

The heterogeneity and complexity of Cannabis extracts as antitumor agents

Review # 1

Joe Goldstrich MD, FACC

Important things to consider when reading this article:

- There are cannabinoids other than THC and CBD that have antineoplastic action
- CBG has heretofore unrecognized antineoplastic activity
- Some tumors will not respond to cannabinoids
- Some high THC, full extract cannabis oils (FECO), will lack antineoplastic activity
- Pure THC is less effective than THC administered as a full extract cannabis oil

The big picture:

- Include CBG in your cannabinoid antineoplastic protocol
- Consider making your FECO from more than one THC rich cultivar to lessen the risk of using an extract that lacks antineoplastic activity and to broaden the spectrum of anti-neoplasia



Review # 2

Trina Hazzah DVM, DACVIM (Oncology), CVCH

Important things to consider when reading this article:

- 1. Specific cannabis extracts may selectively affect cancer cells. And differing cancer cell lines from the same organ origin were affected differently by the same cannabis extract.
- 2. Using whole cannabis extracts is more effective in inducing cancer cell death than applying pure $\Delta 9$ -THC on the studied cells lines. These findings indicate that compounds other than $\Delta 9$ -THC in these extracts might act together in a polypharmacology way and determine the extract efficacy as antitumor agents.
- 3. Not all $\Delta 9$ -THC-rich extracts produce the same effects when applied at the same concentrations on a specific cancer cell line. According to the studies hierarchical clustering analysis, it is apparent that minor constituents can also significantly contribute to the variance among cannabis extracts.
- 4. The two most potent extracts affecting the survival of most cell lines tested contained high amounts of $\Delta 9$ -THC. Interestingly, in certain cell lines (a lung carcinoma cell line), cell survival was weakly correlated to the amount of $\Delta 9$ -THC in the extracts.
- 5. Some cancer cell lines are resistant to cannabis indued cell death. For example, of all the cell lines examined in this study, the HT-29 cell line (colon carcinoma) was the least sensitive to all cannabis extracts and concentrations tested (+42 additional extracts tested). This was correlated to the low or under detectable expression levels of CNR1, GPR55 and TRPM8 receptors.



The big picture:

- 1. The studied cancer cell lines differed in their susceptibilities towards the antitumor effects of various cannabis extracts. Phytocannabinoids work through different pathways and receptors, which vary in different cancer cell populations. This emphasizes the selective nature of cannabis extracts to affect the survival of certain cancer cell lines.
- 2. The fate of specific cancer cells following cannabis extract application is dependent upon the synergistic effects of its phytocannabinoid composition, concentration applied, along with the cell specific characteristics (e.g. cannabimimetic receptor expression). Future studies could focus on matching cannabis extracts with specific phytocannabinoid compositions and their effects on specific cancer subtypes in order to optimize treatment effects.