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Advancing the Application of Critical Fluid Technology in Cannabis Science & Engineering

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ABSTRACT

The value of cannabis products in 2018 is estimated to be currently conservatively at $10 billion (USA) and 5.5 billion (Canada) and to reach ~$60 billion within a decade. The role of critical fluid technology (CFT) in this dynamic growth pattern is significant due primarily in its role in producing extract concentrates for use in infused products [1]. CFT has also in the USA created a dynamic industry in itself characterized by: (a) the use of not only CO_2 in its sub- and super-critical state, but propane or butane, dimethyl ether, tetrafluoroethane, or mixtures thereof; (b) the development of over 20 new companies producing different architectures of extraction equipment – including contributions from pan-Euro and – world contributors[2]. The first portion of this presentation will illustrate these developments. Secondly, this presentation will report of new research in better optimizing CFT, namely: (a) the use of dynamic differential rates of dissolution of THC and CBD – to produce customized extracts of varying cannabinoid content; (b) development of approaches to capture the entourage terpene fraction based on predictive, methods employing both new and old physicochemical data, such as phase equilibria, the solute solubility's, and vapor pressure of terpenes associated with certain cannabis strains[3]. The vapor pressure of cannabis's terpene components are in some cases known under ambient, pressurized, and vacuum conditions from the literature, and is an important in the effective extraction and capture of these volatile or semi-volatile components when extracting cannabis. Hence the relative rates of terpene extraction depend on factors such as the Poynting-effect and their 2nd mixed virial coefficients with the extracting fluid which and can be predicted via an EOS. Recently determined vapor pressures for CBD and THC are identical over the range of conditions typically employed in the SC-CO_2 of cannabinoids [4]; hence one is limited to using the reported literature differential solubility data for these solutes, which results in long extraction times and copious recirculation of CO_2 to avoid extraction of unwanted co-extractives. Finally, solubility parameter theory will be used to explain the above results and use of alternative solvents for producing cannabis extractives.

INTRODUCTION

The development of the medical and recreational cannabis industry in the USA, Canada, and throughout the world has embraced the use of pressurized fluids in both their sub- and supercritical states as applied to extraction, purification and for other unit processing steps. Particularly the use of CO_2 in its sub- and supercritical states with the use of ethanol [5] as a co-solvent is widely practiced. Despite CO_2's environmental and consumer appeal, traditional techniques such as mechanical pressing, propane and butane percolation methods, the use of both

ambient and sub-ambient ethanol still largely persist based on an array of traditional consumer product formats such as “shatter”, “rosin”, “kief”, “crumble”, “butter”, “HBO”, and “Charlotte’s Web” [6]. Recently the use dimethyl ether and tetrafluoroethane as neat fluids or mixtures have also appeared.

It should be appreciated that this array of techniques is employed in the cannabis and hemp industry in the development of the above-derived products. Sub- and super-critical CO_2 extraction is primarily today used in the extraction mode of processing to produce “oils” that can contain up to ~40 % cannabinoid-based ingredients, although this is dependent of the type of cannabis matrix being extracted. Further enrichment of the active cannabinoid ingredients is achieved by using precipitation of contaminating material in such solvents as ethanol at sub-ambient conditions, followed by vacuum distillation techniques such as thin-film and short path, and in the case of cannabidiol (CBD) – seed crystallization from a hydrocarbon-based solvent such as n-pentane.

An example of such a process is show in **Figure 1** as provided by the author’s direction of a Capstone Senior Design II engineering team in the Department of Chemical Engineering at the University of Alberta to produce 99% crystalline CBD. Here a 40 % CBD-containing “oil”, CO_2 - extracted is further treated with cold ethanol (-45^{o}C), the liquid filtrate treated by vacuum distillation at 180-200^{o}C, and the product from the vacuum distillation fed to a forced circulation crystallizer to produce crystalline CBD. Such scaled-up engineering design will be required to serve the cannabis industry commensurate with the anticipated large cannabis or hemp crop yields such as the Aurora Sky operation in Edmonton, Canada anticipated to yield 100,000 kilos of cannabis product in 2018. Hence extraction technology must be also scaled to meet this scale cannabis production.

