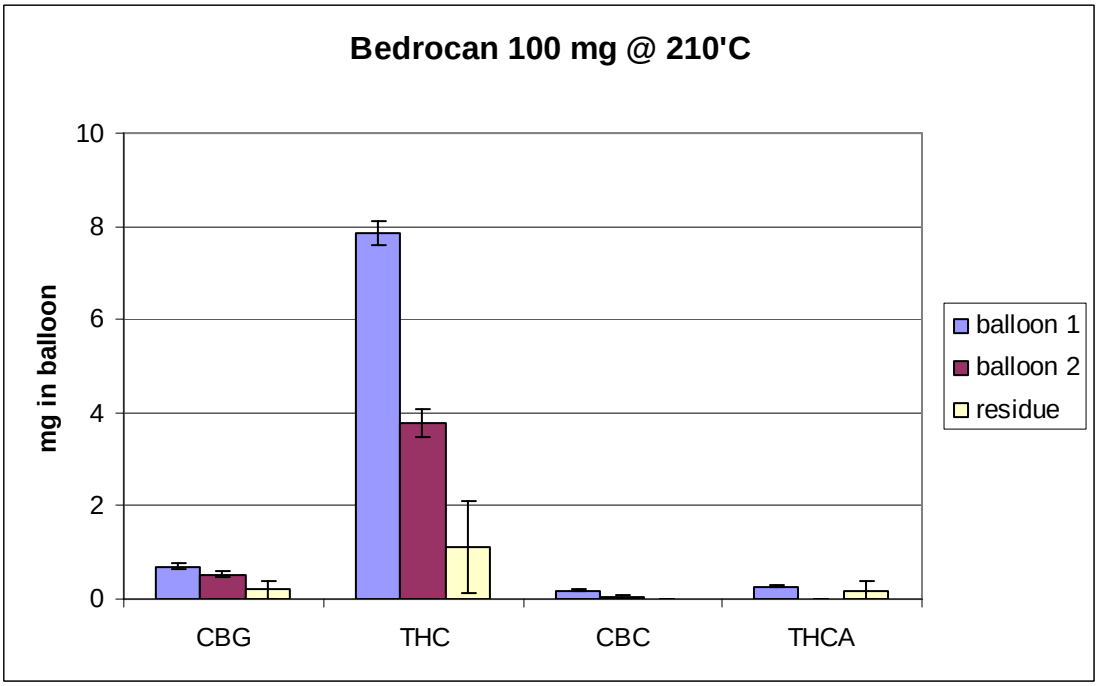
APPENDIX 1: Quick scan of optimal temperature setting(s) for Bedrocan and Bediol. Bars show milligrams of cannabinoids detected in the balloon. Data is based on single experiments.



