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Water content determination in different varieties of *Cannabis* flowers

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Abstract

The potency of the cannabinoids depends on the accuracy of the values of water content in the medicinal *Cannabis* flowers. Since the water in the plant material greatly affects its contamination susceptibility and product consistency, an accurate analysis of water content in medicinal *Cannabis* flowers is necessary to ensure product quality and safety, as well as compliance with numerous state and local regulations. The aim of this research was to develop a specific, accurate, fast, and reliable method for selective determination of water at wide concentration ranges in different varieties of *Cannabis* flowers for medicinal use. The intended use of the method was the evaluation of the quality of the starting material for production of *Cannabis* extract.

Considering that the Karl Fischer titration (Ph.Eur. 2.5.12) is the only established specific test for quantification of water in a wide variety of samples at wide concentration ranges, its suitability for medicinal *Cannabis* flowers was demonstrated by proposing suitable titrant-solvent combination, followed by verification of the accuracy, linearity, and sensitivity of the method.

The obtained results for water content in more than 40 samples of different *Cannabis* varieties were in range from 3.8 to 8.5%. The values indicate only water content and do not include amounts of other volatile compounds, such as terpenes, as well as cannabinoids, which can be incorrectly classified as moisture content when using thermogravimetric methods.

The proposed method has suitable selectivity, accuracy, and sensitivity for the intended purpose. The small sample amount, in addition to the simple operation conditions and fast analysis allows the use of the method for 'in process' control for *Cannabis* flowers.

Key words: medicinal *Cannabis* flowers, water content, semi-micro determination

Introduction

One of the most popular plants, the *Cannabis* plant, defined by international law as 'any plant of the genus *Cannabis*, to cover the species *Cannabis indica* and *Cannabis sativa* and any variety discovered in the future (EMCDDA, 2018), has been grown for several hundred years for fiber, oil, medicines and drugs.

Seeing that the interest in herbal drugs for medical purposes has increased significantly in the past decade, the importance to ensure their pharmaceutical quality and safety and to conform that they are acceptable for its intended use, highlights the importance for implementation of appropriate regulatory requirements for herbal drugs.

Several Pharmacopoeias, including the German pharmacopoeia (DAB), Swiss pharmacopoeia (Ph.Helv.) and the American Herbal Pharmacopoeia (AHP), have

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published monographs for "*Cannabis* inflorescence" as herbal substance obtained from the female plants of *C. sativa L*. (Cvetkovikj Karanfilova et al., 2022). Recently, European Pharmacopoeia has published monograph on *Cannabis* flower (3028) in Supplement 11.5, which will be valid from July 2024 and will maintain in providing harmonized quality requirements.

The specifications for *Cannabis* flower, until now, were set according to the requirements of: European Pharmacopoeia (general monograph Herbal Drugs, 1433); European Medicines Agency (Guideline on specifications: test procedures and acceptance criteria for herbal substances, herbal preparations and herbal medicinal products/traditional herbal medicinal products, 2011); WHO (Guideline on Herbal Medicinal Products) etc. Tests include: identity test (macroscopic and microscopic characteristic); determination of the content of the cannabinoids; tests for contaminants/impurities (residual solvents, microbial limit, inorganic impurities, toxic (heavy) metals, mycotoxins (aflatoxins, ochratoxin A), pesticides, fumigation agents and etc.); physicochemical tests (water and/or alcohol extractable matter, total ash content, loss on drying, water content, volatile oils and etc.) and other tests.

The water content is a critical part of the specification for herbal substances, herbal preparation and herbal medicinal products for their accurate standardization, taking into consideration that the water content in *Cannabis* flower impacts the actual potency of the cannabinoids, susceptibility to contamination, product consistency and more.

Measuring moisture is another important parameter for assuring quality and safety of the plant material, as it not only effects shelf-life and taste sensation but also the percentage of THC in medicinal *Cannabis* products, as it is a substantial part of the total weight. If the moisture changes, the percentage of the THC also changes (Miao et al., 2014). In general, *Cannabis* products should have a moisture content between 10 and 15% to prevent mold growth and ensure proper preservation. It is important to maintain the proper values of these parameters in *Cannabis* products to prevent degradation and ensure their quality. Moisture content for dried herbal materials varies, depending on the tissue structure, however, it is known that it should ideally be below 12%. (Technical Report Series No. 1010, Annex 1- WHO, 2018; Ph.Eur. 07/2024:3028).