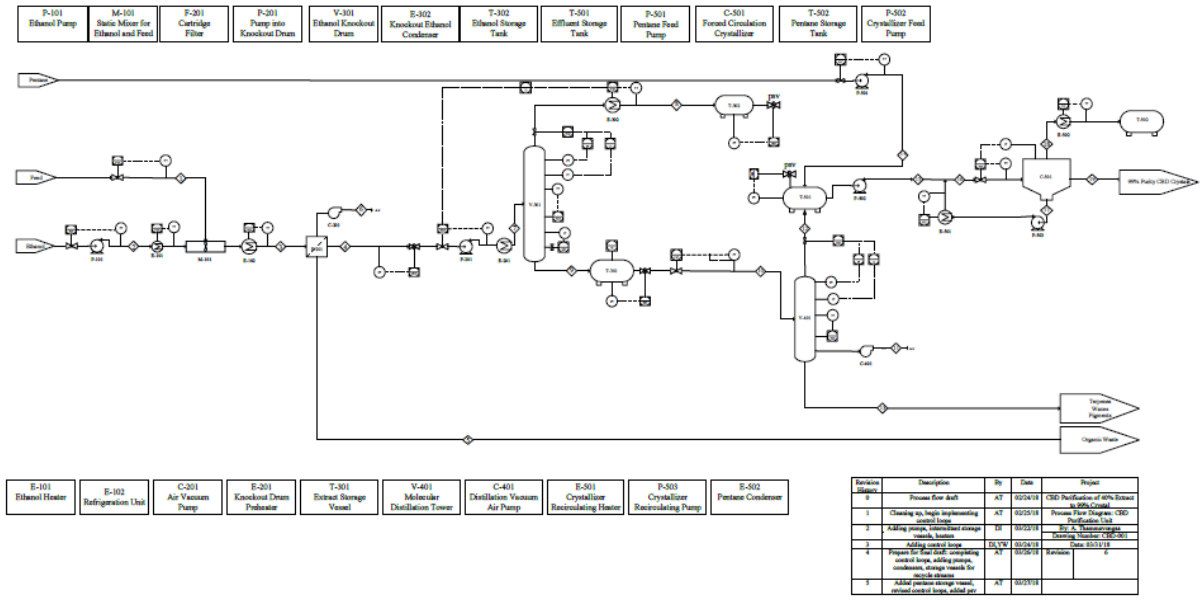

Figure 1, Flow schematic for the post-SFE enrichment of CBD after CO_2 extraction of hemp “flower”.

MATERIALS AND METHODS

The development of extraction equipment and plants to serve the cannabis and hemp industries has been dramatic over the past 4 years, particularly in the USA where well over 20 or more new companies and developed to serve the industry. This continues at a rapid pace with an emphasis on increasing both the speed of extraction, scale-up, automation, and the development of semi- to continuous systems. Aside from these primarily-based CO_2 extractors, advocacy continues for other modes of extraction, such as the sub-critical ethanol, the lower hydrocarbon fluids (propane and butane), specific fluorocarbons (ex. – tetrafluoro ethane), and dimethyl ether. In the USA, state-based regulations make closed loop mandatory even when using CO_2 as the extracting fluid.

Table 1. Companies producing CO_2 – based extractors for the cannabis industry

- Apeks
- Eden Labs
- Waters
- Stripper Cell
- Infinity Supercritical
- Paradigm Supercritical Innovation (PSI)
- Evolab - PIC
- Clean Room Extracts (Applied Separations)
- Vitalis (CANADA)
- Advanced Extraction Systems (CANADA)
- Careddi (CHINA)
- Supercritical Fluid Technologies
- MRX Extractors
- Xact-xtract
- Kiinja Corporation
- Evolabs
- NuAxion Tech (INDIA)
- Thar Technologies
- Ocolabs
- Druk Engineering
- Separeco (ITALY)
- STEP X
- Extraction Tek Solutions
- Pure Extract (Bandit)
- Applied Extracts
- Isolate Extraction Systems
- ExtractLab
- Soma Labs

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Figure 2. Uniquely designed CO_2 extractors: (left) "cathedral or boat" extractor, (b) "washing machine" extractor

