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WHITE PAPER

A Critical Analysis and Comparison of Ethanol and CO_2 Extraction Techniques for CBD Derived from Hemp

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Abstract

Ethanol has been used as a solvent to extract essential oils from botanicals for centuries. Recently, ethanol has been used to extract the cannabinoids CBD and CBG from hemp, and THC from cannabis. Ethanol is an attractive solvent because it is readily available in commercial quantities and relatively inexpensive in a denatured state. *There are two main categories of ethanol: denatured or food grade.* 200-proof food grade ethanol is pure and contains very little water. Denatured ethanol is typically 196-proof or less and contains added chemicals known to be detrimental to health. Most licensed processors of hemp and cannabis employing ethanol extraction use denatured ethanol to greatly reduce the cost of operation, but do so without knowing how this impacts the public. This article compares denatured ethanol vs. CO_2 as an extraction solvent. We discuss chemical residue contaminants, testing issues, solvent reuse, and solvent revalidation requirements. We also discuss and compare solvent loss costs for the two

extraction techniques and show how solvent losses can contribute to high operating costs. Finally, we present a comprehensive comparison of ethanol and CO_2 as extraction solvents.

Chemical Residues in CBD Oil

Consumers demand the highest purity for all ingestible products. Consumers want products to be safe and free of any health harming chemical residues. This is especially true when a remedy is claimed to be derived from a natural botanical source. The dirty little secret in the cannabis and hemp industry: natural CBD products might not be so healthy.

Residual chemical impurities used to denature ethanol can contaminate CBD oil. Denatured ethanol is governed by the Bureau of Alcohol Tobacco and Firearms in the United States and similar agencies in Europe and Canada. Approved denatured recipes include harmful chemicals such as heptane, hexane, methanol, butanol, and distilled mineral spirits.[1]

> *"Residual chemical solvent Impurities from ethanol are **entirely avoidable** using CO_2 production methods."*
>
> *- Dr. Jon Thompson*

Denatured ethanol is chosen by manufacturers instead of food grade ethanol in order to avoid expensive excise taxes. Even though most of the chemical impurities are claimed to be at "safe" levels as described by the United States Pharmacopeia (USP), chemical residuals are still measurable in the CBD oil. These residual chemical contaminants can be harmful to human health. There are more than fifty different denatured ethanol recipes available for hemp extraction, all of them containing solvent health hazards.[2]

Residue Testing for CBD Oil

In the hemp and cannabis industries, third-party lab tests are used to measure and control the quality of wholesale and retail consumer products. Unfortunately, many of these "standard" quality tests are conducted by labs without having first-hand knowledge of the added chemicals in denatured ethanol, these chemicals are labeled "unknowns".

The quality of the denatured ethanol used in extraction affects the end product. These *generic tests* only address a portion of the potential denatured ethanol chemical residues. This is why the International Council for Harmonization (ICH) Q2 specification requires unknowns be identified and assessed in order for a test method to be valid.

"Standard" tests can miss chemical contaminants present in the sample, giving a false "chemical residue free" test result. By adjusting and validating a single "standard" test method

to address other possible contaminants, the consuming public doesn't need to be misled or potentially harmed.

Consumers may have a false sense of product safety when consuming ethanol-derived extracts supported by "standard" lab tests. Without scientific training, denatured ethanol extraction manufacturers may even brag their CBD has LESS residue than their competitors.[3]

Why should a natural product have ANY unnatural chemical residues? It is our belief, backed by growing consumer awareness, manufacturers should be required to disclose low-level chemical contaminants and residuals in their products.

Risk Assessment of Chemical Residues between CO_2 and Ethanol

Chemical residues are entirely avoidable using CO_2 extraction techniques. CO_2 is a pure solvent because it does not use chemical denaturants. There are several different grades of CO_2 including industrial, food, and medical grades. Food grade CO_2 is pure and inexpensive compared to ethanol. (Specifications are available from the Compressed Gas Association and Certificates of Analysis from all CO_2 providers.)

The following table examines the pros and cons of ethanol vs CO_2 as a solvent.

Table 1. Risk Assessment comparing chemical residues in extraction methods.

