The Concentration of THC, 11-OH-THC, 11-COOH-THC, CBD, and CBN in Human Milk from Lactating Persons Who Use Cannabis or Cannabis Derived Products

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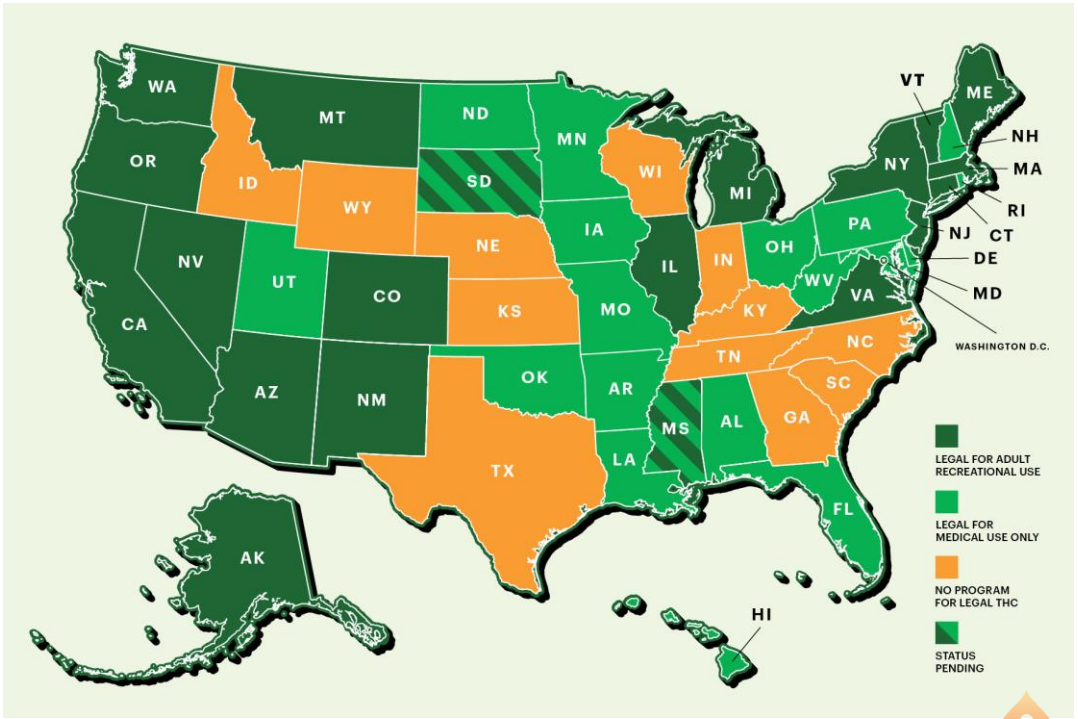
Agenda

- An overview of marijuana
  - Cannabinoids
  - Methods of Using Marijuana
- Mommy's Milk Study
  - Mommy's Milk Study Design
  - Results from Marijuana Analysis

An overview of cannabis



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What is Cannabis?

- The dried leaves, flowers, stems, and seeds from the Cannabis sativa or Cannabis indica plant.
- Sativa = energy
- Indica = drowsy

Cannabinoids: The Major Players

- Cannabinoids are chemical compounds found in the cannabis plant that produce the various effects of cannabis
  - Over 500 cannabinoids
- The main cannabinoids are:
  - Tetrahydrocannabinol (THC)
    - Primary psychoactive compound
  - Cannabidiol (CBD)
    - Primary non-psychoactive compound
  - Cannabinol (CBN)
    - Mild psychotropic- somewhere in between THC and CBD
  - Cannabigerol (CBG)
  - THCv

How are Breastfeeding Women Using Cannabis?

- Inhalation
  - Smoking
    - Hand pipes
    - Water pipes
    - Rolling papers/Blunts
    - Hookah
  - Vaporization
    - Vape pens
    - Dabbing (concentrates)

Dabbing Marijuana Concentrate using a Rig

How are Breastfeeding Women Using Cannabis?

Soda

Gummy Bears

Cookie

Creams and Lotions

- Oral Consumption
  - Tinctures
  - Infused Food and Drinks
- Topical Delivery
  - Includes transdermal patches, creams, and lotions

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How Has Cannabis Changed Over Time?

- The potency of cannabis has increased dramatically
- The THC content present in cannabis has increased from 4% in 1995 to an average of 15% in 2018
- New concentrated extracts (wax and shatter) are readily available- some are up to 90% THC

THC concentrate

What Does The Research Show About Cannabis And Breastfeeding?

