

CADTH RAPID RESPONSE REPORT: REFERENCE LIST

The Use of Medical Cannabis with Other Medications: Safety and Guidelines

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About CADTH: CADTH is an independent, not-for-profit organization responsible for providing Canada's health care decision-makers with objective evidence to help make informed decisions about the optimal use of drugs, medical devices, diagnostics, and procedures in our health care system.

Funding: CADTH receives funding from Canada's federal, provincial, and territorial governments, with the exception of Quebec.

Research Questions

1. What is the clinical evidence regarding the safety of the use of medical cannabis with other medications?
2. What are the evidence-based guidelines regarding the interaction of the use of medical cannabis with other medications?

Key Findings

Two systematic reviews and one non-randomized study were identified regarding the safety of the use of medical cannabis with other medications.

Methods

A limited literature search was conducted on key resources including PubMed, The Cochrane Library, University of York Centre for Reviews and Dissemination (CRD) databases, Canadian and major international health technology agencies, as well as a focused Internet search. No filters were applied to limit the retrieval by study type. Where possible, retrieval was limited to the human population. The search was also limited to English language documents published between January 1, 2012 and February 14, 2017. Internet links are provided, where available.

Selection Criteria

One reviewer screened citations and selected studies based on the inclusion criteria presented in Table 1.

Table 1: Selection Criteria

Population	Any patient taking cannabis to treat a medical condition
Intervention	Q1: Medical cannabis Q2: Recommendations on the use of medical cannabis interacting with other medications (including dosage)
Comparator	Q1: Other medications, including illicit substances and alcohol Q2: No comparator
Outcomes	Q1: Drug-drug interactions, safety, harms Q2: Guidelines
Study Designs	Health technology assessments, systematic reviews, meta-analyses, randomized control trials, non-randomized studies, evidence-based guidelines.

Results

Rapid Response reports are organized so that the higher quality evidence is presented first. Therefore, health technology assessment reports, systematic reviews, and meta-analyses are presented first. These are followed by randomized controlled trials, non-randomized studies, and evidence-based guidelines.

Two systematic reviews and one non-randomized study were identified regarding the safety of the use of medical cannabis with other medications. No relevant health technology assessments or randomized control trials were identified. In addition, no

relevant evidence-based guidelines or recommendations regarding the interaction of the use of medical cannabis with other medications were identified.

Additional references of potential interest are provided in the appendix.

Health Technology Assessments

No literature identified.

Systematic Reviews and Meta-analyses

1. Tsang CC, Giudice MG. Nabilone for the management of pain. *Pharmacotherapy*. 2016 Mar;36(3):273-86.
[PubMed: PM26923810](#)
2. Stout SM, Cimino NM. Exogenous cannabinoids as substrates, inhibitors, and inducers of human drug metabolizing enzymes: a systematic review. *Drug Metab Rev*. 2014 Feb;46(1):86-95.
[PubMed: PM24160757](#)

Randomized Controlled Trials

No literature identified.

Non-Randomized Studies

3. Geffrey AL, Pollack SF, Bruno PL, Thiele EA. Drug-drug interaction between clobazam and cannabidiol in children with refractory epilepsy. *Epilepsia*. 2015 Aug;56(8):1246-51.
[PubMed: PM26114620](#)

Guidelines and Recommendations

No literature identified.