In this regard, the official DAB method, as well as Ph.Eur. method for the determination of moisture in *Cannabis* flowers is performed by loss on vacuum drying and lasts for more than 24 hours. The alternative pharmacopeial method suggested for determination of water content for dried herbal drugs with a high essential-oil content (Ph.Eur. 07/2017:1433) after distillation of the sample dispersed in toluene is given in Ph.Eur. 2.2.13. The main limitation of this method is the large amount of the sample (more than 20 g of flower), which is not acceptable for the industry considering the price of the material, and usage of highly toxic solvent toluene. The durability and sample size of these tests makes them unsuitable for in-process control of *Cannabis* flower.

The Karl Fischer titration (semi-micro determination method) is the only established specific test for the quantification of water. This method is selective quantitative method for semi-micro determination of water and it is the most commonly used in the pharmaceutical industry in a wide variety of samples at wide concentration ranges but is rarely suggested for control of herbal material.

The aim of our work was to develop a method for semi-micro determination of water in different varieties of medicinal *Cannabis* flowers in order to evaluate the quality of the plant material intended for production of *Cannabis* extract. For this purpose, the method should be specific, accurate, fast and reliable for selective determination of water at wide concentration ranges in different varieties of *Cannabis* flower for medicinal use. The accurate value for water content can be used for evaluation of mass loss during the decarboxylation step of the production of *Cannabis* extract.

Material and methods

Solvents, reagents and samples

Aqualine Complete 5 was used as a single-component Karl Fischer volumetric reagent, supplied by Fischer Chemical and Methanol used as a solvent, supplied by Carlo Erba. The Water Standard 1% (10 mg Water / 1 g) supplied by Merck, was used for verification of the method suitability. The tested samples of *Cannabis* flowers were purchased from Replek Farm Ltd, Skopje, Republic of North Macedonia.

Decarboxylation

Forced decarboxylation of the flowers prior to the production of *Cannabis* extract was performed by conditions of the method Ph.Eur. 2.2.32 Loss on drying (LOD). Each sample was accurately weighed (about 1 g) in glass container and dried in oven for 2h at 105 °C. After cooling in desiccator, the sample was weighed again.

Semi-micro determination of water (Karl Fischer Titration method)

Karl Fischer titration was performed on Karl Fischer Titrator V20S, Mettler Tolledo.

The suitability of the method was carried out according to the procedure given in the Ph. Eur. 2.5.12, valid edition, using Water Standard 1% (10 mg Water/1 g).

The critical step of the method development was introducing proper sample preparation method to provide a representative and well homogenized sample. The thorough homogenization of the samples, containing dried, crushed or whole clustered flowers, was obtained by grinding machine (HsiangTai) with a spin speed of 20000

rpm for 30 s, producing fine powder. When the drift value is under 20 µL per minute and stable, an accurately weighted amount of sample (0.2 g) was quantitatively introduced in the titration vessel, containing about 40 mL solvent. The stirring time before titration was 15 s. The endpoint was detected at about 20 min.

Results and discussion

Development of method for semi-micro determination of water in Cannabis flower

Standardization of the titrant concentration and performance verification was done according to the Ph.Eur. 2.5.12 and OMCL Qualification of equipment guideline, Annex 5: Qualification of automatic titrators. The repeatability of the titrant concentration was 0.5%, whereas the mean recovery of the water content determined after six independent additions of Water Standard 1% (10 mg Water /1 g) was found to be 100.1%.. Therefore, the acceptance criteria for repeatability and recovery, were met (Table 1).

In order to confirm the choice of the proposed solvent/ titrant system and to demonstrate that the results are accurate and reproducible, the suitability test, found in the general chapter of Ph.Eur. 2.5.12 was performed.

The accuracy of the method was determined with the standard addition method, by adding accurate quantities of water standard to the medicinal *Cannabis* flowers (exact amount of homogenized medicinal *Cannabis* flowers). First, the water content of the selected medicinal *Cannabis* flower was tested using the determined solvent/titrant system in six replicate titrations of 0.2 g homogenized *Cannabis* flowers and was found to be 5.29%, which corresponds to 10.8 mg initial water content (M) for the sample (Table 2).

