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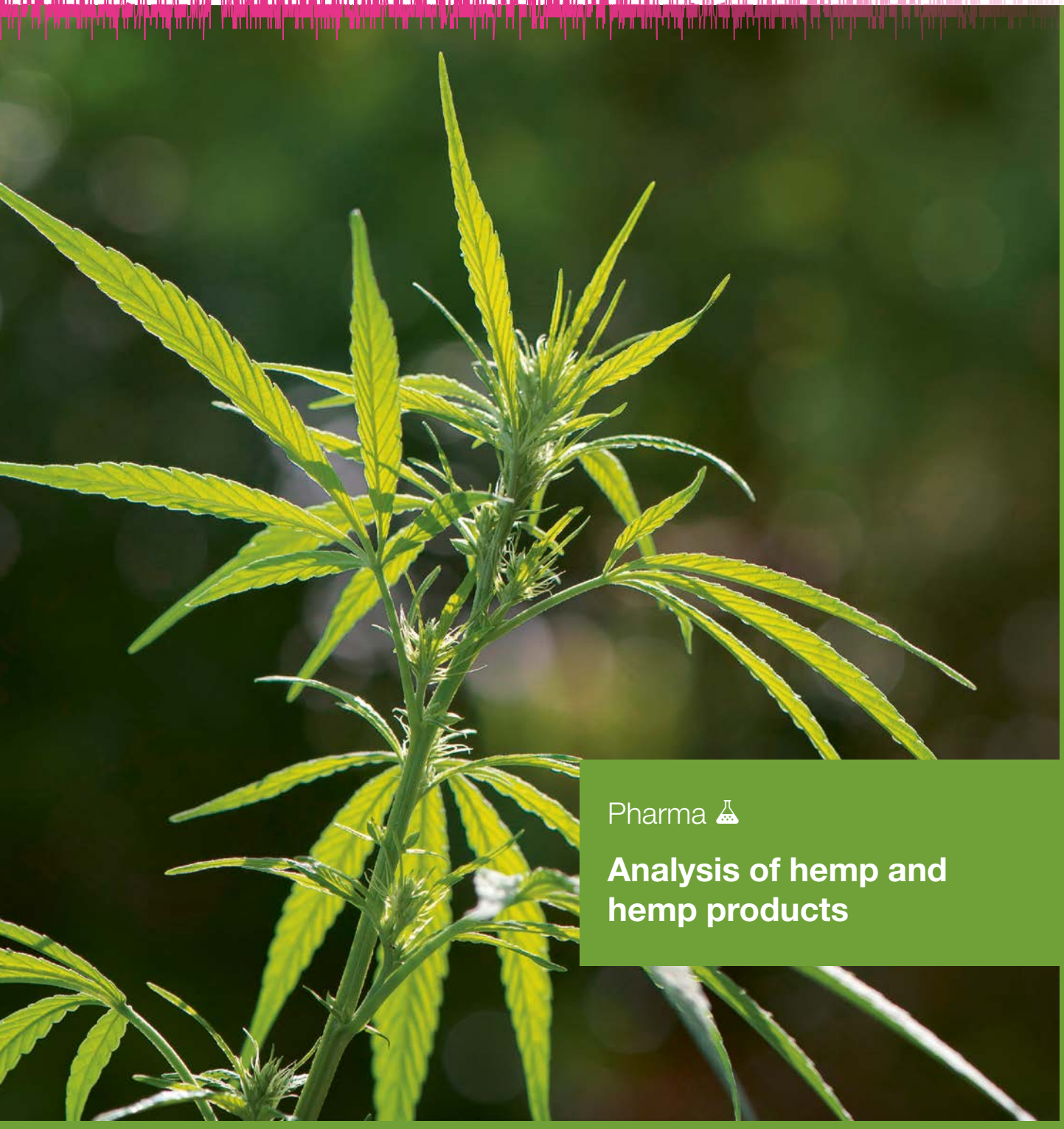

Pharma

Analysis of hemp and hemp products

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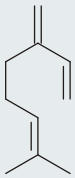
Author: Dr. Tanja Badewien

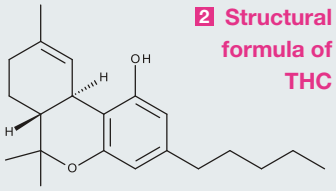
Hemp belongs to the cultivated plants, which have a millennia-old usage history. Thus, the medical use of the plant, which was originally native to Asia, was already described in Chinese texts from the time before the birth of Christ. At latest since the crusades, it has been cultivated in Central Europe and was used as a raw material for textiles, ropes and paper before the development of artificial fibers. Also as a medicinal plant hemp has always been used in many ways – for example for the treatment of pain or rheumatic diseases. The mind-expanding effect of cannabis was also known from early times on and ritually used.