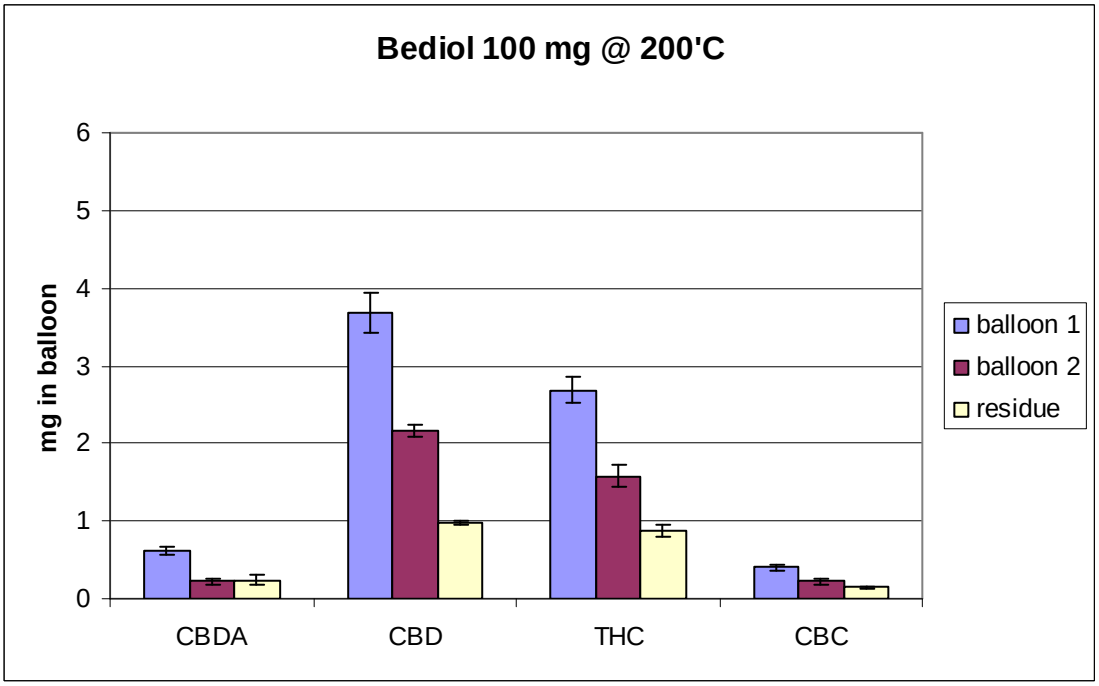


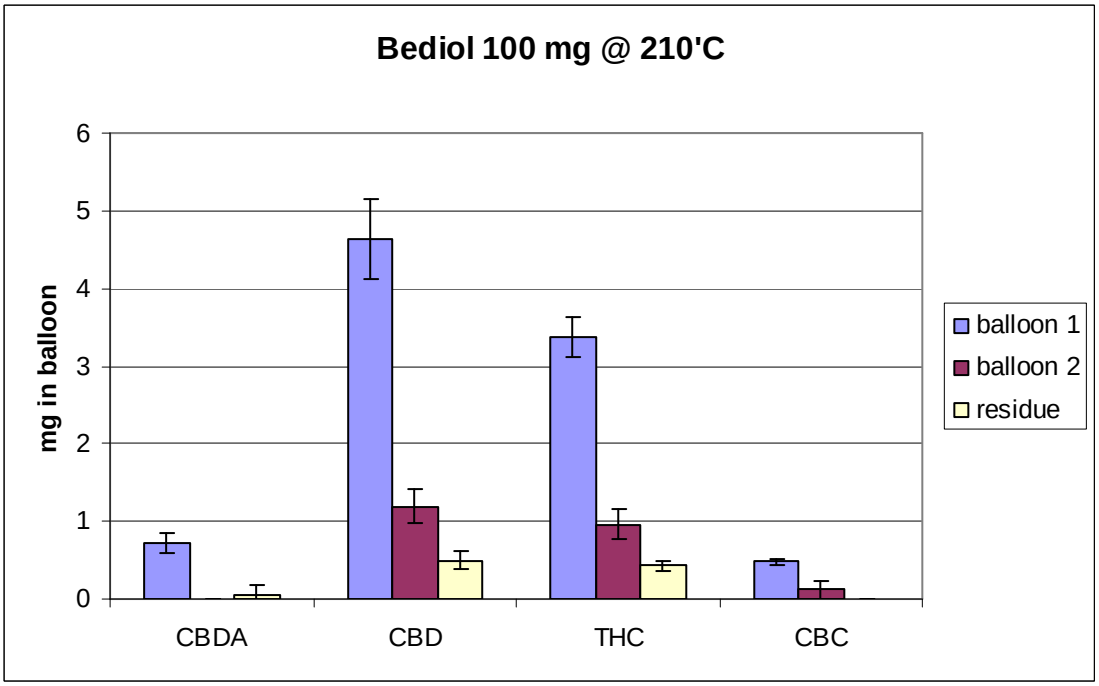
APPENDIX 2: Evaporation of *Bedrocan* at 200ºC en 210ºC. Bars show milligrams of cannabinoids detected in the balloon. Errorbars indicate standarderror, based on n=3 measurements.
N.B.: for the experiments at 200ºC the residue remaining in the filling chamber was not measured.





APPENDIX 3: Evaporation of *Bediol* at 200ºC en 210ºC. Bars show milligrams of cannabinoids detected in the balloon. Errorbars indicate standarderror, based on n=3 measurements.





APPENDIX 4: Evaporation of THC (Dronabinol) at 200ºC en 210ºC. Bars show milligrams of THC detected in the balloon. Errorbars indicate standarderror, based on n=3 measurements.