

Abstract

The market of cannabis products for recreational and medical use is growing quickly, BUCHI strongly supports producers by offering the right instruments and dedicated applications for several main production stages. The industrial scale rotary evaporators R-220 Pro and R-250 are the ideal solutions for efficient concentration of cannabinoid extracts after initial extraction as well as subsequent cannabinoid separation. High purity separation of various cannabinoids (e.g. THC and CBD) is achieved by preparative chromatography using BUCHI's compact PrepChrom C-700 which combines both flash and prep-HPLC purifications.

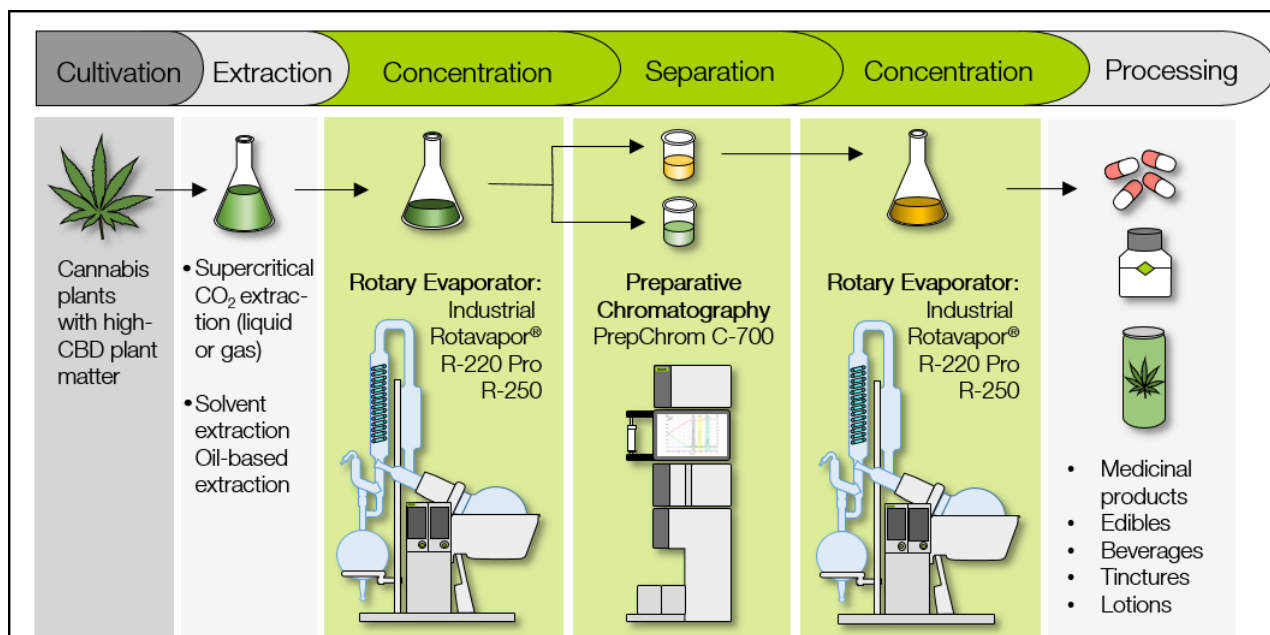


Figure 1: BUCHI covers several processing steps for the production of various cannabis products.

1. Introduction

Cannabis is a versatile plant with a wide range of applications; historically used for textile manufacturing, cannabis is commonly known as recreational drug and has recently been growing in popularity for its medical properties. Cannabis contains more than 80 cannabinoids, a group of chemical compounds concentrated in the plant's resin with unique therapeutic effects [1]. Cannabinoids are used to treat various ailments, as well as to diminish side effects of chemotherapy, inflammatory diseases (e.g. Multiple Sclerosis) or degenerative illnesses (e.g. Parkinson's disease) [2]. Cannabis is believed to relieve nausea and vomiting, boost the appetite, reduce seizure events and muscle spasm pain.

2. Cannabinoids

The most studied cannabinoids to date are tetrahydrocannabinol (THC) and cannabidiol (CBD). Whereas THC is the primary psychoactive component of the cannabis plant, CBD is not intoxicating and is considered a very promising medicine. Recent legalization in a number of states across the USA, as well as a few

European countries, have opened up new opportunities and challenges in the fast-growing market of cannabis products for recreational and medical use. In terms of production of pharmaceutically pure cannabinoids, BUCHI offers several instruments that cover multiple production stages. This whitepaper describes the general manufacturing process from cannabis cultivation to the end product, and presents the suitable solutions provided by BUCHI.

Cannabinoids can be consumed in different ways; smoked, vaporized, eaten as foodstuffs and tinctures, as well as applied via eye drops or lotions. Cannabis edibles are a rapidly emerging market, with products ranging from confectionery to beverages. Cannabis processing is a multi-stage production process starting with the extraction of the desired substances from the cannabis plant to packaging into appropriate edibles. BUCHI offers several instruments covering multiple manufacturing stages and dedicated cannabis applications that were developed in close collaboration with the cannabis pioneering company AI FAME GmbH.

