TRANSFORMATION OF PHYTOCANNABINOIDS BY HEAT -
ISOMERIZATION, DEHYDRATION, AND DERIVATIZATION OF CANNABINOIDS PRESENT IN CANNABIS SATIVA SMOKE

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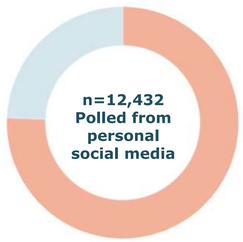
INTRODUCTION

Over 76% of cannabis consumers (both medical and recreational) prefer smoking to edibles



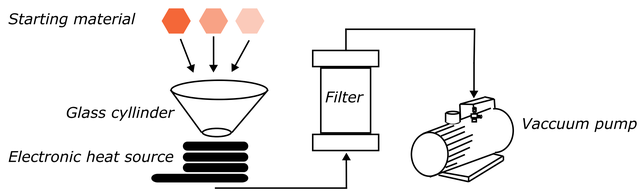
Smoking = 9,412
Edibles = 3,022

Inhaling cannabinoids by smoking Cannabis sativa biomass, primarily flower, is the most common method of ingestion (1). Differences in the therapeutic effects of smoking cannabis versus ingesting cannabis edibles has been reported (2). These differences have been attributed to first-pass metabolism before distribution and variations in pharmacokinetics (2), but transformation of phytocannabinoids into active isomers and derivatives that are present in cannabis smoke may contribute to this phenomenon.

Most methods of smoking Cannabis sativa use high temperatures that create environments for both aerobic and anaerobic pyrolytic reactions to occur (3). The vast array of secondary metabolites present in biomass, particularly flower, serve as the possible chemical reagents for these reactions; many of these compounds are known to be volatile and prone to degradation and derivatization (4). Early work characterizing the constituents of cannabis smoke has identified a large array of chemodiverse compounds (5), but the focus has been either the degradation of D9-tetrahydrocannabinol (THC) or the production harmful byproducts that do not contribute to the therapeutic effects.

It's possible that the transformation of cannabinoids by high heat contributes to the preferred therapeutic effects received by smoking. This study investigates the transformation of phytocannabinoids by applied heat in environments that simulate the process of smoking.

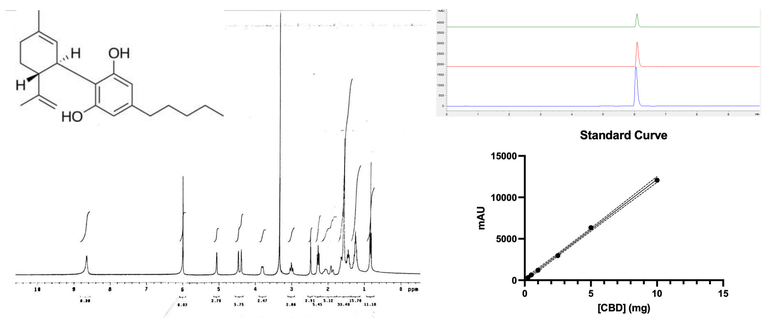
METHODS



Cannabidiol (CBD) isolate (>98% pure), high CBD hemp distillate, and hemp Cannabis sativa flower were placed in a small cylindrical glass chamber. The chamber was heated to temperatures between 250-500°C and the smoke was passed through a selection media by vacuum flopw. Compounds of interested were eluted from the filter with 100% ethanol and the eluants were collected for analysis.

RESULTS

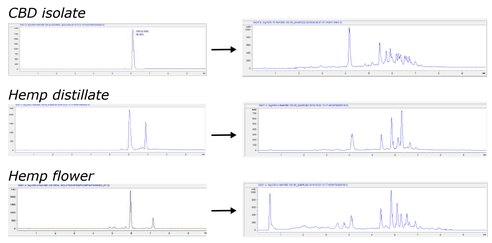
Analysis of CBD isolate:



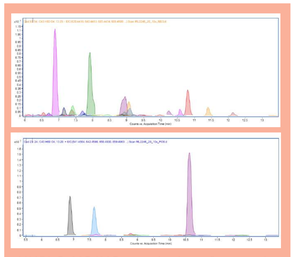
Commercial cannabidiol (CBD) isolate was purchased (EcoGen Laboratories, CO) and was evaluated for purity by NMR and HPLC. It was determined that the isolate was >98% pure and able to be used reproducibly as a research standard.

