L-Università ta' Malta
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Analysis of Minor Cannabinoids

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INTRODUCTION

The two major cannabinoids are Cannabidiol (CBD) and Tetrahydrocannabinol (THC). Minor cannabinoids include acidic minor cannabinoids such as Tetrahydrocannabinolic acid (THCA) and Cannabidiolic Acid (CBDA), neutral minor cannabinoids such as Cannabinol (CBN) and Cannabigerol (CBG), and varinic minor cannabinoids such as Cannabidivarin (CBDV) and Tetrahydrocannabivarin (THCV).

AIMS

- **To identify and compare analytical methods for determination of minor cannabinoids in different matrices.**

METHOD

- **Systematic literature search was carried out to identify analytical methods used for determination of minor cannabinoids.**
- **Sources used were peer-reviewed journal articles published in English between 2015 and 2022 on the University of Malta's HyDI database using key words such as "determination of cannabinoids", "qualitative techniques for cannabinoids", and "quantitative techniques for cannabinoids"**

Table 1 - Inclusion criteria for literature review

Sources	Peer-Reviewed Open Access Journal Articles published in English
Databases	HyDi
Time Period	2015 - 2022
Keywords	"Determination of cannabinoids", "Qualitative techniques for cannabinoids", "Quantitative techniques for cannabinoids"

RESULTS

- **From 622 eligible article, 107 articles were identified and considered in the comparative analysis, with 10 articles being review articles describing more than one method. Determination techniques found can be seen below.**

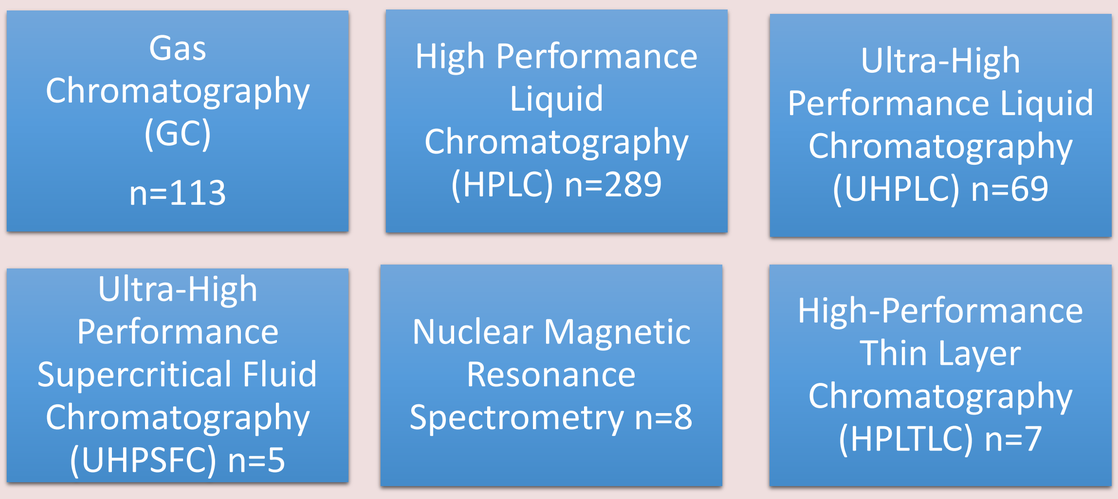

Table 1 - High-performance liquid chromatography (HPLC) methods (n=289)

Cannabinoid analysed	CBN (n=240), THCA (n=150), CBDA (n=137), CBG (n=122), THCV (n=73), CBC (n=57),
Matrix	Biological matrices (n=129), Plant Material (n=99), Cannabinoid products (n=56)
Sample Preparation	Liquid-liquid extraction (n=94), solid-phase extraction (n=63), protein precipitation/ deproteination (n=24)
Stationary Phase	C18 type columns (n=131), Kinetex HPLC column (n=41). Agilent brand columns (n=25)
Mobile Phase	Water and ACN (n=107) with formic acid (n=74), Water and methanol (n=33) with formic acid (n=15)
Detector	Mass spectroscopy (MS) (n=179), UV spectroscopy (n=67), Photodiode-array detection (DAD) (n=43),

Table 2 - Gas Chromatography (GC) methods (n=133)

Cannabinoid analysed	CBN (n=114), THCA (n=54), CBG (n=55), CBC (n=48), CBDA (n=29), THCV (n=25)
Matrix	Plant Material (n=73), Biological matrices (n=62), Cannabinoid Products (n=13)
Sample Preparation	Liquid-liquid extraction (n=75), Solid-Phase extraction (n=33)
Mobile Phase	Helium (n=69), Hydrogen (n=3), Nitrogen (n=1),
Detector	Mass Spectroscopy (MS) (n=117), Flame ionization Detector (FID) (n=23)

Table 3 - Ultra High-performance liquid chromatography (UHPLC) methods (n=69)

Cannabinoid analysed	CBN (n=56), THCA (n=46), CBDA (n=40), CBG (n=25), THCV (n=21), CBC (n=16),
Matrix	Plant Material (n=25), Biological samples (n=24), Cannabinoid Products (n=19)
Sample Preparation	Liquid-liquid extraction (n=21), solid phase extraction (n=4)
Stationary Phase	C18 type columns (n=40), Waters brand column(n=24)
Mobile Phase	Water and ACN (n=50) with formic acid (n=27), Water and methanol (n=17) with formic acid (n=12)
Detector	Mass spectroscopy (n=47), UV spectroscopy (n=17), Photodiode-array detection (DAD) (n=15),

CONCLUSION

From the systematic literature review, CBN was the minor cannabinoid most analysed, with HPLC being the most used chromatographic technique used for the determination of minor cannabinoids. Mass Spectrometer was the most commonly used detector for minor cannabinoids. For Acidic minor cannabinoids (THCA, CBDA), HPLC and UHPLC were preferred, since when using GC, the minor cannabinoids must undergo derivatisation to prevent decarboxylation. Knowledge of parameters used in the analysis of minor cannabinoids could help in the development of more efficient determination techniques.