

## Chronic Pain

Given the growing number of chronic pain patients on opioid treatment and the associated addiction epidemic in both the US and Europe, effective pain treatment alternatives may possibly be found in the use of cannabis.

In this experimental trial, we explored the analgesic and pharmacokinetic effects of pharmaceutical-grade cannabis in patients with chronic pain from fibromyalgia. Here we report on the results of the pharmacokinetic analyses.

Fibromyalgia is a disorder characterized by widespread musculoskeletal pain and sensitivity to touch. Research shows that cannabinoids - the active compounds present in the cannabis plant - can have a beneficial effect on fibromyalgia symptoms by reducing pain and improving sleep quality.

Although cannabis has not been established as an approved medicine for this medical condition, surveys indicate that fibromyalgia patients already self-medicate using cannabis.

## Study

This randomized, double-blind, cross-over study investigated how the symptoms of fibromyalgia are affected by the two major cannabinoids of the cannabis plant: delta-9-tetrahydrocannabinol (THC) and cannabidiol (CBD).

The aims of the study were to investigate the pharmacokinetics and pharmacodynamics of three different standardized cannabis strains, and their effects on spontaneous and experimentally induced pain, as well as mental state. Twenty female patients diagnosed with fibromyalgia were included if they had a pain score  $\geq 5$  (on a scale from 0 = no pain to 10 = most pain imaginable) for most of the day and meet the 2010 American College of Rheumatology diagnostic criteria.

We studied different cannabis varieties: Bedrocan (22.4-mg THC and <1-mg CBD), Bediol (13.4-mg THC and 17.8-mg CBD) and Bedrolite (18.4-mg CBD and <1-mg THC). All cannabis varieties were obtained from Bedrocan BV, The Netherlands. Twenty female fibromyalgia patients inhaled a single cannabis dose within 3-5 min, after which frequent arterial samples were obtained for 3 hours. Determination of the CBD, THC, 11-hydroxy-THC (11-OH-THC) plasma concentrations was performed using liquid chromatography with tandem mass spectrometer detection (LC-MS/MS).

## Results

See Figure 1 for the results of the study. The plasma concentrations observed following treatment with Bedrocan and Bediol were associated with effective pain relief (Figure 2).

The data indicate an important pharmacokinetic interaction between THC and CBD with greater THC plasma concentrations when CBD is present in the inhalant.

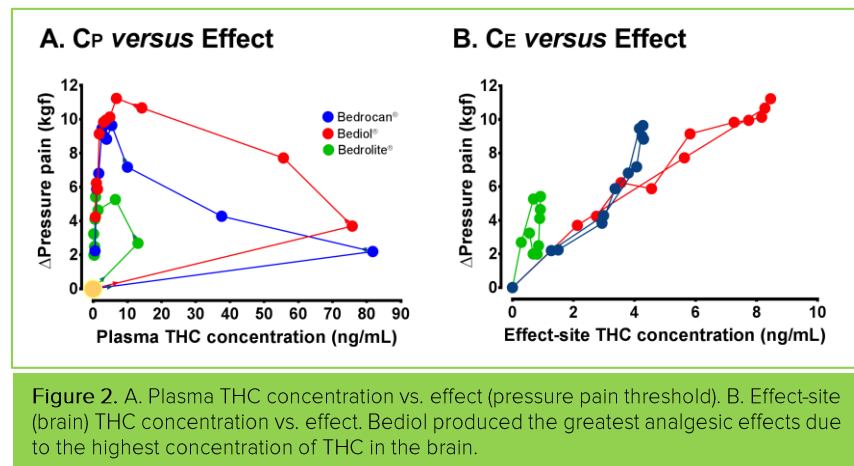


Figure 2. A. Plasma THC concentration vs. effect (pressure pain threshold). B. Effect-site (brain) THC concentration vs. effect. Bediol produced the greatest analgesic effects due to the highest concentration of THC in the brain.

## Conclusions

In a population of chronic pain patients, the inhalation of three cannabis varieties produced effective plasma concentrations of CBD and THC. In the presence of CBD, THC concentrations were 50% greater than expected.

We explain these findings by either an increased absorption of THC in the lung or the inhibition of THC metabolism, both induced by CBD, or the conversion of CBD into THC.

This first study suggests that Bedrocan and Bediol may be attractive alternatives for the treatment of chronic pain.

## Statement

The protocol was approved by the local institutional review board of the Leiden University Medical Center and the Central Committee on Research Involving Human Subjects in The Hague.

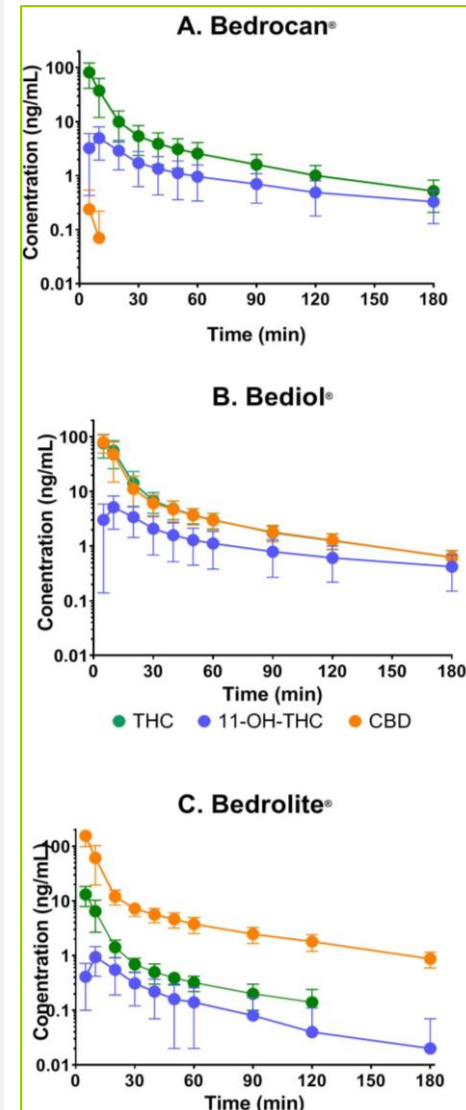


Figure 1. THC, 11-OH-THC and CBD plasma concentrations after inhalation of three cannabis varieties