Cannabinoids in food, feed and Novel Food in the European Union

Jörg Konetzki from Mérieux NutriSciences outlines the current cannabinoid climate, including legality in Europe and some noteworthy aspects of analytics.

CANNABIS SATIVA, or hemp, is gaining increasing significance in food production, with products containing hemp seeds, flowers or oil becoming more readily available. Hemp seeds, hemp expeller and hemp oil are also approved as feed materials.

A legislative big-bang

Since the landmark decision of the European Court of Justice in November 2020 that cannabidiol (CBD) is not considered to be a narcotic drug and EU member states may not prohibit the marketing of CBD legally produced in another member state,[1] »

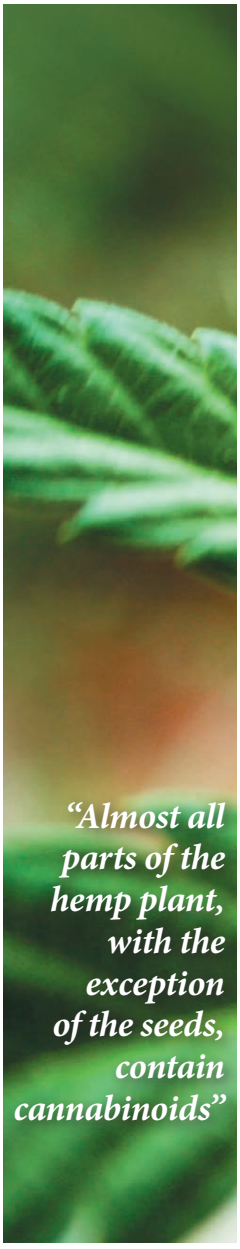
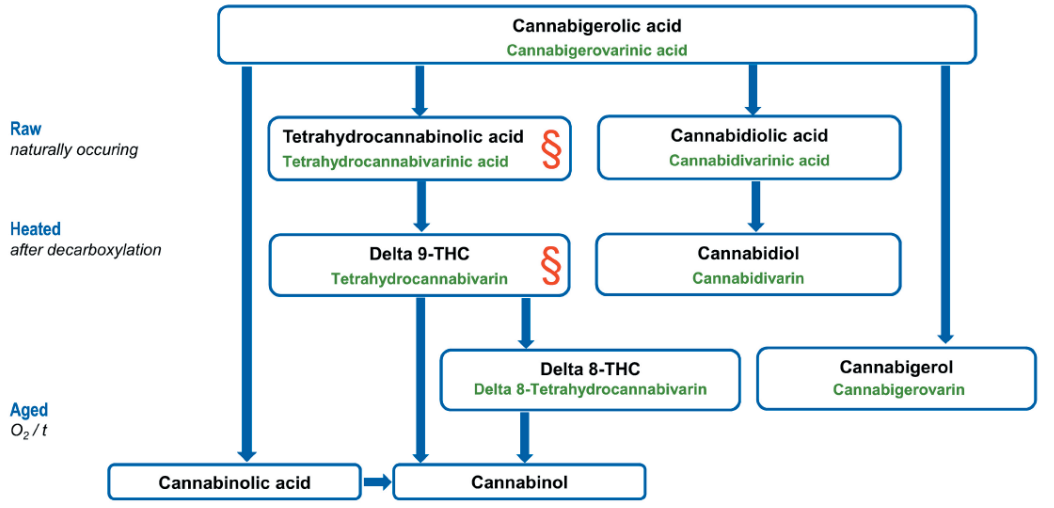


Figure 1



Excerpt from cannabinoid biosynthesis

the European Commission (EC) has resumed the examination of applications for authorisation of CBD products as a Novel Food. But it must be ensured that no delta-9-THC is detectable in CBD products as most food inspection offices will classify CBD products as drugs if delta-9-THC is detectable.

This decision cleared the path for future applications in Novel Food and overturned a ban in France on the marketing of hemp-derived CBD products, which the court said contradicted EU law on the free movement of goods. As such, the enormous market potential for CBD has grown further, driving an increased need for specific and robust analytical methods for the quantification of cannabinoids.