	Denatured Ethanol Extracts	**Food-Grade CO_2 Extracts**
Presence of chemical solvent residual contaminants in extract	High Risk.	No risk.
Health impact of chemical solvent residuals	Unknown risk. The toxicity and carcinogen aspects of the chemical residues in ethanol are significant and defined by the Environmental Health Criteria 170, World Health Organization, 1994, the US National Toxicity Program.	No risk.
Validated test methods for measurement of chemical residuals	High risk of misleading results with standard testing methods of 3rd party labs. The standard list of impurities tested often does not match the impurities in denatured ethanol. Comprehensive testing methods and procedures are readily available, but	No risk.

	must be validated according to USP<467>[4], ICH Q2[5], ICH Q3C[6] and EP 5.4[7] (EHC, IRIS). Testing methods must be developed and validated for each product and each specially denatured ethanol recipe.	
Batch-to-batch solvent revalidation	To ensure purity, solvents must be re-tested between each extraction batch to verify no buildup of contanimants.[8]	Not applicable.

Highly publicized events such as the vaping crisis are quickly raising consumer awareness about the purity and safety of hemp and cannabis derived products. The growing consumer preference for CO_2 extracted products is expected to quickly accelerate as the FDA defines the health and safety requirements for the industry.

Hidden Costs of Ethanol Extraction

Beyond health and safety concerns, there are ***many hidden costs*** of ethanol extraction. These need to be considered before making a large investment in manufacturing equipment and facilities. These include the following:

- Hazardous waste costs
- Electrical power costs
- Solvent recovery and losses costs
- Carbon filtration costs
- Facility costs to comply with fire codes
- Worker safety risks and high business insurance costs
- Storage of flammable solvent costs
- Regulatory compliance costs
- Solvent reconditioning and revalidation costs
- Biomass hazardous waste costs and hazardous volatile and hazardous organic compounds (VOC)
- Revenue losses due to lower extraction efficiency
- Excise tax associated with “organic” solvents

”Ethanol extraction leaves chemical residues in the extract and costs significantly more to produce compared to CO_2 extracts when all the hidden costs are understood.

-Dr. Jon Thompson

We will focus on two hidden costs in the following paragraphs. These include solvent recovery/loss and solvent revalidation. The former has a huge impact on operating cost and the latter is driven by Good Manufacturing Practices (GMP) compliancy.

Solvent Loss as a Key Cost Driver in Ethanol Production

Companies choosing ethanol extraction methods often do so because the cost for ethanol equipment is attractive. But, ethanol extraction also carries the highest operating costs for many reasons. Table 2 shows poor ethanol recovery from extracted biomass translates into a significant loss of solvent and added cost.

Table 2. Estimated Difference in Solvent Cost[b,c] for a 1-ton per day Ethanol and CO_2 system.

	Ethanol	**CO_2**
Approximate Equipment Cost[a]	$2,000,000	$4,000,000
Required Solvent Start-Up Cost	$7,000	$500
Solvent Loss Cost per Day	$2,700-3500[d]	$115
CUMULATIVE COMPARISON		
1 Year Solvent Loss Cost	**$972,000-1,260,000[e]**	**$34,000[f]**
10 Year Solvent Loss Cost	**$2,916,000-3,780,000**	**$102,000**

a. Biomass throughput is 1 ton per day processing to distillate.
b. All costs are approximate and in USD.
c. Costs of infrastructure, recovery, biomass disposal, revalidation costs, losses due to carbon, and energy are excluded.
d. 5% loss per cycle at 1 gallon of ethanol per pound of biomass. 360 days operating per year. Assumes no carbon or filters are used.
e. Cost of one 240-gallon tote including shipping is about $7/l of ethanol.
f. Cost of CO_2 in bulk delivered is about $0.04/lb.

The above table shows solvent loss is a major contributor to operating cost, thus greatly increasing the total cost of ownership. When considering all of ethanol's hidden costs, CO_2 comes in with the lowest operating costs. CO_2 extraction is usually the best choice for your manufacturing equipment foundation. CO_2 extraction supports the broadest addressable market for consumer products, has the highest cannabinoid extraction efficiency levels, and the lowest operating costs.