Presence of delta-9-tetrahydrocannabinol in Human Milk

- Letter to the Editor published in *New England Journal of Medicine* in 1987
- Two human milk samples had Δ9-THC concentrations of 105 ng/mL and 340 ng/mL
- One set of paired milk and maternal plasma samples showed a milk Δ9-THC concentration of 60.3 ng/mL which was eight times higher than the maternal plasma concentration of 7.2 ng/mL[7]
  - Based on the year of the study, the concentration of THC was likely 100-200x less concentrated than today's cannabis
- No developmental follow-up on the child

Perez- Reyes M et al. 1982. N Engl J Med

Maternal Marijuana Use During Lactation and Infant Development at One Year

- Article published in *Neurotoxicology and Teratology* in 1990
- Investigated the relationship between infant exposure to marijuana via breast milk and infant motor and mental development at one year of age
- Marijuana exposure via breast milk during the 1st month post-partum was associated with a decrease in infant motor development at one year of age
- Strong correlation between maternal pre- and postpartum marijuana use that could not be effectively reduced by matching

Simultaneous Analysis of Frequently Used Licit and Illicit Psychoactive Drugs in Breast Milk by LC-MS

- Article published in *Journal of Pharmaceutical and Biomedical Analysis* in 2011
- Barcelona, Spain
- 1 milk sample
- THC was detected and the level reported was 86ng/mL
- No developmental follow-up on the child

Marchei E et al. 2011. J Pharm Biomed Anal

Transfer of Inhaled Cannabis Into Human Breast Milk

- Article published in *Obstetrics & Gynecology* in 2018
- Denver, Colorado
- 8 participants who gave serial samples at 20 minutes, 1, 2, and 4 hours after maternal inhalation of a specific dose of cannabis (0.1g containing 23.18% THC)
- The average concentration detected was 53.5 ng/mL
- Peak was at 1 hour post consumption
- No developmental follow-up on the child

Marijuana Use by Breastfeeding Mothers and Cannabinoid Concentrations in Breast Milk

- Article published in *Pediatrics* in 2018
- 50 participants who provided milk samples following maternal use of cannabis in the two weeks prior to milk sample collection
- The average concentration detected was 9.43 ng/mL
- The concentration present in milk is dependent on the hours since last used and the number of times used per day
- The half-life is about 27 hours
- No infant outcomes

Bertrand, K et al. 2018. Pediatrics

An Update: Mommy's Milk Cannabis Study

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Mommy's Milk, The Human Milk Research Biorepository (HMB)

- Study Design
  - Breastfeeding women who use cannabis, are over the age of 18 years and who reside in the United States
  - A 50 mL (~2 ounces) milk sample is collected, but as little as 1 mL is accepted.
  - Samples can be collected either at the UCSD HMB Research Center or via a mailed milk sample.
  - Women are interviewed with a semi-structured by trained study staff
    - They complete a 14 day recall which the interview guides them through using a calendar
  - Samples are stored in a -80◦ C freezer

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Study Recruitment

- Recruitment Sources
  - Social Media (Facebook)
  - MotherToBaby Pregnancy Studies
  - UCSD General Pediatrics Clinic
  - UCSD NICU and Post-Partum Floors
  - Rady Children's Hospital - San Diego
  - Sharp Mary Birch Hospital for Women and Neonates
  - Breastfeeding Support Groups (digital and in-person)

Data Collection

- Interview Data
  - Demographics, maternal and child health, and breastfeeding habits
  - Current and past exposures to recreational drugs, alcohol, tobacco, caffeine, prescription medications, and over-the-counter medications
  - Infant adverse reactions (i.e., infant “toxicities”)
- Mailed/Online Questionnaires Data
  - Stress, anxiety, and depression questionnaires (PSS-10, STAI, EPDS)
  - Eating habits via a short Block Food Frequency questionnaire
  - Child developmental questionnaires (ASQ, ITSEA, CDI, MCHAT) are various timepoints

Cannabinoid Analysis

- 99 human milk samples with known maternal cannabis exposure were analyzed at the UCSD Skaggs School of Pharmacy
  - 87 unique women with 91 unique children; 10 women provided 2 samples and 1 women provided 3 samples at different time points

- Evaluated the concentrations of THC, 11-OH-THC, NOOR COOH-THC, CBD, and CBN simultaneously

*unpublished data

Selected Maternal Characteristics of Breastfeeding Women with Cannabis Exposure Enrolled in the HMB, 2017-2020