Almost all parts of the hemp plant, with the exception of the seeds, contain cannabinoids (>100 substances known so far) which are produced by glandular hairs. Cannabinoid contents of the seeds primarily result from contamination with other parts of the plant.

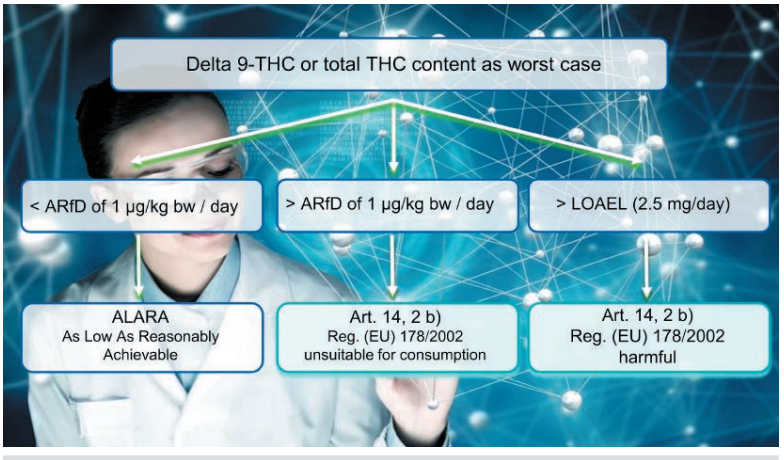
In raw plant material most of the cannabinoids are present as carboxylic acids which can undergo decarboxylation induced by heat in production processes, smoking or even in gas chromatographic analyses (see **Figure 1**). Important acids include tetrahydrocannabinolic acid – the precursor of delta 9-THC (often simply called THC) and delta-8-THC – and cannabidiolic acid – the precursor of CBD. Some cannabinoids are psychoactive (eg, delta-9-THC and delta-8-THC), whereas others are not (eg, delta-9-THC acid, cannabidiolic acid and cannabinol) or they only show slight effects (eg, CBD).

Essential for the analytics of food are the analytes delta-9-THC, the only cannabinoid for which toxicological limits have been established by the EFSA,[2] and delta-9-THC acid for the calculation of potentially formed delta-9-THC as well as for the analytics of CBD products, the analytes cannabidiol and cannabidiolic acid.

Two varieties of hemp are known: drug hemp and fibre hemp, which contains less THC. According to Reg. (EU) No 1307/2013 of the European Parliament, the maximum THC content for state-subsidised fibre hemp is 0.2 percent THC.[3] The CBD content can be used (together with the cannabinol content) for the distinction between drug hemp and fibre hemp.

The monitoring of further cannabinoids is recommended by the EC in the commission recommendation (EU) No. 2016/2115,[4] whereas in case of food of animal origin, only the monitoring of delta-9-THC is recommended. The EC has also asked for the monitoring of even more cannabinoids in hemp-derived foods and foods containing hemp or hemp-derived ingredients, like delta-8-THC (an isomer of delta-9-THC), cannabinol, CBD and delta-9-tetrahydrocannabivarin.

Figure 2



Evaluation of hemp containing food

Analysing CBD

Cannabinoid analytics require certain expertise. Laboratories must apply for approval from national authorities to analyse cannabinoids. The commission recommendation (EU) No. 2016/2115 is an important basis for the selection of a suitable method. A central statement is that cannabinoids shall be determined separately, which makes LC-MS/MS the preferred technique, since GC-MS/MS is not able to distinguish between precursor acid forms and decarboxylated forms. A disadvantage of LC-MS/MS is that the analyst often has to cope with strong matrix effects which require expensive (labelled internal standards) or time-consuming (standard addition) compensation techniques.

Regarding extraction procedures (solvents) and cleanup techniques, there is currently huge variety in the methods used among different laboratories. As such, several state committees are working to develop a harmonised approach.