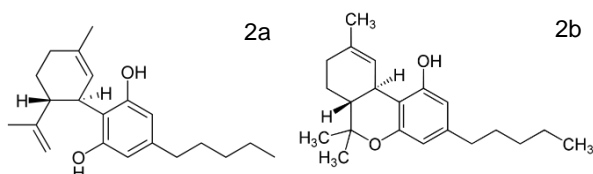


Figure 2: psychoactive Tetrahydrocannabinol (THC, 2a) and non-psychoactive cannabidiol (CBD, 2b)

2. Production process

Cultivation and extraction

In order to maximize the CBD yield, it is most effective to use high-CBD plant matter as raw ingredients. Further, a controlled environment is required to achieve highly reproducible batches of plants. Once the plants are harvested, the valuable cannabinoids can be separated

from the plant by various extraction methods; solvent extraction and supercritical CO₂ extraction are the most commonly used techniques. Solvent extraction is mostly performed with ethanol/water mixtures; a cost-effective method, but additional safety measures and solvent removal is required. The extraction by super-critical CO₂ (liquid or gas) is considered as particularly efficient and environmentally friendly, however, initial costs are high and parameter setting is time consuming.

Concentration by evaporation

As the extraction often uses a large amount of solvent, it is necessary to reduce the volume of the crude extract to facilitate subsequent cannabinoid separation. The concentration of the extract is achieved by evaporating the solvent by an industrial rotary evaporator. BUCHI is the global market leader in rotary evaporators and offers a wide range of solutions for evaporation and drying applications. The ideal instruments for the concentration of the cannabinoids are the models R-220 Pro and R-250 which can be used with 20 L and a 50 L evaporation flask, respectively. All BUCHI industrial evaporators are equipped with FDA-compliant materials suitable for production at medical and food grade levels. In addition, system extension by a foam sensor allows for automatic foam control of the typically strongly foaming extracts saving time for monitoring and cleaning. The concentrated extract is now ready for separation of the desired cannabinoids.

Separation by preparative chromatography

BUCHI's PrepChrom C-700 offers a compact and simple solution to separate and purify cannabinoid extracts of various volumes from small to large size batches. The automated system combines flash chromatography separation and subsequent preparative HPLC purification of the relevant cannabis fractions as well as their separate collection. The concentrated extracts are applied under reversed phase conditions with mostly ethanol and water as the mobile phase. The water solubility of the extract allows for the use of aqueous solvents with associated economic and ecologic advantages over conventional organic solvents.

Separation by preparative chromatography uses the principle that different cannabinoids travel through a specific stationary phase at different speeds. The

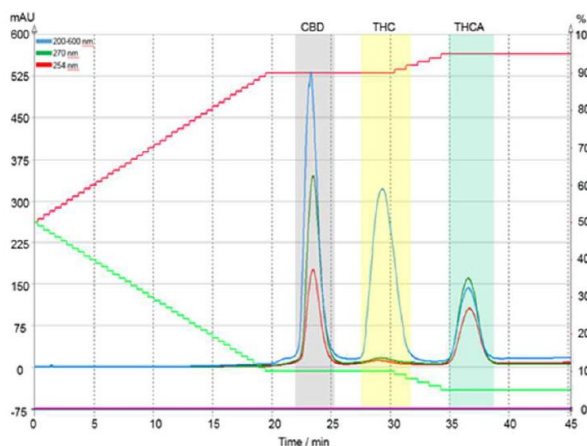


Figure 3: Methanol/water separation of the extracted cannabinoids using the PrepChrom C-700.

substances to separate and purify are eluted and collected successively, as illustrated in Figure 3 for a cannabis extract containing the three cannabinoids, THC, CBD and THCA (tetrahydrocannabinolic acid).

Concentration after separation

The high throughput of the PrepChrom C-700 results in large fractions of valuable cannabinoids at high purity, although in solvent mixtures. Therefore, it is required to evaporate the present solvent, and hence concentrate the cannabinoid fractions for further processing. The industrial rotary evaporator models R-220 Pro and R-250 are also the ideal solution for this concentration step. The possibility of using an amberized glass aids in preserving light sensitive cannabinoids. The continuous version of the R-220 Pro can be used for evaporating and drying large volumes as well as solvent recycling thanks to the automatic draining and filling possibilities.



Figure 4: Amber glass evaporation flask.

Further processing

Once the desired cannabinoids are present separately and at high purity, they can be used for further processing, e.g. pharmaceutical production or food manufacturing.

3. Conclusions

The industrial rotary evaporators (R-220 Pro, R-250) and the PrepChrom C-700 by BUCHI are ideal solutions for the concentration, separation and purification of cannabinoids and support medical research, product development and small-scale production of cannabis products. The automated systems perfectly fulfil the requirements for the cost-effective and straightforward production of pharmaceutically pure cannabinoids, covering several stages in the production process of cannabis products.

4. Acknowledgement

We thank AI FAME GmbH, Switzerland, for sharing their expertise in cannabis production and processing, the good collaboration and valuable discussions.

5. References

- [1] Kuzdzal S. and Lipps W. Unravelling the cannabinome, *The Analytical Scientist* 32 (2015), 24-31
- [2] Sutton, IR. Daeniken, P. (2006). Cannabinoids in the management of intractable chemotherapy-induced nausea and vomiting and cancer-related pain. *The Journal of Supportive Oncology*.
- [3] Kogan, NM. Mechoulam, R. (2007) Cannabinoids in health and disease. *Dialogues Clin Neurosci*. 2007 Dec; 9(4): 413–430.

Detailed instructions are found in the following short notes:
Evaporation (No 220/2015): 'Applied Industrial Rotavapor® solutions for cannabis products'
Chromatography (No 190/2015): 'Separation of Cannabinoids for Clinical Use'