		Overall
n		87
Age	19-25	15 (17.2)
	26-30	24 (27.6)
	31-35	29 (33.3)
	36-40	13 (14.9)
	41-42	6 (6.9)
Ethnicity	Hispanic	18 (20.7)
	Non-Hispanic	69 (79.3)
Race	Asian	2 (2.3)
	Black	5 (5.7)
	Caucasian	76 (87.4)
	Native American	2 (2.3)
	Pacific Islander	2 (2.3)
Education	<10th Grade	1 (1.1)
	Partial High School (10th-11th)	1 (1.1)
	High School Graduate/GED	10 (11.5)
	Some College/Specialization	40 (46.0)
	College Graduate	26 (29.9)
	Post-Graduate	9 (10.3)
Maternal BMI		27.02 (5.54)

*unpublished data

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Selected Characteristics of Children who's mothers used Cannabis while breastfeeding

		Overall
n		91
Infant Sex	Female	49 (53.8)
	Male	42 (46.2)
Infant Age	0-3	17 (18.7)
	3-6	24 (26.4)
	6-12	31 (34.1)
	>12	19 (20.9)
Birth Term	Pre-Term	3 (3.3)
	Term	88 (96.7)
Delivery Mode	Vaginal	66 (72.5)
	C-Section	25 (27.5)

*unpublished data

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THC, 11-OH-THC, NOOR COOH-THC, CBD and CBN Levels Detected in Breast Milk

Analyte	Total Samples	Quantifiable Samples	Min	1st Qu.	Median	3rd Qu.	Max
DELTA-9-THC	99	93 (93.9%)	0.1	5.9	22.8	105.0	1620.0
11-OH THC	99	21 (21.2%)	0.1	1.6	5.4	10.6	30.3
NOR COOH-THC	98	81 (82.7%)	0.1	0.2	0.4	1.9	10.0
CBD	99	41 (41.4%)	0.1	0.6	1.4	7.3	98.0
CBN	98	42 (42.9%)	0.1	0.1	0.1	0.2	1.1

Δ9-THC was detectable in 93 (~94%) samples and the median concentration was 22.8 ng/mL; NOR COOH-THC was detectable in 81 (~83%) samples and the median concentration was 0.4 ng/mL; CBD was detectable in 41 (~41%) samples and the median concentration was 1.4 ng/mL; CBN was detectable in 42 (~43%) samples and the median concentration was 0.1 ng/mL; *unpublished data

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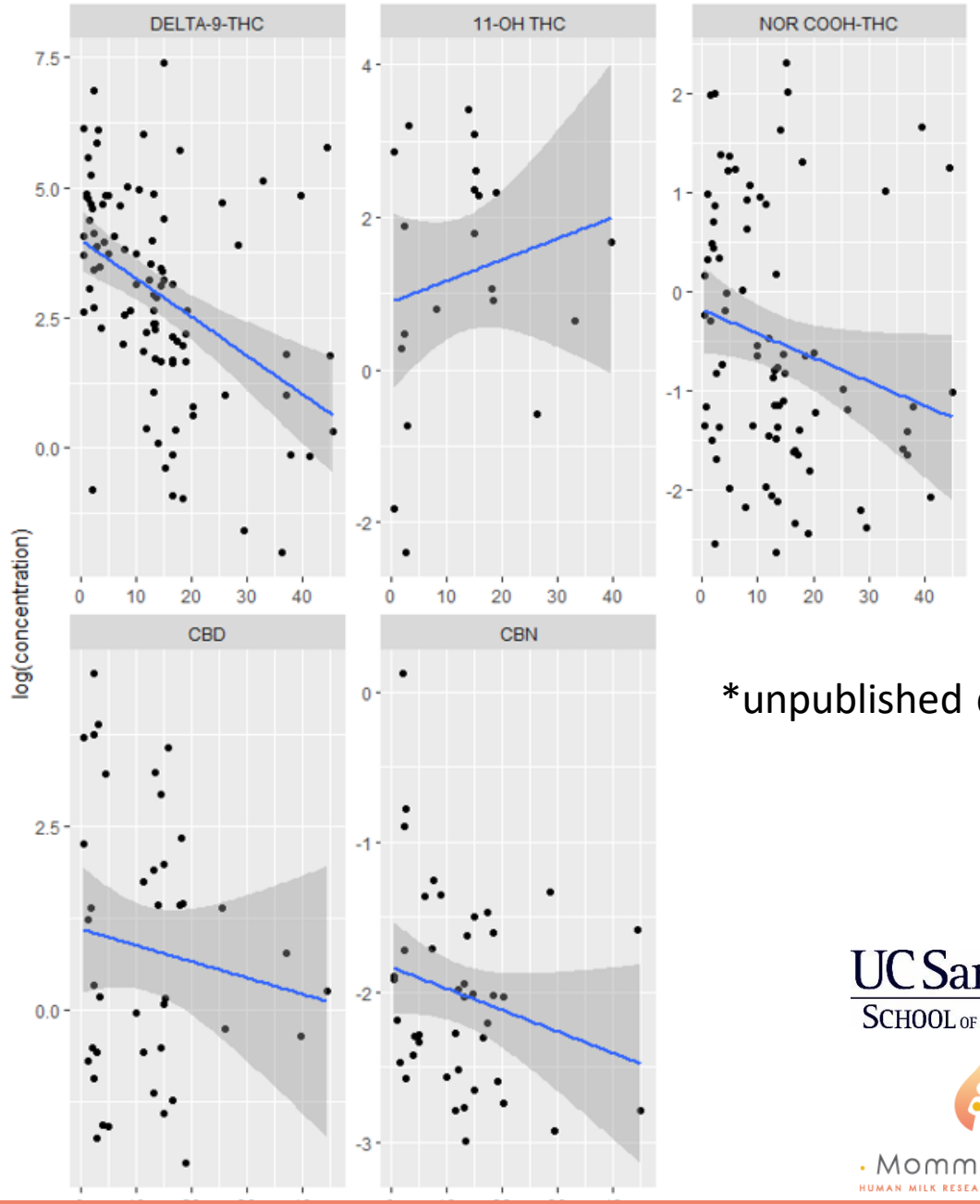
Estimated linear trends for the regression of log concentration on Hours since last use with 95% confidence bands