For the legal evaluation of hemp containing products, the key question is always: 'Is the product food, drug or pharmaceutical?'. Narcotic or psychotropic substances are not accepted as food. "Cannabis and cannabis resin and extracts and tinctures of cannabis" are classified as drugs according to the United Nations Single Convention on Narcotic Drugs of 1961 legislation. Seeds (from fibre hemp) and leaves are excluded from the drug definition. Furthermore, flowering and fruiting tops are not regarded as drugs if the resin has been extracted.

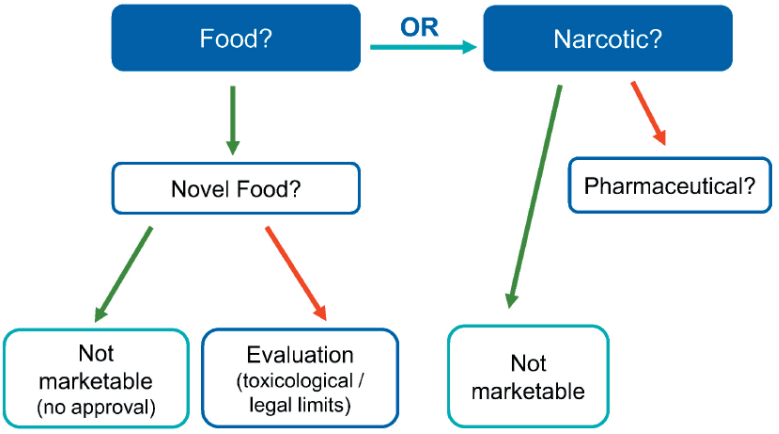
In the European Union (EU), no specific limit for delta-9-THC in food currently exists. The evaluation of THC contents is usually performed by food inspection authorities in consideration of toxicological values published by the European Food Safety Authority (EFSA)[2]:

- Acute Reference Dose (ARfD = estimate of the amount of a substance in food or drinking water that can be consumed over a lifetime without presenting an appreciable risk to health): 1 µg/kg body weight/day
- Lowest Observed Adverse Effect Level (LOAEL = lowest dose at which there was an observed toxic or adverse effect): 2.5 mg/day.

If the content of delta-9-THC (or total THC content, including THC acid in the worst case) is below the ARfD, the content is evaluated according to the ALARA (As Low as Reasonably Achievable) principle. This means that an assessment is carried out if the content could have been technologically avoided or reduced. If the determined content is above the ARfD but below the LOAEL, the product is rated as "unsuitable for consumption" according to art. 14, 2b) of Reg. (EU) No 178/2002,5 and if the determined content is above the LOAEL, the product is rated as "harmful" according to art. 14, 2b) of Reg. (EU) No 178/2002.

Currently, new specific limits for THC in oil from seeds, seeds and food derived from seeds are being discussed.

Figure 3



Product classification (green arrows: yes; red arrows: no)

Conclusion

To conclude the situation of CBD products, three outcomes are currently possible. CBD containing extracts from flowers and leaves are classified as drugs; isolated (pure) or synthetic CBD containing products could be marketed as Novel Food but need approval; and products with highlighted health benefits are classified as pharmaceutical.

Hemp seed, expeller and oil are currently approved as feed materials.[6] Other parts of hemp or the whole plant are not since no feed additives may be placed on the market without an authorisation.[7]

Overall, it can be said that the legal situation in the EU is currently quite complex. There will certainly be some changes in the next few years, but the importance of hemp in food, feed and Novel Food will continue to increase.

References

1. https://eur-lex.europa.eu/legal-content/EN/TXT/PDF/?uri=CELEX:62018CJ0663
2. Scientific Opinion on the risks for human health related to the presence of tetrahydrocannabinol (THC) in milk and other food of animal origin, EFSA Journal 2015;13(6):4141
3. https://eur-lex.europa.eu/legal-content/EN/TXT/PDF/?uri=CELEX:02013R1307-20201229
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