



University of
Nottingham

UK | CHINA | MALAYSIA

Effects of Lipid Vehicles on Cannabidiol Delivery to Brain Regions after Oral Administration

Alice Brookes

PhD Candidate

University of Nottingham, UK





University of
Nottingham

UK | CHINA | MALAYSIA

Can oral lipids affect biodistribution to the brain?

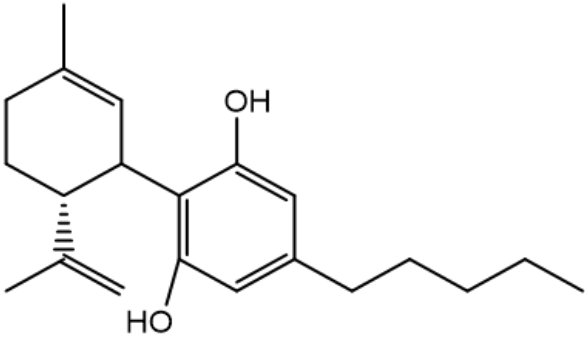
Alice Brookes

PhD Candidate

University of Nottingham, UK



Background: Cannabidiol (CBD)



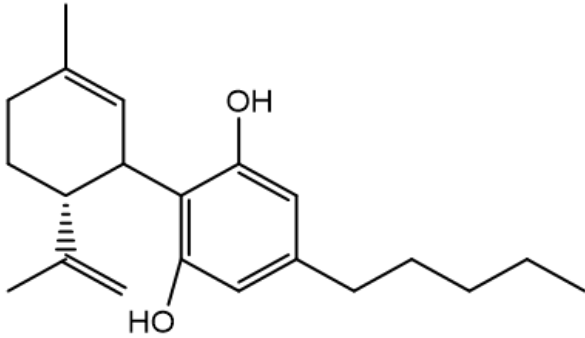
Cannabidiol (CBD)

- Extract of the *Cannabis sativa* plant
- Non-psychoactive cannabinoid
- Anxiety, depression, chronic pain





Background: Cannabidiol (CBD)



Cannabidiol (CBD)

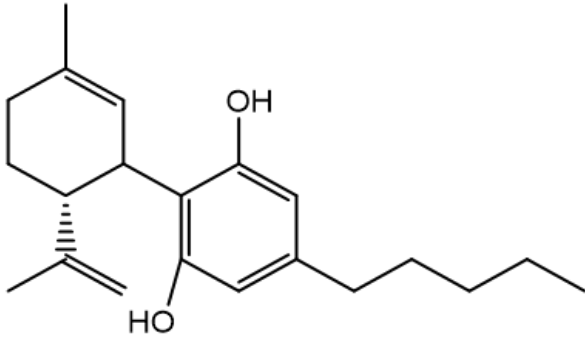
- Extract of the *Cannabis sativa* plant
- Non-psychoactive cannabinoid
- Anxiety, depression, chronic pain



Rare forms of epilepsy
(UK/EU/USA)



Background: Cannabidiol (CBD)



Cannabidiol (CBD)

- Extract of the *Cannabis sativa* plant
- Non-psychoactive cannabinoid
- Anxiety, depression, chronic pain



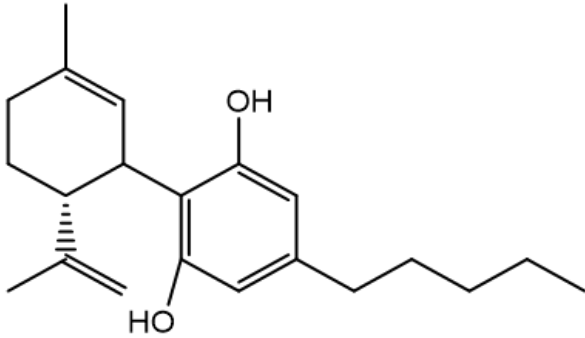
Rare forms of epilepsy
(UK/EU/USA)



MS symptoms
(UK/some EU/Canada)



Background: Cannabidiol (CBD)



Cannabidiol (CBD)