The extraction equipment listed in **Table 1** and shown in **Figure 2** are largely designed for batch, semi-continuous operation at pressures of 200-350 bar and up to 2 X 50L vessel configurations. The commensurate capitalization costs to implement CO_2 extraction in the cannabis industry and their current limited production capacity makes alternatives such as liquified hydrocarbon fluids and ethanol competitive with sub- and supercritical CO_2 extraction, but the ability of SFE using CO_2 to control extract composition and, hence final extract product "appearance" in product formulation are not matched by these extraction methods. Carbon dioxide-based extraction avoids the inherent dangers of propane- or butane-extraction and copious co-extractives that must be removed when using ethanol as the primary extraction solvent. An example of the selectivity afforded using SC-CO_2 extraction is shown in **Figure 3** for the extraction of a non-decarboxylated cannabis. It can be seen that the cannabinoid composition nature of the extract varies over the time of the extraction which, when coupled with the co-extraction of non-cannabinoid solutes, can produce different unique extracts with respect their appearance and taste. Alternatively, cannabis CO_2 extracts can be fractionated by using multiple separator vessels which allows for isolation of enriched fractions of cannabidiol and tetrahydrocannabinol (THC) and the terpenes associated with a strain of cannabis. Depending on the desired end-product, either non- or fully-decarboxylated cannabis can be extracted.

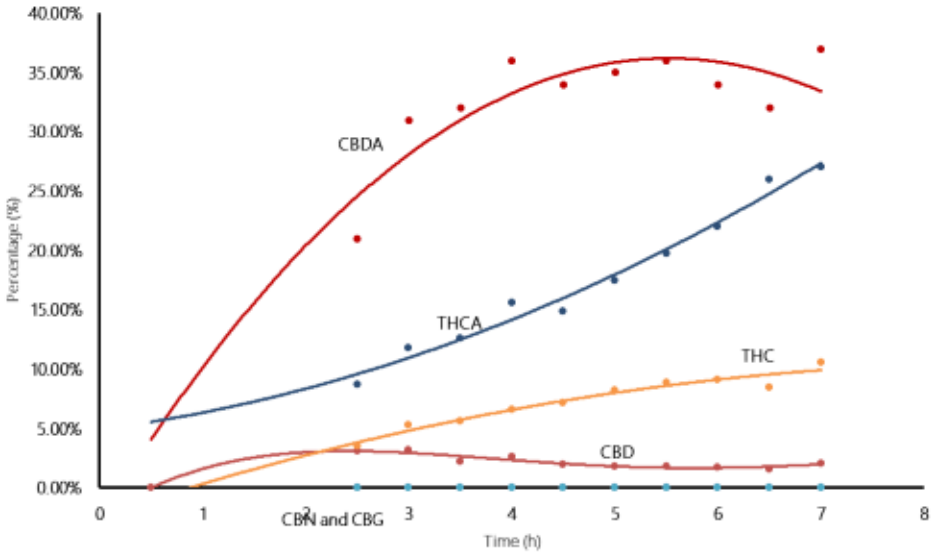

Figure 3. Variation in the cannabinoid composition during SC-CO_2 extraction of cannabis.

The design and optimization of cannabis extraction has largely been empirical, in part, due to legal restrictions that have limited research in this field. In addition, the lack of requisite data particularly for cannabis constituents such as THC and CBD and their acidic analogues, as well as the associated terpene solutes, hinders the development of rationale extraction protocols. There is however associated data for terpene solutes which can be used in modeling their extraction from cannabis – particularly from studies on the extraction of essential oil terpene components. Examples of this can be found in the classic supercritical extraction literature, such as the excellent book by Stahl and co-workers [7], physicochemical data from the predictive

methods of Martins et al [8], experimental results of De Mello, et al. [9], and older essential oil data [10].

We have also have also found solubility parameter theory to be of aid in selecting and optimizing processing conditions for cannabis, as well as beneficial in understanding the results obtained using various extraction solvents and methods. **Figure 4** shows in a columnar format for the relative solubility parameters for some of the major cannabinoid and terpene compounds found in cannabis in contrast to those for the solvents, sub- and super-critical CO_2 - and ethanol as a function of temperature. This tells us that under the stated extraction conditions being commonly used for CO_2 overlap with those for the terpenoid compounds but are compromised with respect to the major cannabinoid values. This means at best CO_2 provides a relative poor solubility for the cannabinoids relative to ethanol at the stated extraction conditions, while ethanol is a poorer solvent for removing-retaining the terpene fraction – which is what is found in extracting cannabis, as well as post-extraction processing. Typical conditions and the relevant solubility parameters for propane and butane when using them as percolation solvents show a significant overlap with the terpene components, but a more limited capacity to extraction a major amount of the cannabinoid components. However, it must be appreciated that the solubility parameters for unwanted compounds in the extract, such as the waxes and pigments [11] associated with the cannabis or hemp plant also overlap with those shown for the cannabinoids and terpenes, making further post-extraction purification necessary on the extracts.