This measurement was considered as blank and the average volume of Aqualine-Complete 5® consumed for titration was subtracted from the volumes consumed for titration of samples with standard addition of water. A known amount of water standard 1% (in the range from 0.0033 g to 0.0110 g, corresponding to 30-100% of the amount of water found in the sample) were added to the titration vessel five consecutive times, and the water content was determined after each addition (Table 3). Recovery was acceptable in all cases (i.e. within the limits of 97.5 – 102.5%), with mean recovery of 98.3%.

The regression line equation was calculated from the six points calibration curve obtained by plotting the cumulative amount of water (g) added against the sum of the initial water content determined for the sample and cumulative amount of water (g) determined after each addition. The slope (b) of the regression line was 0.9839, whereas the y-axis intercept (a) was found to be 21.584. The correlation coefficient of the regression line was found to be 1.000. The x-axis intercept (d), needed for the calculation of the percentage errors e1 and e2 (Ph.Eur.2.5.12) related to the water content determined, was calculated as a ratio between the intercept and the slope. The value of d was found to be 21.937. The calculated values for e1 and e2 were -0.05 and 1.59, correspondingly. The the acceptance criteria given in Ph. Eur. 2.5.12 (the |e1| and |e2| are not greater than 2.5% and the slope (b) is between 0.975 and 1.025) were met, thus the reagent/solvent system is considered to be acceptable.

Table 1. Repeatability of the system (system precision) and recovery after additions of Water Standard 1%

Sample Number	Sample size (g)	Water content (mg/g)
1	1.179	10.00
2	0.968	10.09
3	0.981	9.96
4	0.936	10.01
5	0.999	10.00
Mean water content R1 (mg/g)		10.012
Recovery of R1 (%)		100.1
Relative standard deviation of R1 (RSD, %)		0.5
System suitability of the method		
Parameter	*Acceptance criteria*	*Conclusion*
Precision	RSD < 1.0%	met
Recovery	97.5 <R1< 102.5%	met

Table 2. Method repeatability (replicate titrations of homogenized *Cannabis* flowers)

Sample N°	Calculated % of water	Titrant (mL) consumed for titration of 0.2 g sample	Calculated mg of water (1)
1	5.32	2.24	10.91759
2	5.35	2.21	10.74972
3	5.30	2.22	10.79838
4	5.25	2.20	10.70228
5	5.26	2.23	10.83974
6	5.28	2.22	10.77433
Average =	5.29	2.22	10.8
RSD (%) =	0.7	0.7	0.7

Water content determination in medicinal Cannabis flower samples

Once the chosen solvent/titrant system was found suitable and all the requirements in the suitability test were met, the proposed method was applied for determination of the water content in the selected samples of medicinal *Cannabis* flowers (Table 4 and 5). The obtained results by semi-micro determination of water content in more than 40 samples of different cannabis varieties for medicinal use, already characterized by the content of cannabinoids for the purpose of standardization of the plant material, were in range from 3.76 to 8.48%. The values obtained with the proposed semi-micro method indicate only water content and do not include amounts of other volatile compounds, such as terpenes, as well as loss of mass due to decarboxylation of cannabinoids, which can be incorrectly considered as moisture, when using the thermogravimetric methods.

Mass loss of Cannabis flowers during decarboxylation step of the production of Cannabis extract

Cannabis plant contains variety of chemical constituents including terpenes, flavonoids, and cannabinoids, which are the most prominent and predominant constituents in *Cannabis* flowers (Pourseyed Lazarjani et al., 2020; Stefkov et al., 2022). In the process of *Cannabis* extract production, there is significant mass loss of the starting material during the decarboxylation step that should be well recorded, explained and justified for regulatory purposes. However, the total mass loss during this process, exceeds the expected mass theoretically calculated from the molecular weight of the carbon dioxide molecules, lost from the carboxylic group of the acidic forms of the cannabinoids. Evaporated water can have considerable input in the excess mass loss, during decarboxylation. Therefore, the accurately determined values of the water content in the starting material is one of the important input information on the mass loss.