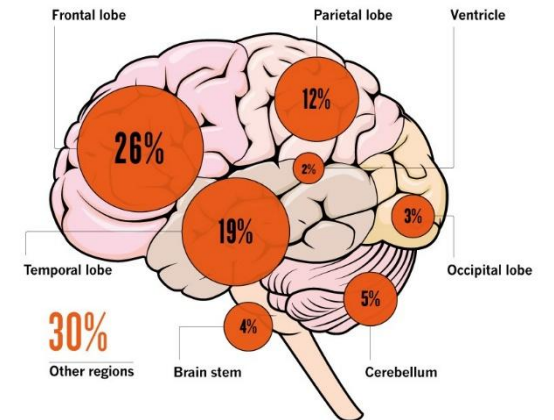
- Extract of the *Cannabis sativa* plant
- Non-psychoactive cannabinoid
- Anxiety, depression, chronic pain



Rare forms of epilepsy
(UK/EU/USA)



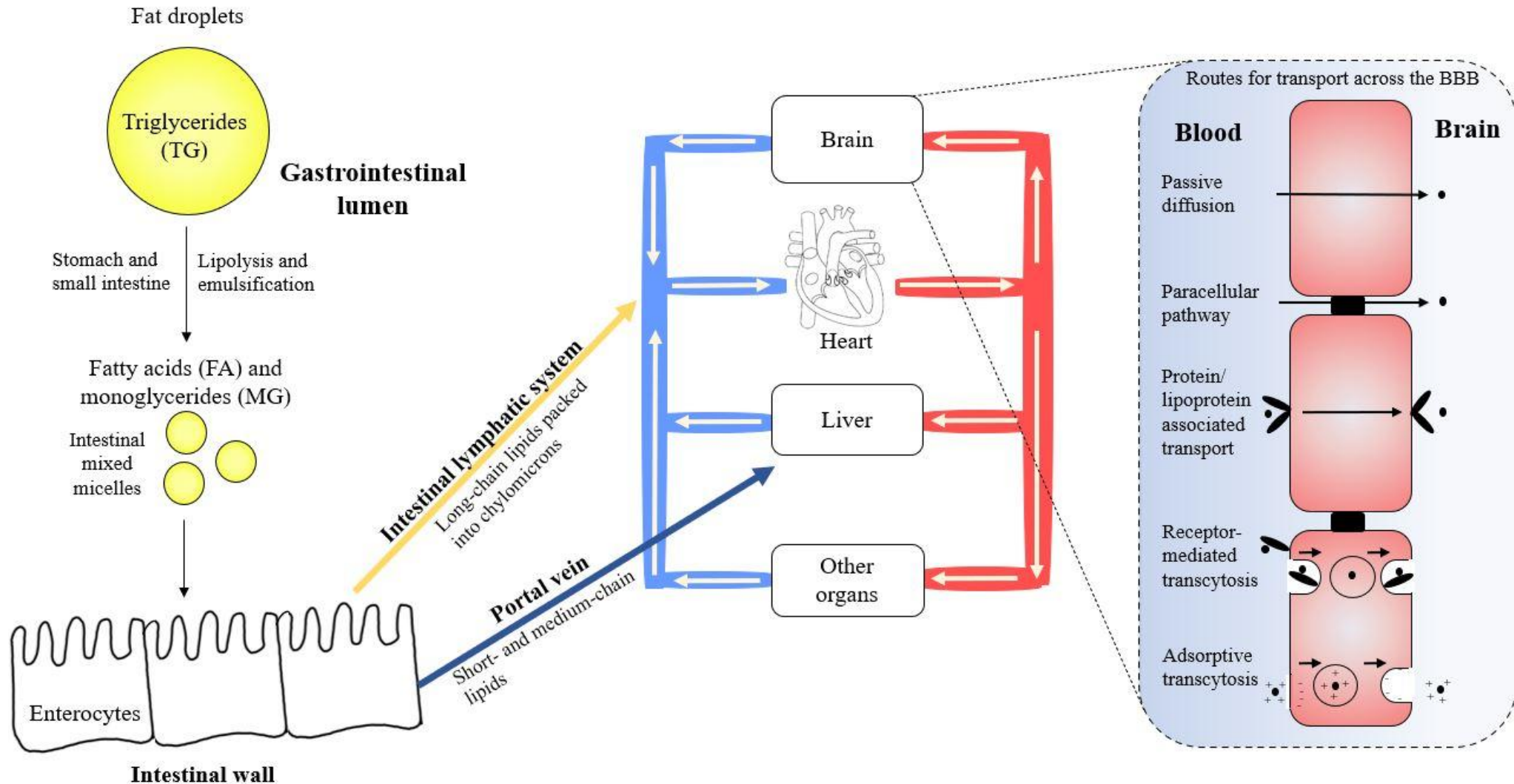
MS symptoms
(UK/some EU/Canada)