Solvent Revalidation

Solvent revalidation is the sampling and testing of a solvent once it has been used, recovered, and reconditioned to show it is suitable to be reused. According to the USFDA manufacturing guidelines published in 2010[8], solvents "have no therapeutic benefit" and any solvent used in the manufacturing process must not show an increase in contaminants over time when reused. This means, in order to show contaminants have not built up, it is the manufacturer's responsibly to test and demonstrate the lack of contaminant concentration over sequential extraction cycles.

By using headspace GC-MS, it can be easily demonstrated, a solvent can only be reused 10-20 times before it needs to be discarded for fresh solvent. This is determined by looking at the residues, denaturants, pesticides, and insecticides extracted from the solvent concentrates.

Since it is inevitable for contaminants to build up with repeated use from batch to batch, solvent reuse carries either: a high cost of testing and remediation or frequent solvent changes with fresh solvent. Either situation has a major impact to the overall cost effectiveness of ethanol as an extraction solvent. Indeed, the only way to eliminate this cost and make ethanol extraction manufacturing profitable, is to forgo testing and prolong the reuse of the extraction solvent while the concentration of contaminants rises.

Other Key Comparisons Between Extraction Methods

There are many other factors contributing to these hidden ethanol extraction costs. The following table compares the pros and cons of ethanol and CO_2 extraction machines, processes, and methods:

Table 2. Ethanol vs CO_2 Extraction Comparison

Parameter	**Ethanol Extractor**	**CO_2 Oil Extractor**
Organic products	Organic ethanol required.[9]	No special requirements. Already an approved organic solvent.[9]
Cannabinoid Recovery	50-80% typical cannabinoid recovery including carbon scrubbing. Method may require carbon to remove chlorophyll. Carbon absorbs THC and CBD, lowering recovery. Carbon is a high cost consumable.	85-95% typical cannabinoid recovery. No carbon is required due to the lack of chlorophyll extracted.
Solvent Recovery	Ethanol is expensive and therefore needs to be recovered. Typically, 90-95% recovery of ethanol leads to high operating costs. Losses come from ethanol remaining in biomass and extract.	CO_2 naturally separates from extract as pressure is lowered. No need for any recovery process. CO_2 maintains purity and can be recycled for subsequent extraction runs.
Disposal of Raffinate (Extracted Biomass)	Biomass extracted with ethanol is hazardous waste and may be flammable due to type of ethanol used and the amount of remaining VOC and HAP.[10] Subject to regulations 40 CFR 261.21. Transportation subject to DOT hazardous waste rules.	Biomass extracted is VOC and HAP free and is a decent source of food grade essential amino acids and digestible protein. Recyclable with potential biomass tax credits available in Europe. Transportation is not regulated.
Winterization	Warm ethanol extractions need to be winterized. Winterization may be avoided if extraction is at << -20°C leading to high energy expense.	Winterization may be avoided with subcritical extraction. However, extraction is much slower at low pressure.

Safety, Infrastructure Cost	Significant fire hazard risk for indoor deployment.[11] High cost for hazardous building occupancy and special room classifications and limitations.[11,a]	Inert. No fire hazard risk.[12] Proper installation mitigates static and asphyxiation risks. Minimal requirements. May operate in industrial building (F2) classification.
Equipment Cost	$2-3M USD for 1 ton per day	$3-4M USD for 1 ton per day
Operating Cost	High variable costs and overhead, including but not limited to: ethanol cost, ethanol losses, consumables, reduced recovery, high insurance premiums, hazardous waste disposal, and energy costs.	Very low variable cost for CO_2 No difficulty getting business insurance. No hazardous waste disposal.
Scalability	Easily scales to 10 tons per day in less than 450 m^2 with hazardous (H2,3) occupancy, with about ~7000 amps, 230V, 3 phase cooling capacity and C1D2 special rooms.[13]	Easily scales to 10 tons per day in less than 450 m^2 in F occupancy with ~2400 amps 230V 3 phase.
Solvent-Sourced Cross Contamination Risk	Herbicide, pesticide, solvent contamination, extraction byproduct contamination and risk.[b]	CO_2 is not generally used across lots. No risk of cross contamination.
Solvent Purity Revalidation Costs	Required by GMP. Solvent must not show an increase in contaminants over time.[8] High cost for validation testing, potential remediation, filtration and testing for contaminants.	None required.
Cost of Solvents	Food grade ethanol is safest and comes with little to no chemical contamination risk, but with higher cost. Specially denatured solvents are less expensive but carry a myriad of non-food grade contaminants.[1]	Low price per kg.
Terpenes for full spectrum flavor and aroma	Lost during processing.	Captured during processing.
Environment	High carbon footprint to produce ethanol. Cooling capacity needed to cool to <20°C. Disposal of hazardous biomass waste after processing.	Byproduct of existing industrial processes, nontoxic, non-ecotoxic, renewable, and recaptured.[14] Considered a green solvent.