Table 3. Results from water content in *Cannabis* samples and recovery after addition of a known amount of water

Added mg of water	Titrant (mL) consumed for 0.2 g sample + added water	Titrant (mL) consumed, corrected for Blank	Calculated mg of water (after addition)	Calculated mg of water (after addition) - average calculated mg of water (1)	Recovery (%)
3.3	2.89	0.67	14.044497	3.2474895	98.41
5.5	3.30	1.08	16.181631	5.3846235	97.90
7.7	3.74	1.52	18.408085	7.6110775	98.85
8.8	4.01	1.79	19.444535	8.6475275	98.27
11	4.46	2.24	21.608106	10.8110985	98.28
				Average =	98.3
				RSD (%) =	0.35

Table 4. Results from quality control of the plant material, THC var. (cannabinoid content analysis, water content determination) and mass loss during decarboxylation step (total mass loss, theoretical decarboxylation and calculated other volatiles)

	Quality control of the plant material (content, %)			Mass loss (%) during decarboxylation (105 °C for 2 hours)		
THC Var. Sample N°	THC	THCA	Water (KF)	Total mass loss	Theoretical decarboxylation (calculated)[a]	Other volatiles-terpenes (calculated)
1	4.73	11.19	6.24	9.21	1.37	1.60
2	1.64	8.12	6.39	8.44	1.00	1.05
3	2.42	6.59	7.01	9.18	0.81	1.36
4	2.7	22.58	5.64	9.93	2.77	1.52
5	0.89	12.86	6.97	9.71	1.58	1.16
6	2.6	19.47	5.5	10.02	2.39	2.13
7	1.21	31.69	4.95	10.20	3.88	1.37
8	1.54	14.88	5.8	10.13	1.82	2.51
9	0.53	7.97	6.71	11.38	0.98	3.69
10	0.5	11.83	6.49	11.11	1.45	3.17
11	0.62	12.34	6.97	11.87	1.51	3.39
12	1.49	11.1	7.32	10.3	1.36	1.62
13	0.5	18.99	6.25	10.86	2.33	2.28
14	0.9	12.83	6.61	11.1	1.57	2.92
15	1.45	16.63	6.41	11.81	2.04	3.36
16	3.23	19.48	5.79	11.06	2.39	2.88
17	0.76	22.28	6.02	11.97	2.73	3.22
18	1.04	23.7	5.87	10.51	2.90	1.74
19	1.5	23.27	5.71	9.85	2.85	1.29
20	1.06	20.69	6.11	8.8	2.54	0.15
21	0.53	18.61	8.48	12.65	2.28	1.89
22	0.64	22.7	6.24	11.92	2.78	2.90
23	0.58	19.26	5.61	10.16	2.36	2.19
24	0.57	15.93	4.39	8.05	1.95	1.71
25	0.65	10.5	5.34	7.37	1.29	0.74
26	0.63	16.48	5.17	8.03	2.02	0.84
27	0.66	10.78	6.17	9.91	1.32	2.42
28	0.52	15.28	4.32	8.17	1.87	1.98
29	0.68	9.77	4.95	7.62	1.20	1.47
30	0.57	17.03	5.1	8.22	2.09	1.03
31	0.49	16.73	4.21	8.53	2.05	2.27
32	0.48	15.61	6.61	10.99	1.91	2.47

33	0.48	10.07	3.76	6.97	1.23	1.98
34	0.84	18.99	5.09	10.82	2.33	3.40
35	0.54	10.32	6.31	8.58	1.26	1.01
36	4.19	16.23	5.81	9.93	1.99	2.13
37	1.46	13.79	6.01	10.49	1.69	2.79
38	2.9	18.06	5.34	10.85	2.21	3.30
39	1.95	11.86	6.63	10.15	1.45	2.07
40	0.65	18.85	4.26	8.22	2.31	1.65
41	1.95	11.86	5.96	10.15	1.45	2.74
42	1.95	11.86	5.51	10.15	1.45	3.19
MIN. (%)	0.48	6.59	3.76	6.58	0.81	0.15
MAX. (%)	4.73	31.69	8.48	13.65	3.88	3.69

[a]Calculated as ratio between molecular weight of carbon dioxide (M = 44 g/mol) and THCA (M = 359 g/mol), expressed as %, related to the amount of the THCA.