Until the early 20th century, cannabis supplements were by far the best-selling drugs. Due to dosing difficulties and the increasing displacement by synthetic drugs, the prescriptions decreased continuously. In the middle of the 20th century, cannabis was banned almost worldwide in the context of the intensified discussion about illegal drugs. Moreover, the controversial view of cannabis is due to the use as a psychoactive drug: Some demonize it as a gateway drug, others exaggerate it as a natural panacea, others again transfigure it in memory of Woodstock or the hippie era.

More recently, the therapeutic effect of hemp has increasingly become awareness. This is not least due to the cannabinoid cannabidiol (CBD), which, in contrast to Δ9-tetrahydrocannabinol (THC), does not have a psychoactive effect, but also features anti-inflammatory and analgesic properties. In addition, cannabis products with a THC content of < 1 %, with the exception of cannabis resin (hashish) among others, are no longer subject to the Narcotics Act in Switzerland; not least because of this they are increasingly being commercialized. The products range from cannabis-containing foods to remedies and tobacco substitute products to cosmetics. However, it should be considered that the legal sale is besides the limit for the THC content also subject to all requirements for the specific product categories. Details about the legal framework conditions are further described in a leaflet of BAG [1].



1 Structural formula of myrcene



2 Structural formula of THC

Ingredients of hemp and hemp products

Cannabis contains two very different substance classes as pharmacologically relevant ingredients. On the one hand, there are varying amounts of cannabinoids, on the other hand, cannabis has volatile terpenes, which are responsible for the characteristic hemp smell.

The effects of the terpenes themselves are still largely unexplored, with some arguing that they can enhance the effects of cannabinoids. Depending on the hemp variety, both the species and the amount of terpenes vary greatly. Often myrcene (see 1) makes up about 50 % of the plant's essential oils. In addition, pinene, limonene, linalool and numerous other terpenes are included in lower proportions.

In contrast to terpenes, the effects and properties of cannabinoids, in particular of THC (see 2) and CBD, have been the subject of numerous scientific studies. For a long time, the main focus was on THC, which affects the central nervous system in many ways. For example, the substance is said to have a muscle-relaxing, calming and nausea-suppressing effect. In addition, THC has strong mind-altering properties that can lead to addiction. The transitions between drugs and intoxicants are therefore often fluid. In this context, other representatives of cannabinoids such as CBD are interesting; they have similar effects as THC, but they have a much lower psychoactive potential.

In order to obtain perfect starting material for different uses, extensive efforts are made in variety selection and breeding for specific traits. While in the past the focus was mainly on low-THC (industrial hemp) and high-THC varieties, the breeding goals today are quite differentiated.

The following UPLC-HRMS chromatograms (see 3) visualize the cannabinoid spectrum of three completely different hemp varieties.

Sample A contains both high concentrations of cannabidiolic acid / cannabidiol (CBDA/CBD) and Δ9-tetrahydrocannabinoleic acid / Δ9-tetrahydrocannabinol (THCA/THC) and is used for medical purposes.

Sample B contains only THCA and THC and therefore belongs to the intoxicants.

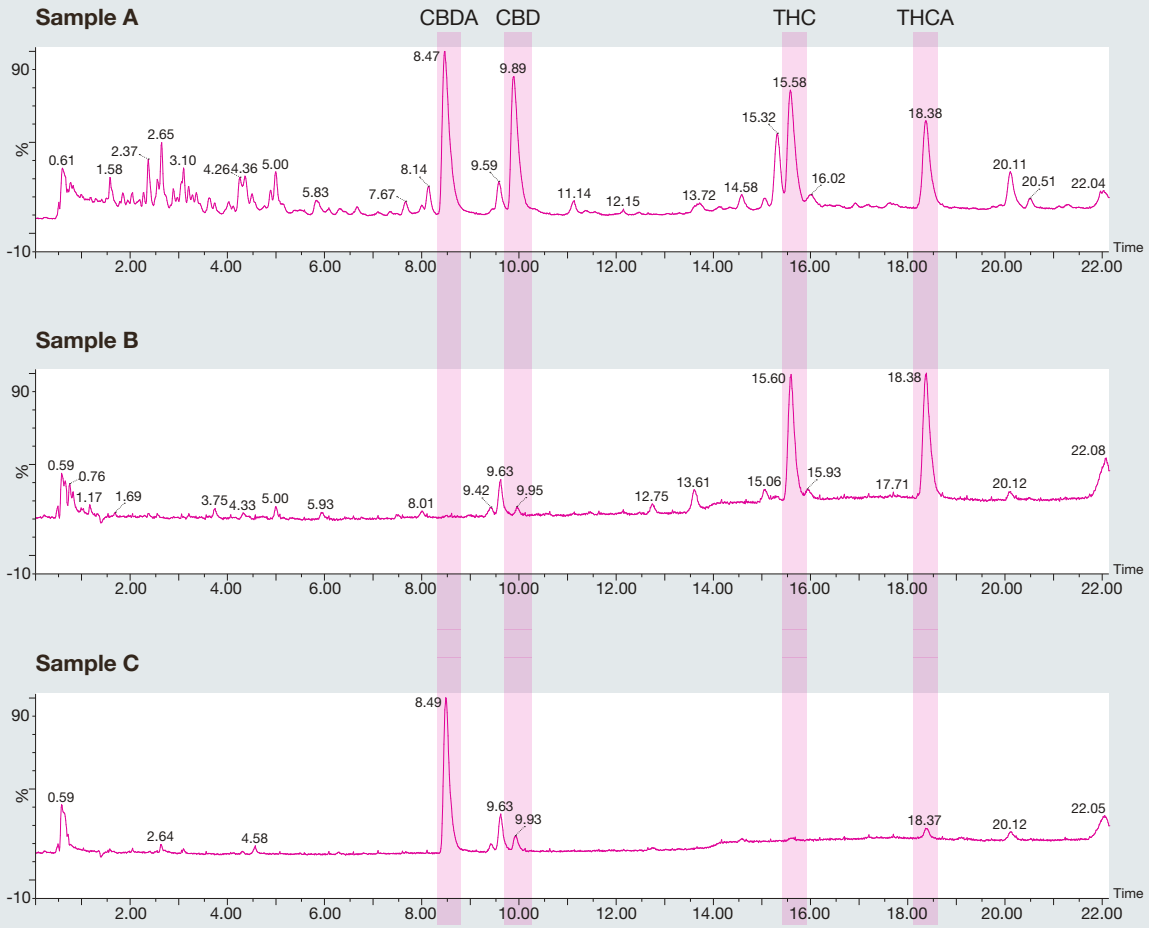
Sample C contains almost exclusively CBDA and CBD, but only traces of THC. Sample C is thus a typical representative of THC-free hemp, which is used as a tobacco substitute.