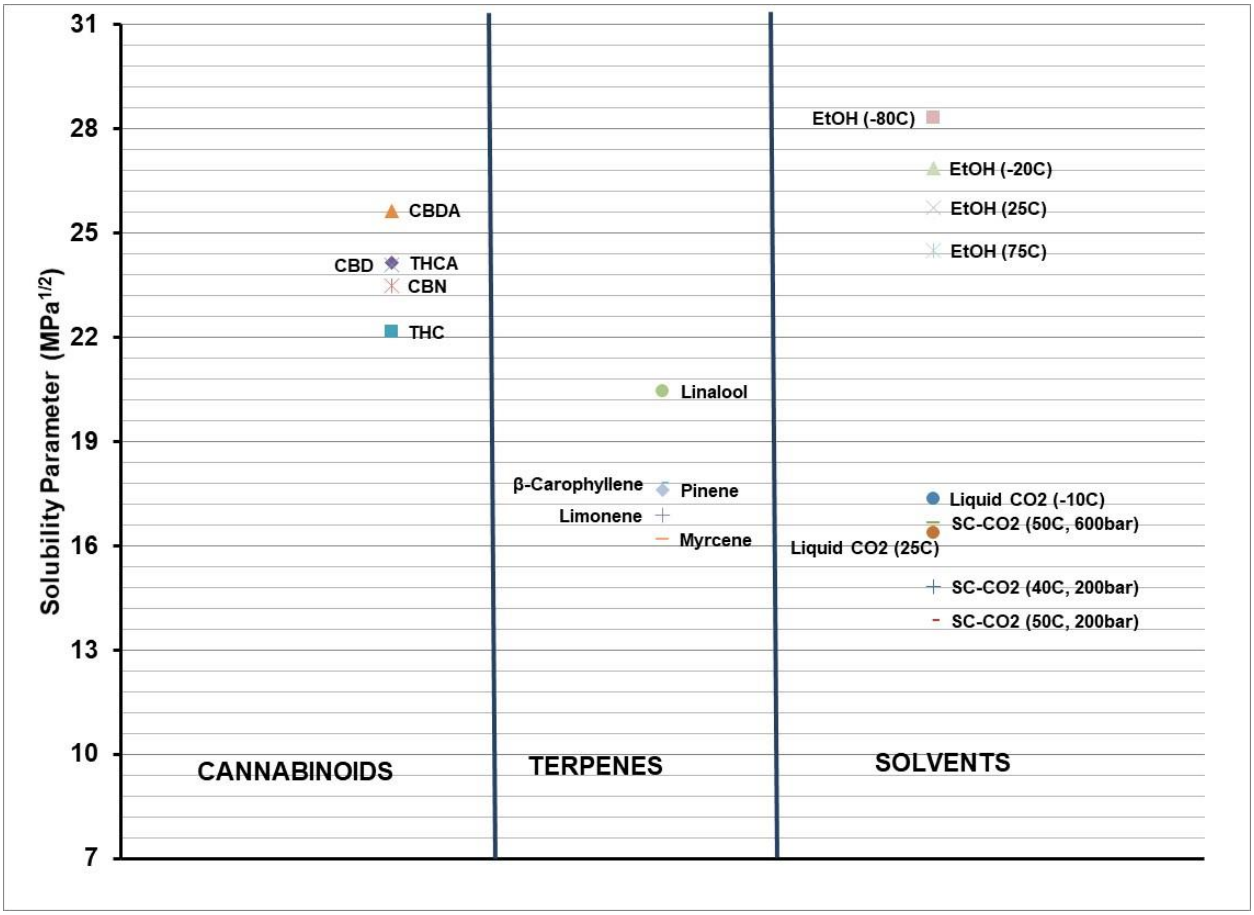

Figure 4. Relative solubility parameter values for cannabis compounds and the extraction solvents CO_2 and ethanol (EtOH) under specified extraction conditions.

RESULTS

The solubility of cannabinoids in SC-CO_2 are low under the stated conditions as rationalized in the previous section as well as the experimental results of Perrotin-Brunel, et al. [12]. This can be improved by conducting CO_2 extractions at higher pressures, but unfortunately a high level of unwanted co-extractives will also be extracted from the cannabis and hemp matrix. Conversely, this is also true using ethanol (EtOH) as well as when using other solvents due to the complex chemical composition of the cannabis plant. This fact manifests itself in several other problems facing the cannabis industry, namely; (1) the removal or minimization of the THC content in the resultant extract, (2) retention of the terpene fraction during extraction and post-extraction processing, and (3) the extraction of unwanted contaminants (i.e., pesticides, fungicides) found in the cannabis feedstock.