Table 5. Results from quality control of the plant material, CBD var. (cannabinoid content analysis, water content determination) and mass loss during decarboxylation step (total mass loss, theoretical decarboxylation and calculated other volatiles)

CBD Var. Sample N°	Quality control of the plant material (content, %)			Mass loss (%) during decarboxylation (105 °C for 2 hours)		
	CBD	CBDA	Water (KF)	Total mass loss	Theoretical decarboxylation (calculated)[a]	Other volatiles - terpenes (calculated)
1a	0.35	8.8	7.21	11.39	1.08	3.10
2a	0.22	8.52	7.35	10.79	1.05	2.39
3a	0.47	9.79	6.84	11.45	1.20	3.41
4a	0.51	14.5	6.09	10.31	1.78	2.44
5a	0.59	14.13	7.22	12.58	1.73	3.63
6a	1.97	17.93	6.05	9.66	2.20	1.41
7a	2.34	20.51	5.92	10.22	2.52	1.78
8a	1.76	15.82	6.12	9.9	1.94	1.84
MIN. (%)	0.22	8.52	5.92	9.66	1.05	1.41
MAX. (%)	2.34	20.51	7.35	12.58	2.52	3.63

[a]Calculated as ratio between molecular weight of carbon dioxide (M = 44 g/mol) and CBDA (M = 359 g/mol), expressed as %, related to the amount of the CBDA.

For the purpose of this study, all samples (characterized by cannabinoids content (THC, THCA, CBD and CBDA) and water content) were subjected to decarboxylation (105 °C for 2 hours). The theoretical mass loss due to decarboxylation was also calculated as ratio between molecular weight of carbon dioxide (M = 44 g/mol) and of THCA/CBDA (M = 359 g/mol), expressed as %, related to the amount of the THCA and CBDA, respectively (Table 4 and 5).

The difference between the total mass loss (after decarboxylation) and the sum of the accurately determined water content (KF) and theoretically calculated loss of mass

due to carbon dioxide (CO_2) from the acidic forms of the canabinoids, most probably equals the mass of other volatiles, such as terpenes (Table 4 and 5). Usually the content of terpenes in the *Cannabis* flowers are generally up to 3-5% (Chacon et al., 2022) depending on the strain (higher for CBD strains).

The production and processing of medicinal *Cannabis* is highly regulated process and keeping the records of all stages, including the records for the exact mass of starting plant material, is of substantial importance. For that purpose, the accurate water content determination is an essential element. Considering the fact that during the decarboxylation process of dry cannabis flower material the mass loss can be much higher than the expected theoretical loss of the CO_2 molecule, water content and a certain remaining percentage originating from the volatile components, such as terpenes should be taken into account in order to estimate the cannabinoid yield in the extract and to justify inevitable mass loss during the manufacturing process.

Conclusion

A specific, selective, accurate, fast and reliable method for semi-micro determination of water in different varieties of *Cannabis* flower for medicinal use was developed. The proposed method was proved suitable for quality control of the starting material, as well as for in-process control during production of *Cannabis* extract. It has advantages over other compendial methods intended for determination of moisture in terms of durability (less than 30 min total analysis time) and sample amount needed to run the test (1 g powdered flowers). Additionally, the obtained results in more than 40 samples of different *Cannabis* varieties (water content in range from 3.76 to 8.48%) reflect only water content in samples of medicinal *Cannabis* flowers, excluding the possibility to misinterpret other volatile compounds (such as terpenes and some cannabinoids) as moisture.

Accurate determination of water content in medicinal *Cannabis* flowers as starting plant material for production of *Cannabis* extract is critical not only as quality control parameter of the starting material, but also for justification of the mass loss during the manufacturing process.

References

Chacon, F.T., Raup-Konsavage, W.M., Vrana, K.E., Kellogg, J.J., 2022. Secondary Terpenes in Cannabis sativa L.: Synthesis and Synergy. Biomedicines 10(12), 3142. https://doi.org/10.3390/biomedicines10123142

Cvetkovikj Karanfilova, I., Stoilkovska Gjorgievska, V., Stefkov, Gj., Karapandzova, M., Trajkovska, A., Davkova, I., Acevska, J., Kulevanova, S., Brezovska, K., 2022. DAB method transfer for potency of cannabinoids in dry cannabis flower. Mac. Pharm. Bull. 68(2) 2022.