Analyses of hemp and hemp products

Cannabis is still most commonly tested for the various cannabinoids. In addition, as with all plants used as pharmaceuticals, contaminants from the environment such as heavy metals and pesticides are of particular importance. In the analysis of cannabinoids, sampling and homogenization pose a particular challenge. Since the cannabinoids occur mainly in the inflorescences of the female plant and are enriched in their resinous excreta, the samples must be very carefully mixed and crushed before analysis. Only in this way it is possible to obtain a representative statement on the content in the respective sample. For this purpose, Interlabor has developed a special process based on fragmentation with a cryomill. As a result, homogeneous powdery mixtures are obtained even with highly enriched resin samples, which are very suitable for further analysis steps. Likewise, suitable methods are available for other cannabis products, for example hemp oil.

When analyzing cannabinoids, it must also be taken into account that they are mainly found in the form of acids in the fresh state. These split off carbon dioxide under the influence of heat. This reaction is of great importance, since the acid forms of cannabinoids (THCA, CBDA) in many cases have a different effect than the corresponding decarboxylation products. For example, the psychotropic THC is produced only when the plant dries or when burning (smoking) from tetrahydrocannabinoleic acid, which itself has no psychotropic properties. Therefore, the analysis of cannabinoids must include both forms.

3 TIC-chromatograms of different hemp varieties



Offer of cannabis analyses: INTERLABOR offers support in the following issues:

Analysis	Method	Technique
Examination of cannabinoids CBDA/CBD and THCA/THC	Internal method	HPLC-UV
Examination for by-products such as THCV (tetrahydrocannabivarin) or CBN (cannabinol)	Internal method	HPLC-UV; UPLC-HRMS
Screening cannabinoids	American herbal pharmacopoeia, 2013 (cannabis inflorescence)	HPLC-UV
Plant protection products	Ph. Eur. 2.8.13 [2]	GC-MS/MS; HPLC-MS/MS
Heavy metals (Cd, Pb, Hg)	Ph. Eur. 2.4.27	ICP-MS
Terpenes and terpenoids	Internal monograph	GC/FID; GC/MS
Aflatoxin B1/Ochratoxin A	Ph. Eur. 2.2.18/2.8.22	HPLC-FLD
Structural suggestions for unknown cannabinoids	Internal method	UPLC-HRMS
Cannabidiol (CBD)	DAC C-052, 2016-2	Various such as HPLC-UV

The majority of these methods are validated or verified and can also be offered under GMP.

Forecast

Legal cannabis products are currently experiencing an unprecedented boom as lifestyle, enjoyment and health products. As a result, more and more companies are entering the hemp crop business. With regard to consumer protection and product safety, it is recommended to develop an analytical concept which, on the one hand, allows the content of cannabinoids and other key product components to be determined; on the other hand, it aims to detect the exceedance of critical substances in order to guarantee a stable product quality. □

About the author

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Literature

1) Leaflet "Cannabidiol (CBD) – Überblick und Vollzugshilfe für die Kantone" (BAG, 27.02.2017)

2) European Pharmacopeia, Edition 9.2

Abbreviations

DAC:	*Deutscher Arzneimittel-Codex (German Pharmaceutics Codex)*
FID:	*Flame ionization detector*
GC:	*Gas chromatography*
HPLC:	*High performance liquid chromatography*
HRMS:	*High resolution mass spectrometry*
MS:	*Mass spectrometry*
TIC:	*Total ion count*
UV:	*Ultraviolet*

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