

REPORT OF FINDINGS

Page 1 of 2

STILLWATER
FOODS

SUMMARY

Following a number of anecdotal consumer reports claiming that RIPPLE SC-infused edibles offered faster subjective effect onset versus competing cannabis edibles, Stillwater Foods undertook an effort to quantitate the absorption profile of RIPPLE SC into the bloodstream. Subsequent testing confirmed significant tetrahydrocannabinol (THC) absorption into the bloodstream within 15 minutes and peak absorption within 60 minutes. It is hypothesized that the formulation and production processes used with RIPPLE SC to render cannabinoids water-soluble (patent pending) increases the absorption rate of cannabinoids (THC in this study) versus traditional cannabis edibles.

Based on these findings of faster absorption rates, future testing is planned to further quantify blood absorption profile of RIPPLE SC-infused cannabinoids in other functional food applications.

INTRODUCTION

Published data on water-soluble cannabinoid absorption is minimal at best. Formulation and process factors such as homogenization levels, emulsifier type and amount, carrier oil type, and cannabinoid composition and levels are all believed to affect cannabinoid absorption rates, but to what degree is so far untested. This scoping study is believed to be a first of its kind for water-soluble THC in a functional food application.

This blood absorption test was conducted as an initial scoping study to validate consumer observations and build an empirical understanding of RIPPLE SC's absorption profile. To control initial testing costs, an N of five test subjects were selected, with each subject submitting to six blood draws over 120 minutes for a total of thirty data points. Future tests of increased scope and magnitude are planned to more deeply investigate the results.

The initial test focused on Δ^9 -tetrahydrocannabinol (THC) blood absorption when delivered in a water-soluble format. Ripple Pure 10 was selected as the delivery mechanism for its simplified cannabinoid profile comprised solely of THC distillate. Water was selected as the test matrix to minimize confounding variables.

Cannabinoids such as THC are fat soluble. When ingested, absorption is generally poor, with an overall bioavailability rate of 4-12% and a highly variable rate of total absorption.¹ Once ingested, THC is converted by the liver before entering the bloodstream. This absorption/conversion process adds to the time it takes between consumption and significant increases detected in the blood.

Absorption pharmacokinetics studies of water-soluble cannabinoids are limited. However, studies around improving absorption of fat-soluble nutrients are more abundant, with such studies generally focusing on the creation of a water-soluble version of the parent fat-soluble active component. In such studies, the water-soluble version is generally found to have enhanced absorption characteristics, indicating that the water-soluble version of fat-soluble actives improves the pharmacokinetics for absorption into the blood.² It is believed that such compounds are absorbed directly through the small intestines into the bloodstream rather than through the hepatic system.

METHODOLOGY

Subjects. Five individuals from Stillwater Foods were selected for the March 3, 2018 test. Three females and two males, ages 27 to 50 years of age, all of good health, volunteered for the blood absorption study. Test subjects ranged from "light" users (typical THC dose = 5 to 10mg) to "heavy" users (typical THC dose = 30 to 50mg). Subjects were asked to avoid all cannabis for five days as a THC "washout" period for their blood. Subjects were tested on an empty stomach (12 hour fast).

Normalization. Test Subject 3 was called in as a backup the day before the test and so did not undergo the washout period, which led to significantly adulterated results that were excluded from the final analysis. In addition, Subject 2's results were normalized to a baseline of 0 by subtracting the quantity of carboxy-THC measured at time 0 (5.3 ng/ml) from the result of each draw.

Product. Ripple Pure 10, batch 1512, produced on March 1, 2018 was used for the test. THC content was verified by Agriscience Labs, an unaffiliated, licensed cannabis testing facility in Denver, Colorado. Results indicated a packet content of 9.87 mg THC per 400 mg serving of Ripple Pure 10 powder (i.e., 1 packet). All test product was drawn from a single Ripple container (10 packets per container). For each subject, the content of one Ripple Pure 10 packet (9.87 mg THC) was dissolved in 240 ml of water at room temperature (22° C). Following a baseline blood draw (time 0), each subject then drank the entire 240 ml of water within 30-60 seconds.

Protocol. Blood testing was coordinated through Infinite Lab Phlebotomy Services in Denver, Colorado. Each test subject was set up with an intravenous test port to allow multiple blood draws over time. Subjects had blood drawn at 0, 15, 30, 60, 90 and 120 minutes. THC blood levels at time 0 were used as the subjects' baselines. Blood draws were performed direct into suitable vials, which were then sealed, labeled, and immediately refrigerated. The vials were then sent overnight to the blood testing lab in compliance with all HIPAA requirements. Total testing time, from phlebotomy setup to completion of all blood draws was approximately three hours for all individuals.

Continued on next page

REPORT OF FINDINGS

Page 2 of 2

Testing Services. MEDTOX Laboratories, a division of Labcorp located in St. Paul, Minnesota, was selected as the blood testing partner for its ability to quantitate THC levels at the 1ng/ml threshold (cf. 5 ng/ml at other testing labs we surveyed).