European Monitoring Centre for Drugs and Drug Addiction (EMCDDA), 2018. Cannabis legislation in Europe: an overview, Publications Office of the European Union, Luxembourg. ISBN: 978-92-9497-328-3. https://doi.org/10.2810/566650 TD-01-18-663-EN-N

European Medicines Agency, 2011. Guideline on specifications: test procedures and acceptance criteria for herbal substances, herbal preparations and herbal medicinal products/traditional herbal medicinal products. EMA/HMPC/162241/2005 Rev. 2 Available at: https://www.ema.europa.eu/en/documents/scientific-guideline/guideline-specifications-test-procedures-acceptance-criteria-herbal-substances-herbal-preparations_en.pdf

European Directorate for the Quality of Medicines & HealthCare (EDQM), European Pharmacopoeia, 2023. Guide for the elaboration of monographs on Herbal drugs and herbal drug preparations, 2nd edition, Council of Europe, Strasbourg, France Available at: https://www.edqm.eu/en/ph-eur-technical-guides

European Directorate for the Quality of Medicines & HealthCare (EDQM) 2023. European Pharmacopoeia (Ph. Eur.) 11th Edition. EDQM Council of Europe, Strasbourg, France

European Directorate for the Quality of Medicines & HealthCare (EDQM), Council of Europe, 2022. General European OMCL Network (GEON), Quality Management Document, Qualification of equipment Annex 5: Qualification of automatic titrators (PA/PH/OMCL (07) 108 R11), Council of Europe, Strasbourg, France

European Directorate for the Quality of Medicines & HealthCare (EDQM), Council of Europe, 2000. General European OMCL Network (GEON), Quality Management Document. Validation and Verification of Analytical Procedures (EPA/PH/OMCL (13) 82 R5), 1-12. Council of Europe, Strasbourg, France Available at: https://www.edqm.eu/en/quality-management-qm-documents.

German Pharmacopoeia, 2018. Geschäftsstelle der Arzneibuch-Kommissionen. Bundesinstitut fur Arzneimittel und Miedizinprodukte, Monografie Cannabis blüten. In German Pharmacopoeia, Geschäftsstelle der Arzneibuch-Kommissionen: Bundesinstitut fur Arzneimittel und Miedizinprodukte: Bonn, Germany

International Conference on Harmonization, 2022. ICH guideline Q2(R2) on validation of analytical procedures, EMA/CHM:P/ICH/82072/2006.

International Conference on Harmonization, 2000. ICH guideline Q6A: Specifications: Test procedures and acceptance criteria for new drug substances and new drug products: Chemical substances, CPMP/ICH/367/96.

Manns, D., Norwig, J., Reh, K., 2019. Cannabis for medicinal purposes: development of pharmacopoeia monographs as a quality standard. Bundesgesundheitsbl 62, 806-810. https://doi.org/10.1007/s00103-019-02963-5

Miao, P., Bell, S.A., Rujan, M., Mugurel, G., McIlroy, C., 2014. Report on literature review of recent development in loss on drying method for moisture determination. National Physical Laboratory Report Eng 52.

Moreno, T., Dyer, P., Tallon, S., 2020. Cannabinoid decarboxylation: a comparative kinetic study. Ind. amp; Eng. Chem. Res. 59(46), 20307-20315. https://doi.org/10.1021/acs.iecr.0c03791

PourseyedLazarjani, M., Torres, S., Hooker, T., Fowlie, C., Young, O., Seyfodin, A., 2020. Methods for quantification

of cannabinoids: a narrative review. J. Cannabis Res. 2, 35. https://doi.org/10.1186/s42238-020-00040-2

Perrotin-Brunel, H., Buijs, W., Spronsen, J., Roosmalen, M.J.E., Peters, C.J., Verpoorte, R., Witkamp, G.J., 2011. Decarboxylation of Δ9-tetrahydrocannabinol: Kinetics and molecular modeling. J.Mol.Struct., 987 (1–3), 67-73. https://doi.org/10.1016/j.molstruc.2010.11.061

Radwan, M.M., Chandra, S., Gul, S., ElSohly, M.A., 2021. Cannabinoids, phenolics, terpenes and alkaloids of cannabis. Molecules, 26(9), 2774. https://doi.org/10.3390/molecules26092774

Reason, D.A., Grainger, M.N. and Lane, J.R., 2022. Optimal Storage Conditions of Commercial Cannabis Crops. Ind. amp; Eng. Chem. Res. 61(39), 14691-14701. https://doi.org/10.1021/acs.iecr.2c02071