a. Limits on the amount and storage of flammable solvents in addition to specific alarm lights and deflagration alarms and detectors, emergency phones and alarm systems with 24-hour third party monitoring, alarm levers every 150 ft, setbacks from property lines or other adjacent occupants, automatic and special sprinkler systems, fire distance offsets, deratings

on maximum solvent volume for multi-story, emergency power for vents, fail safe electrical systems, spark proof venting, certified equipment for hazardous locations, and explosion control plans.[11,14] There is no limitation on the amount of CO_2 a factory can have on site, so the mentioned infrastructure is not required.[9]

b. Ethanol derived chemical contaminants remaining in the extracted oil after removal of the ethanol, may increase the risk of safety and health for the consumer.[16] For example, residual contaminants listed in various ethanol recipes have a higher boiling point compared to ethanol and are therefore not removed from the oil during distillation. Furthermore, solvent analysis for contaminants are not always included in a typical certificate of analysis.

In a subsequent article, we will explore and estimate the magnitude of these additional hidden costs.

Conclusion

In conclusion, ethanol extracts carry with them known and unknown risks related to prolonged and repeated exposure to the unnatural denaturant chemical additives used to make ethanol affordable. Although these chemicals are often removed to "safe" levels, they are 1) not fully removed and 2) not generally tested for "safety" with validated methods, but rather general methods.

Health dangers of such additives are well documented (but only partially understood) in the context of cross factors including age, health, drug interactions, effects on the brain, effects on cognitive and emotional function, and susceptibility to negative health consequences. Solvents such as methanol, hexane and heptane are given a "pass" based on extrapolations of rat studies by the same agencies scrutinizing CBD as a drug. It is our opinion that **all** unnatural contaminants should be listed as ingredients– even when they are evident at so-called "safe" levels.

Marginally higher capital cost is no excuse for the risk of compromising public health. ***CO_2 derived hemp and CBD oils are widely regarded as the highest quality and chemical residue free oils produced.*** Tables 2 & 3 show CO_2 extraction has advantages over ethanol as the extraction media in every compared factor, except capital equipment cost. Drastically lower operating costs are a key benefit of CO_2 extraction. Over time, lower operating costs accumulate and will continue to build value throughout the life of the equipment.

Disclaimer

United Science and extraktLAB manufacture and sell both ethanol processing equipment and supercritical CO_2 extractors. The views expressed in this white paper are meant as a guide and a starting point to help investors and potential manufacturers obtain the information they need to make an informed business decision. Numbers presented are only estimates with assumptions listed in the footnotes and must be updated to match the exact scenario being assessed. The reader is encouraged to ask further questions and use the information presented to build their own model of understanding.

References

(1) eCFR — Code of Federal Regulations- TTB Alcohol and Rules for Specially Denatured Alcohol https://www.ecfr.gov/cgi-bin/text-idx?c=ecfr&sid=fc3be5d2e97afdd4aed5fb7b5c26309c&rgn=div5&view=text&node=27:1.0.1.1.17&idno=27#se27.1.21_1112 (accessed Dec 8, 2019).

(2) Ahuja, S. *Overview: Isolation and Characterization of Impurities*; Elsevier Inc., 2004; Vol. 5. https://doi.org/10.1016/S0149-6395(03)80003-X.