Samples were submitted through Holos Health, a licensed medical practitioner located in Boulder, Colorado. Testing was performed under test code 700881, a THC screen with confirmation whole blood executed according to MEDTOX's internal proprietary methodology. The following compounds were quantitated; Δ^9 -tetrahydrocannabinol (THC), carboxy-THC, hydroxy-THC, cannabidiol (CBD) and cannabinal (CBN). The testing assay threshold was 1 ng/ml.

FINDINGS

The scope of this study encompassed THC absorption rates as measured through blood chemistry biomarkers. The main observed biomarker is carboxy-THC, a THC metabolite. Carboxy-THC has a plasma half-life reported at 4 to 12 hours.³ THC pharmacokinetics in the human body was out of this study's scope.⁴

All test subjects experienced rapid absorption of THC within 15 minutes of consumption, with absolute changes from baseline levels that ranged from 3 to 9 ng/ml. Carboxy-THC was the primary biomarker present in the subjects' bloodstreams, but a smaller amount of hydroxy-THC was identified in several test results. Cannabidiol and cannabinal were not present in any of the test samples (1ng/ml threshold).

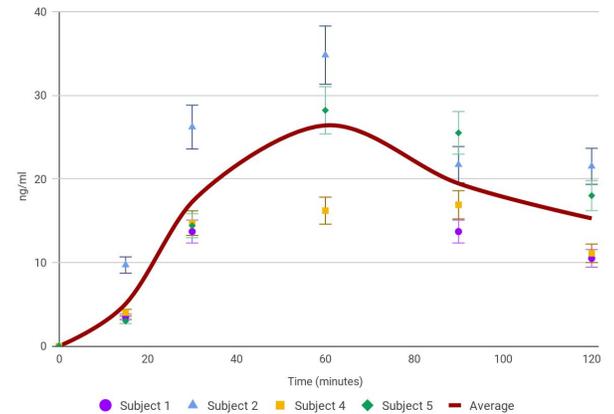
Peak change in carboxy-THC levels was identified in all subjects at time 60, with results ranging from 16.2 to 34.8 ng/ml. The levels of carboxy-THC steadily decreased from 60 minutes through the final blood draw at 120 minutes. Results from the 120 minute draws ranged from 10.5 to 21.5 ng/ml. As measured through the blood metabolites, THC uptake rates were significantly faster than previously understood metabolism rates.

ADDITIONAL OBSERVATIONS

Due to the nature of THC breakdown, metabolites may be detectable for weeks or even months following use. Therefore, it is important to establish baseline blood levels in all test subjects to calibrate and normalize data on absorption rates. This is most relevant for heavy users, who tend to live with a measurable baseline level of THC metabolites in their blood at all times.

While past research has focused on subjective reporting (e.g., "On a scale of 1-10, how high do you feel?"), this study demonstrated that subjective experience is a poor proxy for blood chemistry levels. For example, Subject 1 (light user) reported significant THC effects at 30 minutes with blood levels of 13.7 ng/ml carboxy-THC. Meanwhile, Subject 2, a heavy user, reported no THC effects at 30 minutes with blood levels of 31.5 ng/ml carboxy-THC. It is recommended that future studies further explore the relationship between usage rates and subjective experience.

Observed Change in Carboxy-THC Blood Levels



It is recommended that future studies extend the time period for measurement to 240 minutes or longer to gain a clearer understanding of how the body metabolizes THC throughout the digestive cycle.

CONCLUSION

RIPPLE SC water-soluble cannabinoids were absorbed into the bloodstream at measurable levels within 15 minutes of consumption. Peak uptake, as measured by blood absorption, was observed 60 minutes after consumption. These observations indicate that RIPPLE SC is absorbed into the bloodstream via a more rapid mechanism than the hepatic absorption route followed by traditional cannabis edibles.

Based on these findings, future absorption studies are being planned to further investigate the absorption rates of RIPPLE SC water-soluble cannabinoids in other food and beverage systems.

REFERENCED WORKS

- McGilveray, IJ. *Pharmacokinetics of cannabinoids*. Pain Res Manag. 2005 Autumn; 10 Suppl A:15A-22A.
- Im, Krishnakumar & Kumar, Dinesh & Ninan, Eapen & Kuttan, Ramadassan & Maliakel, Balu. (2015). *Enhanced absorption and pharmacokinetics of fresh turmeric (Curcuma Longa L) derived curcuminoids in comparison with the standard curcumin from dried rhizomes*. Journal of Functional Foods. 17. 10.1016/j.jff.2015.04.026.
- ARUP Laboratories. Laboratory Test Directory. *THC Metabolite, Serum or Plasma, Quantitative*.
- Huestis, Marilyn. *Human Cannabinoid Pharmacokinetics*. Chem Biodivers. 2007 Aug; 4(8): 1770-1804.

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