*unpublished data

There is a reduction in milk Δ9-THC concentration of 7.6% per hour after last use, which can be used to estimate a half-life of approximately 10 hours for Δ9-THC in human milk.

There is a reduction in milk CBD concentration of 2.2% per hour after last use.

There is a reduction in milk CBN concentration of 1.4% per hour after last use

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The concentration of Δ9-THC and NOR COOH-THC in milk is dependent on the hours since last used and the number of puffs consumed during a smoking session

Metabolite	n	Term	Estimate (95% CI)	Std. Error	% Change (95% CI)	p-value
DELTA-9-THC	62	(Intercept)	3.274 (2.586, 3.962)	0.351	---	<0.001
		hours	-0.068 (-0.109, -0.027)	0.021	-6.6 (-10.3, -2.7)	0.001
		Puffs	0.165 (0.107, 0.223)	0.030	18.0 (11.3, 25.0)	<0.001
11-OH THC	11	(Intercept)	1.559 (0.407, 2.710)	0.588	---	0.008
		hours	0.003 (-0.068, 0.074)	0.036	0.3 (-6.6, 7.6)	0.942
		Puffs	0.001 (-0.069, 0.071)	0.036	0.1 (-6.6, 7.4)	0.969
NOR COOH-THC	51	(Intercept)	-0.864 (-1.384, -0.344)	0.265	---	0.001
		hours	-0.023 (-0.047, 0.001)	0.012	-2.3 (-4.6, 0.1)	0.060
		Puffs	0.121 (0.088, 0.153)	0.017	12.8 (9.2, 16.6)	<0.001
CBD	22	(Intercept)	0.588 (-0.331, 1.506)	0.469	---	0.210
		hours	-0.010 (-0.051, 0.030)	0.021	-1.0 (-5.0, 3.1)	0.614
		Puffs	-0.010 (-0.072, 0.051)	0.032	-1.0 (-7.0, 5.3)	0.740
CBN	25	(Intercept)	-1.781 (-2.343, -1.220)	0.287	---	<0.001
		hours	-0.015 (-0.043, 0.013)	0.014	-1.5 (-4.2, 1.3)	0.292
		Puffs	-0.007 (-0.041, 0.026)	0.017	-0.7 (-4.0, 2.7)	0.668

*unpublished data

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Study Limitations

- Samples were collected under different conditions, and not all breast milk collections were directly observed.
- We relied on maternal report of cannabis exposure. However, all participants completed a 14-day recall guided by trained study staff who prompted for specific daily use with the aid of a calendar.

Future Directions

- Within the next year, Mommy's Milk will finish conducting neurodevelopmental questionnaires and testing
    - Maternal report questionnaires
    - Face to Face standardized assessments
- Future studies are required to better characterize the degree of distribution of cannabinoids into human milk through more intensive and paired (milk/plasma) sampling.

Summary and Conclusions

- All 5 cannabinoids measured pass into breast milk
- The concentration of Δ9-THC and NOR COOH-THC in milk is dependent on the hours since last used and the number of puffs consumed during a smoking session
- The half-life is about 10 hours.
- We need more data in order to better advise breastfeeding women on how infant/ child exposure to marijuana via breast milk impacts health and neurodevelopment.

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Questions?

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Learn more about Mommy's Milk:

MommysMilkResearch.org

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