(3) Executive Profile: Stephen Mueller, Founder and CEO of Mile High Labs https://mgretailer.com/business/stephen-mueller-founder-ceo-mile-high-labs/ (accessed Jan 3, 2020).

(4) *USP 467 Residual Solvents*; 2007.

(5) ICH Q2(R1) Validation of Analytical Procedures: Text and Methodology - ECA Academy https://www.gmp-compliance.org/guidelines/gmp-guideline/ich-q2r1-validation-of-analytical-procedures-text-and-methodology (accessed Dec 30, 2019).

(6) Medicines Agency, E. *ICH Guideline Q3C (R6) on Impurities: Guideline for Residual Solvents Step 5*.

(7) *LIMITING RESIDUAL SOLVENT LEVELS IN ACTIVE SUBSTANCES, EXCIPIENTS AND MEDICINAL PRODUCTS The International Conference on Harmonisation of Technical Requirements for Registration of Pharmaceuticals for Human Use (ICH) Has Adopted Impurities Guidelines for Residual*.

(8) CVM. *Guidance for Industry Drug Substance Chemistry, Manufacturing, and Controls Information*; 2010.

(9) Guidance & Instructions for Accredited Certifying Agents & Certified Operations | Agricultural Marketing Service https://www.ams.usda.gov/rules-regulations/organic/handbook (accessed Dec 8, 2019).

(10) Hazardous Waste from Cannabis Extraction - Extraction Magazine https://extractionmagazine.com/2019/08/14/hazardous-waste-from-cannabis-extraction/ (accessed Dec 15, 2019).

(11) Chapter 3: Use and Occupancy Classification, Building Code 2015 of Utah | UpCodes https://up.codes/viewer/utah/ibc-2015/chapter/3/use-and-occupancy-classification#3 (accessed Dec 8, 2019).

(12) CGA P-1-2015 - Standard for Safe Handling of Compressed Gases in Containers - 12th Edition https://webstore.ansi.org/standards/cga/cga2015-1531002?gclid=CjwKCAiA27LvBRB0EiwAPc8XWflJxH6MAC74YxV5upUoi5lt6OakcaPK5L_mu7CrSSu5CMXTjcG9mxoCrikQAvD_BwE (accessed Dec 8, 2019).

(13) 2006 International Building Code https://www.optasoft.com/applications/codes/2006IBC/HTMLHelp/414.htm (accessed Dec 8, 2019).

(14) Chapter 9: Fire Protection Systems, Building Code 2015 of Utah | UpCodes https://up.codes/viewer/utah/ibc-2015/chapter/9/fire-protection-systems#903 (accessed Dec 8, 2019).

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About extraktLAB

ExtraktLAB is a brand of United Science and manufactures leading-edge, CBD hemp and cannabis processing equipment in a ASME accredited, ISO 9001:2015 certified, 30,000 ft^2 facility in St Croix Falls, WI. ExtraktLAB also operates its *Institute for the Advancement of Bioprocessing and Formulations* in a fully operational, GMP Certified, USDA Certified Organic hemp processing facility occupying an 80,000 ft^2. Demonstrations and tours are held weekly. The facility is located in Osceola, WI.

Founded in 2008 by Ph.D. separation chemists and engineers, extraktLAB equipment is renowned for full turnkey extraction facilities. These include: winterization equipment, short path distillation, wiped film evaporators, bucking machines, supercritical CO2 extraction and manufacturing execution software with batch recording capability.

ExtraktLAB's equipment is known for having the highest throughput, smallest footprint, lowest energy consumption and most scalable CO_2 extraction process in the industry. In fact, customers can scale to process 10 tons of hemp extracted per day in an extremely small area using only a small amount of power. Conversely, it is important for cannabis businesses to keep their operation sized for smaller cannabis extraction applications. We fully service both industries and small business clients.

ExtraktLAB provides extraction equipment, engineering, consulting and design services. Our team is standing by to help both experienced and novice producers create and operate manufacturing facilities designed to meet or exceed ISO and GLP/GMP standards.

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