Anti-cancer properties
(currently in trial)



Background: Lipids & the blood-brain barrier





Materials: Lipid vehicles

Fatty acid			Sesame oil	Rapeseed oil	Coconut oil
Saturated	Lauric acid	C12:0			29%
	Myristic acid	C14:0			21%
	Palmitic acid	C16:0	13%	5%	18%
	Stearic acid	C18:0	8%	2%	8%
Unsaturated	Oleic acid	C18:1	44%	62%	13%
	Linoleic acid	C18:2	30%	21%	2%
	Linolenic acid	C18:3	<1%	8%	



Method: Biodistribution

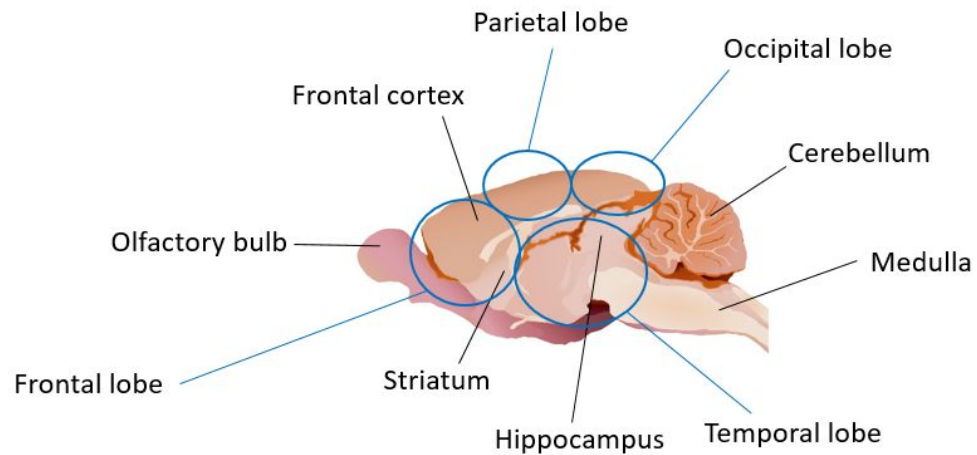
12 mg/Kg
CBD formulation





Method: Biodistribution

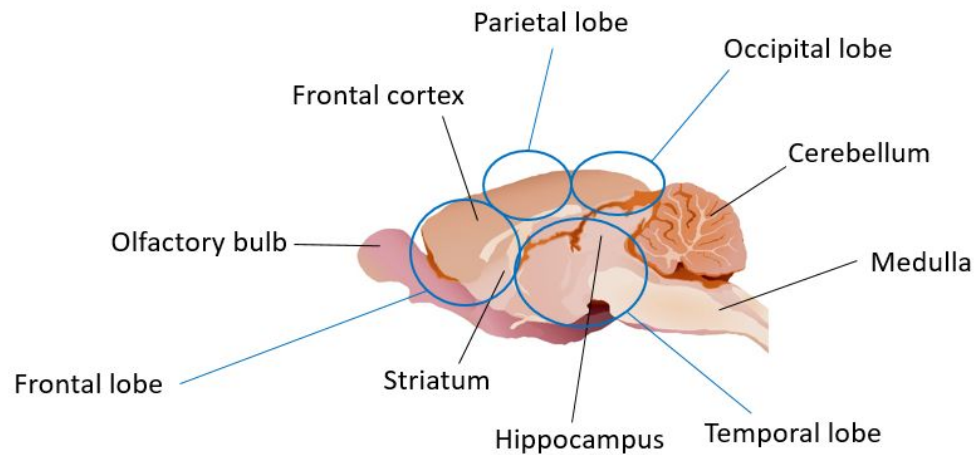
12 mg/Kg
CBD formulation





Method: Biodistribution

12 mg/Kg
CBD formulation

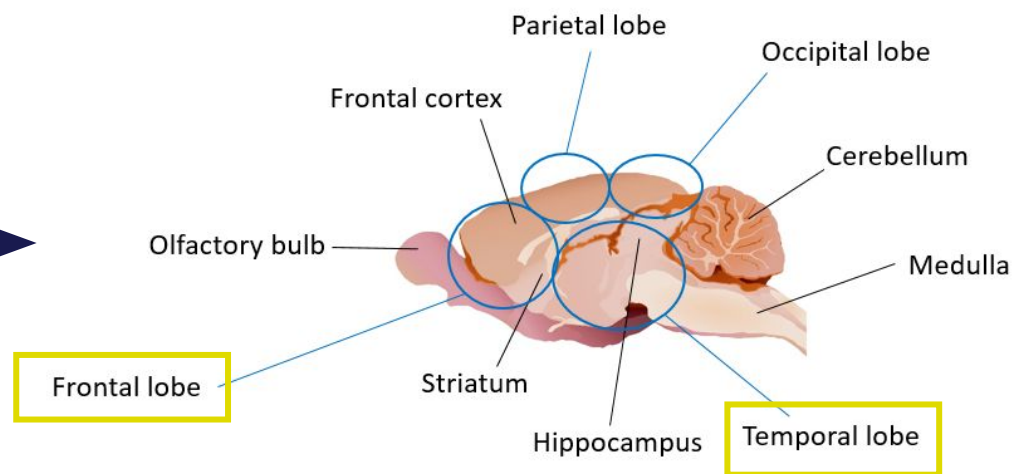


Zgair, A. *et al.*, *J. Pharm. Biomed. Anal.*,
2015



Method: Biodistribution

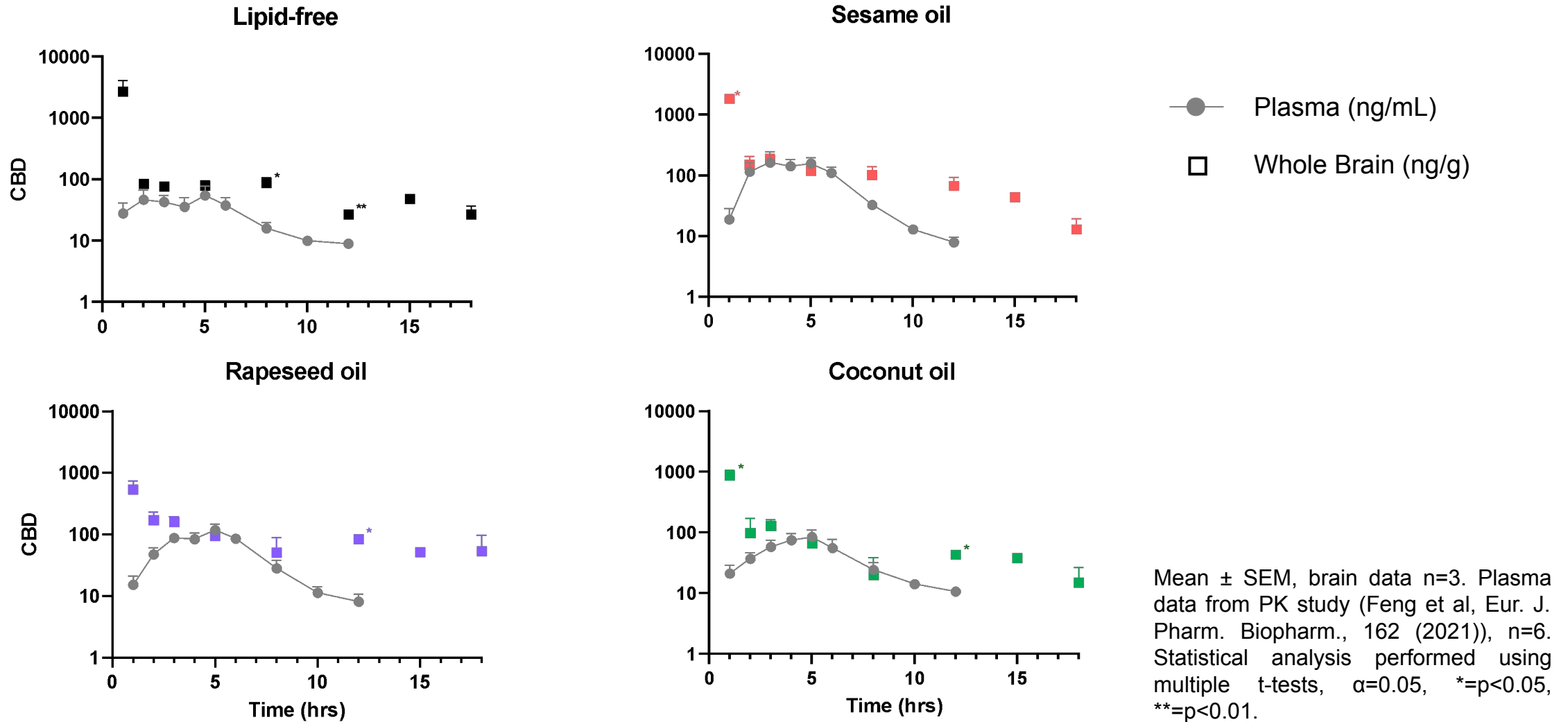
12 mg/Kg
