# Cannabinoid Disposition After Human Intraperitoneal Use: An Insight Into Intraperitoneal Pharmacokinetic Properties in Metastatic Cancer

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## ABSTRACT

**Background:** Medicinal cannabis is prescribed under the provision of a controlled drug in the Australian Poisons Standard. However, multiple laws must be navigated in order for patients to obtain access and imported products can be expensive. Dose-response information for both efficacy and toxicity pertaining to medicinal cannabis is lacking. The pharmacokinetic properties of cannabis administered by traditional routes has been described but to date, there is no literature on the pharmacokinetic properties of an intraperitoneal cannabinoid emulsion.

**Case description:** A cachectic 56-year-old female with stage IV ovarian cancer and peritoneal metastases presented to hospital with fevers, abdominal distension and severe pain, vomiting, anorexia, dehydration and confusion. The patient reported receiving an intraperitoneal injection, purported to contain 12 g of mixed cannabinoid (administered by a deregistered medical practitioner) two days prior to presentation. Additionally, cannabis oil oral capsules were administered in the hours prior to hospital admission.

**Results:** THC concentrations were consistent with the clinical state but not with the known pharmacokinetic properties of cannabis nor of intraperitoneal absorption. THC concentrations at the time of presentation were predicted to be ~60 ng/mL. Evidence suggests that blood THC concentrations >5 ng/mL are associated with substantial cognitive and psychomotor impairment. The predicted time for concentrations to drop <5 ng/mL was 49 days after administration.

**Discussion:** The unusual pharmacokinetic properties of the case suggest that there is a large amount unknown about cannabis pharmacokinetic properties. The pharmacokinetic properties of a large amount of a lipid soluble compound given intraperitoneally gave insights into the absorption and distribution of cannabinoids, particularly in the setting of metastatic malignancy. (*Clin Ther*. 2018;▮:▮▮▮–▮▮▮) 

**Key words:** cannabinoids/pharmacokinetics, injections, intraperitoneal delta(9)-tetrahydrocannabinol, cannabinoids/blood.

## BACKGROUND

Medicinal cannabis is prescribed under the provision of a controlled drug in the Australian Poisons Standard. However, multiple laws must be navigated for patients to obtain access, and imported products can be expensive. Some patients are growing and using their own supply while awaiting the health outcomes research required for streamlined access. There is currently a lack of good quality evidence pertaining

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to medicinal cannabis. Dose response information for efficacy and toxicity is lacking but is unlikely to be consistent across patient groups.

The pharmacokinetic properties of cannabis administered by traditional (inhaled and oral) and alternative (oromucosal, sublingual, buccal, and transdermal) routes have been described. It is known, for example, that the absorption of cannabinoids differs with route of administration, and bioavailability is variable with all modes of administration.[1] Data are even more limited with respect to patients with cachexia, and to date there is no literature on the pharmacokinetic properties of an intraperitoneal cannabinoid emulsion.

## CASE DESCRIPTION

A cachectic 56-year-old woman with stage IV ovarian cancer and peritoneal metastases presented to the hospital with fevers, abdominal distension and severe pain, vomiting, anorexia, dehydration, and confusion (paranoia, anxiety, hallucinations, cognitive distortions, sleepiness). The patient reported that 2 days prior she had received an intraperitoneal injection of cannabis oil, purported to contain 12 g of mixed cannabinoid.

A subsequent regulatory investigation elicited that a "Health clinic" had injected intraperitoneal cannabis oil manufactured from illegally purchased cannabis resin of uncertain potency, solubilized in coconut oil (a medium chain triglyceride), and diluted with saline. In addition, cannabis oil oral capsules (of unknown strength) had been administered in the hours before hospital admission, as had an intravenous injection of ascorbic acid (dose, formulation, and contaminants unknown).

Although 2 days after injection the patient's relative was able to state that the patient had had a cannabinoid injection into the abdomen, it was not until 7 days after injection that the full history became clear. Patient and next-of-kin consent was then obtained to perform opportunistic pharmacokinetic analysis when blood, urine, and ascitic fluid were taken for other medical reasons. A urine sample had already been taken on day 5 and stored; cannabinoid analysis was subsequently undertaken. In summary, pharmacokinetic measurements revealed $\Delta^9$-tetrahydrocannabinol (THC) concentrations consistent with the clinical state but not with the known pharmacokinetic properties of cannabis or of intraperitoneal absorption (Table and Figure).

Plasma concentrations of THC and the active metabolite 11-hydroxytetrahydrocannabinol 7 days after administration were measured as 43 and 25 ng/mL, respectively, and remained elevated at 4 weeks after administration. The assay was performed at the Discipline of Clinical Pharmacology, University of Newcastle. Plasma samples (50 μL) were prepared by

Table. Cannabinoid concentrations in biological fluids after intraperitoneal injection of a cannabis preparation.

| Sample | Days After Administration | Concentration, ng/mL | | | |
|---|---|---|---|---|---|
| | | THC | OH-THC | COOH-THC (Unhydrolyzed)* | COOH-THC (Hydrolyzed) |
| Urine | 5 | 0 | 4 | 1977 | |
| Urine | 7 | 0 | 0 | 1000 | 3734 |
| Blood | 7 | 43 | 25 | 374 | |
| Blood | 8 | 47 | 33 | 432 | |
| Blood | 13 | 34 | 33 | 645 | |
| Urine | 14 | 0 | 0 | 839 | >4000 |
| Ascites | 14 | | | | >4000 |
| Blood | 27 (community sample) | 16 | 13 | 304 | |

COOH-THC = carboxy-tetrahydrocannabinol; OH-THC = 11-hydroxytetrahydrocannabinol; THC = $\Delta^9$-tetrahydrocannabinol.
*Assay validated to 500 ng/mL.