Separation by reverse-phase HPLC as follows: A gradient elution profile of 100% mobile phase B (DiH2O with 0.1% phosphoric acid) to 100% mobile phase A (acetonitrile) was employed on an Agilent HP 1200 with separation on a Zorbax Eclipse XDB-C18 column (4.6 x 50mm, 3um, Agilent Technologies, CA) at a 1mL/min flow rate.

Simulated Smoking Experiments:

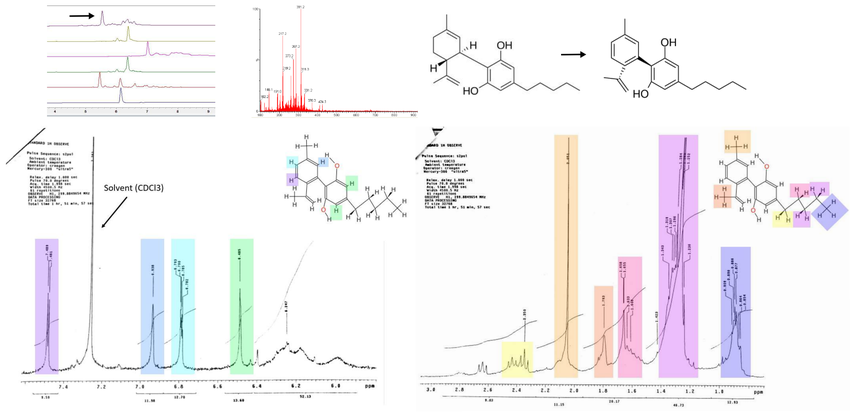


Samples were heated to an approximate temperature of 500°C under atmospheric pressure and open to the environment. In all samples, there was a significant transformation of the profile of compounds present. Most notably, the CBD isolate which was >98% pure transformed into over 18 separate peaks.



UHPLC-MS/MS analysis of sample created from hemp flower biomass identified 78 known cannabinoid isomers.

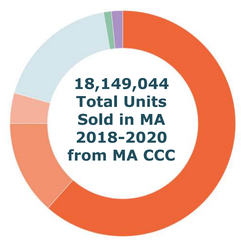
Isolation and Identification of Cannabinodiol (CBND):



The eluant was concentrated by rotary evaporation and partially purified by short-path distillation. The resulting sample was separated using flash chromatography on a 12g cartridge (Teledyne, NE) on a Yamazen W-PREP 2XY system. The fraction containing CBND was concentrated by rotary evaporation and analyzed by HPLC, LCMS, and NMR.

DISCUSSION & CONCLUSION

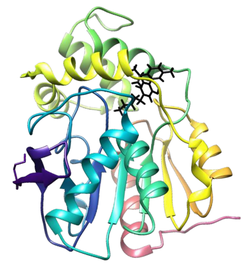
Flower, concentrates that are smoked, and vape cartridges dominate the market for both the recreational and medical cannabis industry



Flower = 61.5%
Concentrate = 13.5%
Vapes = 4.4%
Edibles = 17.9%
Trim = 1.1%
Other = 1.6%

Edible cannabis products are created from extractions that focus on preserving the primary phytocannabinoids in the plant; the total cannabinoid composition present in cannabis smoke is substantially different. There are many variables that may contribute to the final cannabinoid composition in smoke such as temperature, pressure, heat source, gas composition, moisture content, ambient humidity, variations in pH, etc.

When smoking cannabis at high temperature, transformation of phytocannabinoids is significant. While the total activity of these cannabinoid compositions containing pyrolytic cannabinoids, or pyrocannabinoids, at endogenous targets is unclear, it is likely that their combined interactions contribute to the difference in effects between smoking cannabis and edible cannabis products.



The transformation of CBD into CBND is only a small fraction of the total chemodiverse formulation produced in cannabis smoke. There is a huge gap in pharmacological information between the known cannabinoids, rare cannabinoids, and undiscovered pyrocannabinoids. A better understanding of these total cannabinoid compositions, especially the interactions between pyrocannabinoids, will aid in the understanding of the therapeutic potential of cannabis and the development of therapeutic cannabis products.

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