CBD formulation



Zgair, A. *et al.*, *J. Pharm. Biomed. Anal.*,
2015

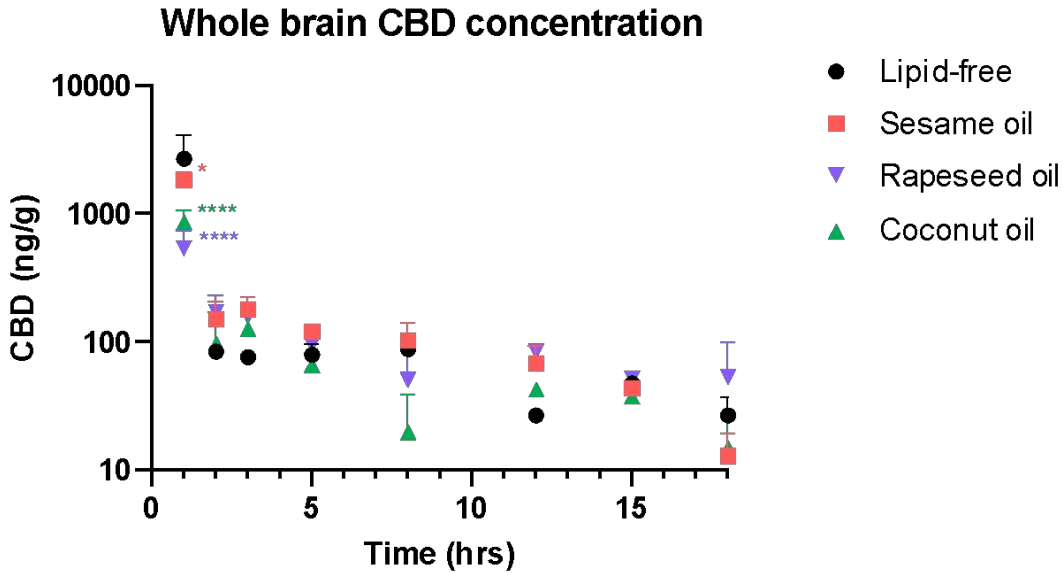


Results: Fast delivery to the whole brain





Results: Lipid-free yields high delivery to the whole brain



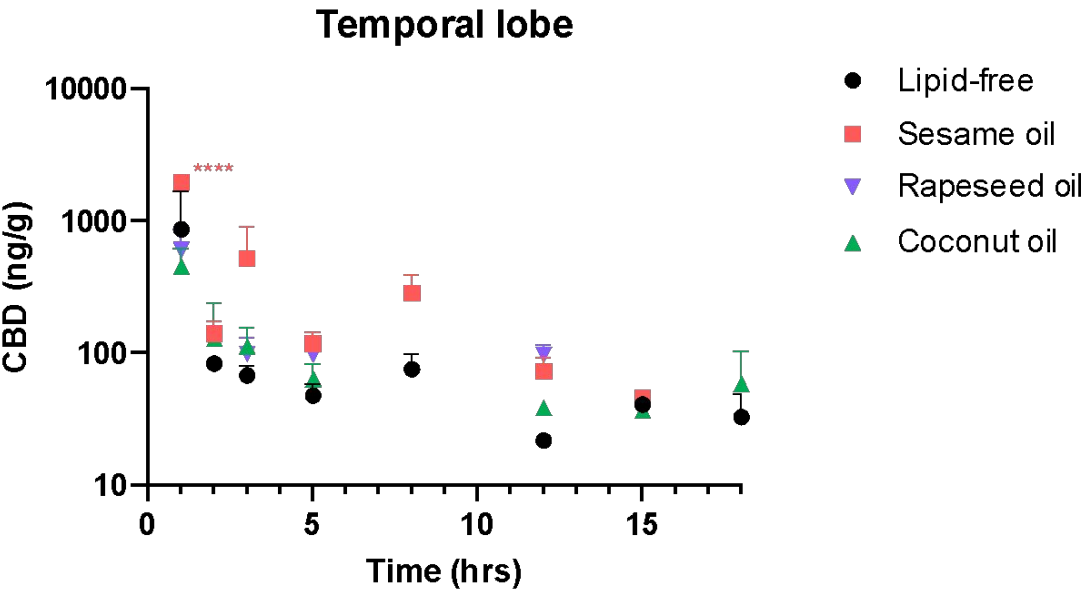
Lipid-free vs. oil shown on graph. Other significant differences found were at 1 hr sesame vs. coconut (**), and sesame vs. rapeseed (***).