Extract consistency when performing extractions and post extraction processing is important in terms of final cannabis product formulation. Aside from THC content of in the extract (0.3 wt. % THC according to regulations in the USA), the ability to produce a consistent cannabinoid and terpene profile content is critical to product formulators. The latter (terpene content) is largely being addressed by back-addition of expensive terpene compounds after extraction (based on the analysis of the original pre-extraction terpene profile) due to loss of the terpene components during the various processing steps. Erratic extraction results (for example an extract having a CBD/THC ratio of 22.6:1 vs. 20.8:1) requires the formulator to consistently adjust the stoichiometry of the final product composition due to specific regulatory labeling requirements Hence immediate access to cannabinoid "potency" analysis via HPLC or SFC is important to the extractor and formulator of the end product.

There is a need for additional physicochemical data in support of the extraction and purification processes for the cannabis industry and the anticipated scale-up of these processes. Aside from the previously mentioned data and studies in the literature, the following physicochemical data tabulated in **Table 1** would greatly aid toward putting the extraction and purification of cannabis constituents on a more-sound basis.

Table 1. Physicochemical data needed for cannabis constituent extraction and purification.

Accurate Solute Boiling and Melting Points under Pressure or Vacuo
Solute Liquid or Solid Density – Ambient and as a Function of P and T
Solute Solubility Data in Various Solvent Media as a f (T)
Critical Parameters for Solutes and Solvents (P, T, ρ)
Vapor Pressure Data of Cannabinoid and Terpenes
Solubility Parameters of Solutes and Solvents
Equation-of-State for Individual Cannabis Components
Effect of Co-Extractives on the Extraction of Cannabis Constituents

It should be noted that the recent studies of Lovestead and Bruno for forensic purposes [4], show that the vapor pressures for CBD and THC are almost identical for an extended range of temperature. This is not encouraging with respect to separating effectively the THC from CBD

found in cannabis extracts, but a further indication as to the role that solvent-based fractionation based on both pressure and temperature along with chromatographic-based purification methods may find an increasing role in resolving this problem and those associated with pesticide-fungicide removal from extract concentrates. The above listed physicochemical data is also of importance to the final product formulator in the cannabis industry with respect to the array of products offered (tinctures, edibles, vape oils, encapsulates, sublingual sprays, patches, and topicals) as well as added incipient such as vegetable oils and cutting or dilution agents.

It should be appreciated that in the real-world cannabis-processing lab or production facility that several extraction methodologies may exist side-by-side. For example, it is not uncommon to find hydrocarbon-based extraction being utilized along with CO_2 – extraction, rosin pressing, and the use of ethanol for extraction and post-extraction purification schemes – all in the same facility. It should also be noted that government regulations from one state or province to another regarding the use of solvents impact on the choice of extraction methods and associated equipment. For example, some states in the USA do not allow the use of hydrocarbon solvents at all; the country-city of San Diego in the USA does not allow the use of butane or ethanol during processing, but allows CO_2 extraction.

CONCLUSIONS

There is a need for the extraction and processing of cannabis to be conducted on a more rationale basis than is currently being executed. Aside from the comments noted previously, there are several reasons for this. The cannabis and hemp processing communities are overall not aware of the "supercritical" fluid community in terms of what it can contribute to solving their processing problems. Aside from this lack of interaction, there are additional reasons for this. One is the lack of educational-based training; the major "cannabis" conferences tend to be "business" conferences as typified by the gigantic MJBiz Conference held annually in Las Vegas, NV-USA. There are probably over 25 conferences held annually in the USA and Canada on both a national and regional basis. In the USA, several professional societies have begun addressing the needs of the cannabis community with respect to interaction and education, e.g.: ACS, ASTM, AOAC, IFT. Especially noteworthy is the existence of the "Cannabis Chemistry" sub-division of the ACS. The efforts of Emerald Scientific Company are exemplary with respect to guidance in the area of the extraction of cannabis. In this regard, an interesting 6-part video series is available gratis at their website [13] (see in **Figure 5** below). In general universities and colleges and been slow and remiss to offer training relevant to the cannabis industry, impart due to existing regulations regarding legalized use of cannabis. However, with the anticipated "state" legalization of medical marijuana to occur in over 40 of the 50 states in the USA in 2018, Federal de-scheduling of the use of CBD from particularly hemp feedstocks is in progress.

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Figure 5. Extraction Efficiency Series available at http://www.emeraldscientific.com