Sarma, N.D., Waye, A., ElSohly, M.A., Brown, P.N., Elzinga, S., Johnson, H.E., Marles, R.J., Melanson, J.E., Russo, E., Deyton, L., Hudalla, C., Vrdoljak, G.A., Wurzer, J.H., Khan, I.A., Kim, N.C., Giancaspro, G.I., 2020. Cannabis inflorescence for medical purposes: USP considerations for quality attributes. J. Nat. Prod. 83, 1334-1351. https://dx.doi.org/10.1021/acs.jnatprod.9b01200?ref=pdf

Stefkov, G., Cvetkovikj Karanfilova, I., Stoilkovska Gjorgievska, V., Trajkovska, A., Geskovski, N., Karapandzova, M., Kulevanova, S., 2022. Analytical techniques for phytocannabinoid profiling of cannabis and cannabis-based products-A comprehensive review. Molecules 27, 975. https://doi.org/10.3390/molecules27030975

Therapeutic Good Administration, 2022. Guidance on quality requirements for medicinal cannabis products: Conforming with Therapeutic Goods (Standard for Medicinal Cannabis) (TGO 93), Order 2017 - including 2022 Amendments, Version 1.5. https://www.tga.gov.au/sites/default/files/guidance-on-quality-requirements-for-medicinal-cannabis-products.pdf

Tolomeo, F., Russo, F., Kaczorova, D., Vandelli, M.A., Biagini, G., Laganà, A., Capriotti, A.L., Paris, R., Fulvio, F., Carbone, L., Perrone, E., 2022. Cis-Δ9-tetrahydrocannabinolic acid occurrence in Cannabis sativa L. J Pharm Biomed Anal. 219, 114958.https://doi.org/10.1016/j.jpba.2022.114958

United Nations Office on Drugs and Crime. 2009. Recommended methods for the identification and analysis of cannabis and cannabis products. ISBN: 978-92-1-148242-3

United States Pharmacopeia. 2023. USP-NF. Rockville, MD: United States Pharmacopeia.

Warner, M.L., Alford, I., Lawrence, D.M., Kohl, A.C., Williams, S.J., Yeatman, D.T., 2017. Comparative analysis of freshly harvested cannabis plant weight and dried cannabis plant weight. Forensic Chem, 3, 52-57. https://doi.org/10.1016/j.forc.2017.02.001

World Health Organisation. 2018. Technical Report Series No. 1010, Annex 1- WHO guidelines on good herbal processing practices for herbal medicines. https://www.gmp-compliance.org/files/guidemgr/TRS1010annex1.pdf

Резиме

Определување на вода во различни видови на цвет од Канабис

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Клучни зборови: цвет од канабис за медицинска употреба, содржина на вода, семи-микро определување

Потенцијата на канабиноидите зависи од точноста на вредностите за содржина на вода во цветот од канабис за медицинска употреба. Бидејќи водата во суровината во голема мера влијае на нејзината подложност на контаминација и конзистентност на производот, точното определување на содржината на вода во цветот од канабис ја обезбедува неговата безбедна употреба, како и усогласеност со бројни национални и локални регулативи. Целта на ова истражување беше да се развие специфичен, точен и брз метод за селективно определување на вода во широк концентрациски опсег во различни видови на цвет од канабис за медицинска употреба. Со употребата на предложениот метод беше направена евалуација на квалитетот на почетната суровина за производство на екстракт од канабис.

Соодветноста за примена на титриметриски метод според Карл Фишер (Ph. Eur. 2.5.12), како единствен докажан специфичен тест за определување на вода за употреба во цвет од канабис за медицинска употреба беше докажана за предложената комбинација на титрант-растворувач, преку проверка на точноста, линеарноста и чувствителноста на методот.

Добиените резултатите во повеќе од 40 примероци од различни сорти медицински канабис беа во опсег од 3,8 до 8,5%. Овие вредности укажуваат само на содржината на вода и не вклучуваат количества на други испарливи соединенија, како што се терпени и канабиноиди, кои може погрешно да се класифицираат како влага доколку се користат термогравиметриски методи. Предложениот метод покажува соодветна селективност, точност и осетливост за неговата намена. Потребната мала количина на примерок, покрај едноставните услови за изведба и брзата анализа, овозможуваат негово користење во процесна контрола на цветот од канабис за медицинска употреба.