	Lipid-free	Sesame oil	Rapeseed oil	Coconut oil
T_{max} (hrs)	1	1	1	1
C_{max} (ng/g)	2712 ± 2365	1836 ± 473	539 ± 341*	876 ± 338*
$t_{1/2}$ (hrs)	9.6	4.6	10.1	3.9
AUC_{0-18} (hr*ng/g)	3703	3311	1902*	1691*
$AUC_{0-\infty}$ (hr*ng/g)	4078	3396	2686	1776*

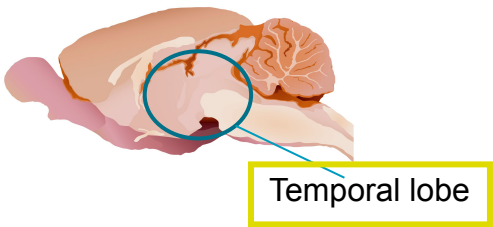
Mean ± SEM, n=3. Two-way ANOVA performed, α=0.05, *=p<0.05, **=p<0.01, ***=p<0.001, ****=p<0.0001. Lipid-free vs. oil shown.



Results: Sesame oil yields high delivery to the temporal lobe (not lipid-free)



Lipid-free vs. oil shown on graph, other differences found were at 1 hr sesame vs. coconut (****) and vs. rapeseed (****).



	Lipid-free	Sesame oil	Rapeseed oil	Coconut oil
T_{max} (hrs)	1	1	1	1
C_{max} (ng/g)	874 ± 1388	1979 ± 378*	611 ± 433	455 ± 282
$t_{1/2}$ (hrs)	12.0	2.6	1.7	7.2
AUC_{0-18} (hr*ng/g)	1696	4527****	1971	1271
$AUC_{0-\infty}$ (hr*ng/g)	2269	4700****	1994	1882

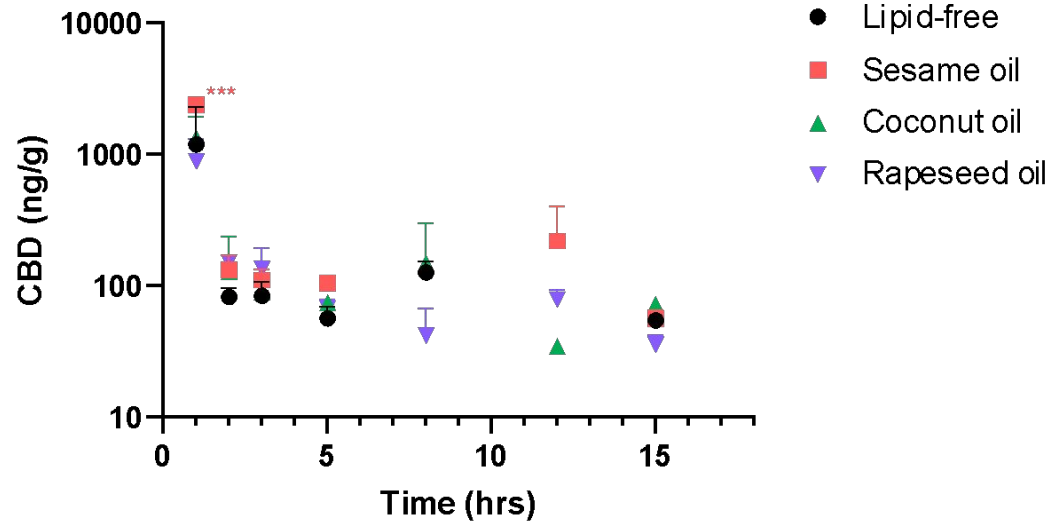
Lipid-free vs. oil shown. Other differences in C_{max} : sesame vs rapeseed (*) and coconut (**), AUC_{0-18} : sesame vs rapeseed (****) and coconut (****), $AUC_{0-\infty}$: sesame vs rapeseed (****) and coconut (****).

