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*Short communication*

# Comparative analysis of the advantages and disadvantages of olive oil and supercritical $CO_2$ extraction in producing Cannabis extracts for medicinal purposes in the production area with GMP standards

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## Introduction

Nowadays, more than ever, pharmaceutical products with extracts from the Cannabis plant are often chosen in treatment for different diagnoses or taken like preventive medicines for everyday usage. Because of it, the industry of Cannabis is noticing a very rapid transition from a black market to a legal market. So, product development and extraction methods have become a focal point.

Over the years, most chemical compounds of the Cannabis plant have been identified. Because of the different chemical properties of every compound, the choice of extraction method is essential. The challenge of purification and separation of compounds of interest has recently become an exciting topic for the pharmaceutical industry. This interest is substantiated by an increased understanding and correlation of the structures of bioactive compounds in plant material with extraction conditions like solvent, temperature, pressure and time (Azmir et al., 2013).

Different extraction methods show different yields and extracts with different potency and quality. These results depend on the applied conditions and techniques correlated with the extracted herbal material. Generally, extraction methods are divided into four groups: solventless, solvent-based, convention, and alternative methods. This paper focuses on a comparison between two methods of solvent-based extractions, vegetable oil, i.e., olive oil, versus supercritical $CO_2$ extraction.

Vegetable oils are considered lipophilic due to their non-polar characteristic, which enables selective dissolving properties. Olive oil is a very often solvent in the field of cannabis extraction. The high yield of terpenes obtained from olive oil as a solvent is attributed to its efficient solubility and limited product loss by protecting the compounds from evaporation (Romano and Hazekamp, 2013).

Supercritical fluid extraction (SFE) is used to displace conventional extraction methods. SFE uses safe and capable solvents (i.e., $CO_2$ gas) in their critical state to efficiently extract chemicals. Also, these procedures decrease environmental impacts and reduce toxic residue on products by using supercritical fluids (Cunha et al., 2018).

## Materials and methods

The Cannabis plant material used in this study was THC-rich floss from a relevant supplier, cultivated under standardized conditions according to the requirements of Good Agricultural Practice (GACP) and Good Manufacturing Practice (GMP).

Preheating of cannabis samples has been recommended to potentiate the final extract, i.e., to decarboxylate the acidic forms of cannabinoids naturally present in cannabis plant material, such as THCA and CBDA, and turn them into their more potent counterparts such as THC and CBD (Romano and Hazekamp, 2013;

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Veress et al., 1990). This was performed with the help of an appropriate chamber for drying at a strictly controlled temperature and duration of the performance.

For olive oil extraction, herb was mixed with appropriate amount of solvent. The solvent used for extraction was of quality in accordance with European Pharmacopeia. The process was performed in stainless steel vessels, with controlled heating to the required temperature, with addition of the new amounts of the solvent to stimulate better extraction of the active ingredients during the process.

Supercritical $CO_2$ extraction was performed on a supercritical extractor according to a recipe with controlled parameters considering temperature and pressure.

Quantification of the present cannabinoids, more precisely the content of CBD, CBDA, THC and THCA, was obtained using a suitable analytical procedure that employs HPLC system Shimadzu with UV DAD detector, quaternary pump, and attached DELL pc with Labsolution software 5.97.

## Results and discussion

### *Olive oil extraction*

Decarboxylated dried flowers were extracted with olive oil at a temperature with repetitive solvent addition cycles in order to extract the active ingredient from THC-rich herbal material. Obtained results for quantification of THC as the active ingredient (1.3 % *W/V*), have confirmed a good extraction yield, taking into consideration the amount of starting material for extraction and its declared concentration of THCA. The main drawback that needs to be stressed out is that the extracted amount of THC is present in the extract in low concentration, more precisely, less than 2 % THC (*W/V*).

### *Extraction by Supercritical Fluids ($CO_2$)*

The previously ground and chopped flowers are decarboxylated in a heated dryer. Decarboxylated flowers are placed in the recipient of the extractor. The extraction begins by selecting the appropriate recipe in which the required temperature and pressure are defined. The obtained extract is collected at a specific time interval. The results of the chemical analysis showed a good yield, with a crude extract that is qualified with a concentration of the active ingredient, THC of about 75 % THC (*W/W*).

## Conclusion

No matter whether the dried cannabis flower is the product of choice, we are currently facing an increased interest in products containing Cannabis extract, which promotes the need to develop new technological processes and new pharmaceutical dosage forms. Therefore, in selecting the technological process, i.e., extraction method, several factors must be taken into account to obtain the desired product.

However, this paper focuses on olive oil and supercritical $CO_2$ extraction.

Olive oil has performed much better as an extraction solvent for making cannabis oil, extracting all terpenes and cannabinoids tested very efficiently. In addition, this solvent is not harmful, expensive, flammable or toxic, and the oil only needs to be heated to the boiling point of water. One of the main drawbacks is that olive oil extract is characterized by low THC concentration, which makes its use more complicated.

Supercritical $CO_2$ behaves like a non-polar solvent, capable of extracting a broad range of non-polar solutes, cannabinoids included. Therefore, due to low critical temperature and pressure, $CO_2$ is also the solvent of choice. It is non-flammable, non-toxic, inert, renewable, easy to remove, abundant, and relatively low-cost.

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