Appendix — Further Information

Non-Randomized Studies - Non-Medical Cannabis Use

4. Jamil M, Zafar A, Adeel FS, Zawar I. Stroke from vasospasm due to marijuana use: can cannabis synergistically with other medications trigger cerebral vasospasm? *Case Rep Neurol Med* [Internet]. 2016 [cited 2017 Feb 21];2016:5313795. Available from: <http://www.ncbi.nlm.nih.gov/pmc/articles/PMC5090067>
[PubMed: PM27833768](#)
5. Hartman RL, Brown TL, Milavetz G, Spurgin A, Gorelick DA, Gaffney G, et al. Controlled cannabis vaporizer administration: blood and plasma cannabinoids with and without alcohol. *Clin Chem*. 2015 Jun;61(6):850-69.
[PubMed: PM26019183](#)
6. Kollins SH, Schoenfelder EN, English JS, Holdaway A, Van Voorhees E, O'Brien BR, et al. An exploratory study of the combined effects of orally administered methylphenidate and delta-9-tetrahydrocannabinol (THC) on cardiovascular function, subjective effects, and performance in healthy adults. *J Subst Abuse Treat* [Internet]. 2015 Jan [cited 2017 Feb 21];48(1):96-103. Available from: <http://www.ncbi.nlm.nih.gov/pmc/articles/PMC4250392>
[PubMed: PM25175495](#)
7. Manini AF, Yiannoulos G, Bergamaschi MM, Hernandez S, Olmedo R, Barnes AJ, et al. Safety and pharmacokinetics of oral cannabidiol when administered concomitantly with intravenous fentanyl in humans. *J Addict Med* [Internet]. 2015 May [cited 2017 Feb 21];9(3):204-10. Available from: <http://www.ncbi.nlm.nih.gov/pmc/articles/PMC4449284>
[PubMed: PM25748562](#)

Review Articles

8. Gaston TE, Friedman D. Pharmacology of cannabinoids in the treatment of epilepsy. *Epilepsy Behav*. 2017 Jan 10. [Epub ahead of print]
[PubMed: PM28087250](#)
9. O'Connell BK, Gloss D, Devinsk O. Cannabinoids in treatment-resistant epilepsy: a review. *Epilepsy Behav*. 2017 Feb 7. [Epub ahead of print]
[PubMed: PM28188044](#)

Non-Medical Cannabis Use

10. Kumar S, Rao PS, Earla R, Kumar A. Drug-drug interactions between anti-retroviral therapies and drugs of abuse in HIV systems. *Expert Opin Drug Metab Toxicol* [Internet]. 2015 Mar [cited 2017 Feb 21];11(3):343-55. Available from: <http://www.ncbi.nlm.nih.gov/pmc/articles/PMC4428551>
[PubMed: PM25539046](#)

11. Scavone JL, Sterling RC, Van Bockstaele EJ. Cannabinoid and opioid interactions: implications for opiate dependence and withdrawal. *Neuroscience* [Internet]. 2013 Sep 17 [cited 2017 Feb 21];248:637-54. Available from: <http://www.ncbi.nlm.nih.gov/pmc/articles/PMC3742578>
[PubMed: PM23624062](#)
12. Valverde O, Rodriguez-Arias M. Modulation of 3,4-methylenedioxymethamphetamine effects by endocannabinoid system. *Curr Pharm Des.* 2013;19(40):7081-91.
[PubMed: PM23574444](#)
13. Lindsey WT, Stewart D, Childress D. Drug interactions between common illicit drugs and prescription therapies. *Am J Drug Alcohol Abuse.* 2012 Jul;38(4):334-43.
[PubMed: PM22221229](#)

Clinical Practice Guidelines – Uncertain Methodology

14. Clinical guidance: for the use of medicinal cannabis products in Queensland [Internet]. Brisbane (Australia): Queensland Health; 2016 Dec. [cited 2017 Feb 21]. Available from: https://www.health.qld.gov.au/_data/assets/pdf_file/0023/634163/med-cannabis-clinical-guide.pdf

Additional Resources

15. Position statement: use of medical marijuana for neurologic disorders [Internet]. Minneapolis (MN): American Academy of Neurology; 2014. [cited 2017 Feb 21]. Available from: https://www.aan.com/uploadedFiles/Website_Library_Assets/Documents/6.Public_Policy/1.Stay_Informed/2.Position_Statements/3.PDFs_of_all_Position_Statements/Final%20Medical%20Marijuana%20Position%20Statement.pdf
See: "The interaction of these compounds with prescription medications is also unknown."
16. Cannabis (marihuana, marijuana) and the cannabinoids. Dried plant for administration by ingestion or other means. Psychoactive agent [Internet]. Ottawa: Health Canada. 2013 Feb. [cited 2017 Feb 21]. Available from: <http://www.hc-sc.gc.ca/dhp-mps/marihuana/med/infoprof-eng.php>
See: Section 6.2 on Drug Interactions.