Mean ± SEM, n=3. Two-way ANOVA performed, α=0.05, *p<0.05, ****=p<0.0001. Lipid-free vs. oil shown.

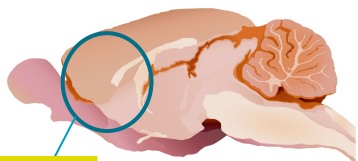


Results: Low degree of saturation yields high delivery to the frontal lobe

Frontal lobe



Lipid-free vs. oil shown on graph, other significant differences found were at 1 hr sesame vs. coconut (**) and rapeseed (***).



Frontal lobe

	Lipid-free	Sesame oil	Rapeseed oil	Coconut oil
T_{max} (hrs)	1	1	1	1
C_{max} (ng/g)	1206 ± 1858	2413 ± 234	893 ± 724	1355 ± 1008
$t_{1/2}$ (hrs)	6.2	6.1	7.8	5.2
AUC_{0-18} (hr*ng/g)	2392	4387*	1895	2565
$AUC_{0-\infty}$ (hr*ng/g)	2883	4888*	2300	3112

Lipid-free vs. oil shown. Other differences in AUC_{0-18} : sesame vs rapeseed (**) and coconut (**), $AUC_{0-\infty}$: sesame vs rapeseed (**) and coconut (*).

Mean ± SEM, n=3. Two-way ANOVA performed, $\alpha=0.05$, *= $p<0.05$, ****= $p<0.0001$. Lipid-free vs. oil shown.



Key points...



Fast brain delivery (1 hr) after oral administration in all formulations



Key points...



Fast brain delivery (1 hr) after oral administration in all formulations



Lipids affect the brain delivery profiles, but lipid-free results in the highest delivery to the whole brain



Key points...



Fast brain delivery (1 hr) after oral administration in all formulations



Lipids affect the brain delivery profiles, but lipid-free results in the highest delivery to the whole brain



Studying individual anatomical regions of the brain is important for optimal delivery to the site of action



Key points...

- Fast brain delivery (1 hr) after oral administration in all formulations
- Lipids affect the brain delivery profiles, but lipid-free results in the highest delivery to the whole brain
- Studying individual anatomical regions of the brain is important for optimal delivery to the site of action
- In general, a decrease in fatty acid saturation (Coconut->Rapeseed->Sesame) yields higher exposure to temporal and frontal lobes

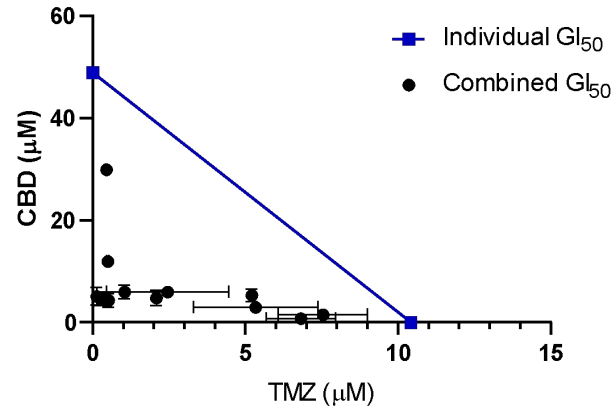


I didn't mention...

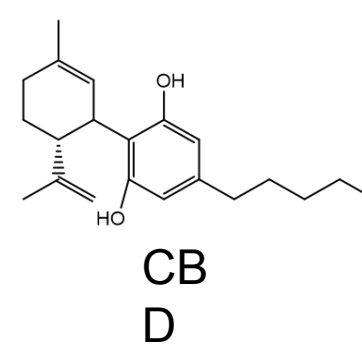
Glioblastoma Multiforme



GBM Cell line U373-V



Fluorinated cannabinoids





Acknowledgements

This work was funded by EPSRC [EP/L01646X/1]:
CDT in Advanced Therapeutics and Nanomedicines

alice.brookes@nottingham.ac.uk



@AliceBrookes11

Dr Pavel Gershkovich

Dr Tracey Bradshaw

Prof Morgan Alexander

Dr David Scurr

Dr James Butler (GSK)

Dr Wanshan Feng

Dr Adelaide Jewell

Haojie Chen



Engineering and
Physical Sciences
Research Council

CDT in Advanced Therapeutics
and Nanomedicines

