

EXECUTIVE SUMMARY

The Center for Medicinal Cannabis Research (CMCR) at the University of California was created in 2000 to conduct clinical and pre-clinical studies of cannabinoids, including smoked marijuana, to provide evidence one way or the other to answer the question “Does marijuana have therapeutic value?” To accomplish this objective, the CMCR issued calls for applications from researchers at leading California institutions, developed a close working relationship with state and federal agencies to gain regulatory approvals, established panels of nationally-recognized experts to rigorously review the merit of applications, and funded carefully designed studies that have now been published in high impact scientific journals, making significant contributions to the available literature on cannabis and the cannabinoids.

Summary of Results to Date

In total, the CMCR has approved fifteen clinical studies, including seven clinical trials, of which five have completed and two are in progress. The CMCR has also approved four pre-clinical studies, all of which have completed.

By design CMCR clinical studies focused on conditions identified by the Institute of Medicine for which cannabis might have potential therapeutic effects, based on current scientific knowledge (Institute of Medicine, 1999). To date, four CMCR-funded studies have demonstrated that cannabis has analgesic effects in pain conditions secondary to injury (e.g. spinal cord injury) or disease (e.g. HIV disease, HIV drug therapy) of the nervous system. This result is particularly important because three of these CMCR studies utilized cannabis as an add-on treatment for patients who were not receiving adequate benefit from a wide range of standard pain-relieving medications. This suggests that cannabis may provide a treatment option for those individuals who do not respond or respond inadequately to currently available therapies. The efficacy of cannabis in treatment-refractory patients also may suggest a novel mechanism of action not fully exploited by current therapies. In addition to nerve pain, CMCR has also supported a study on muscle spasticity in Multiple Sclerosis (MS). Such spasticity can be painful and disabling, and some patients do not benefit optimally from existing treatments. The results of the CMCR study suggest that cannabis reduces MS spasticity, at least in the short term, beyond the benefit available from usual medical care.

Donald Abrams, M.D.

UC San Francisco

Cannabis for Treatment of HIV-Related Peripheral Neuropathy

Donald Abrams, M.D.

UC San Francisco

Vaporization as a Smokeless Cannabis Delivery System

Jody Corey-Bloom, M.D., Ph.D.

UC San Diego

Short-Term Effects of Cannabis Therapy on Spasticity in MS

Ronald Ellis, M.D., Ph.D.

UC San Diego

Placebo-controlled, Double Blind Trial of Medicinal Cannabis in Painful HIV Neuropathy

Mark Wallace, M.D.

UC San Diego

Analgesic Efficacy of Smoked Cannabis

Barth Wilsey, M.D.

UC Davis

Double Blind, Placebo Controlled Trial of Smoked Marijuana on Neuropathic Pain

Table 1. Clinical Studies Published or Submitted for Publication

To date, six of the studies have published (or are in the process of publishing) results in respected medical journals, garnering national and international attention from other researchers, media outlets, governmental agencies, and the general public (see Table 1). These results have helped to bring together accomplished international experts on cannabis and cannabinoids and foster scientific dialog on the possible utility of cannabis as a therapeutic agent.

Adverse side effects experienced by participants included cough, nausea, dizziness, sedation and changes in cognition. However, these effects were typically mild and resolved rapidly after treatment. Currently approved analgesics are not without side effects, and the effects observed in CMCR studies tended to be no worse than would be expected with other potent analgesics. Following the conclusion of the two studies currently in progress, CMCR will have exhausted its available funding for clinical work, though the CMCR will continue to maintain a sample bank and to consult with researchers and policymakers as needed.

The majority of CMCR studies that have been discontinued were cancer studies that experienced difficulty in recruiting participants. Many severely ill individuals were reluctant to volunteer for a rigorous research protocol where the experimental treatment addressed disease symptoms (i.e. nausea, pain) but did not affect tumor growth directly. Other factors, such as requirement that patients have stable pain scores over a period of time leading into the study, prohibition from driving for the duration of the study, and difficulty in providing cannabis for home administration may also have played a role in the lack of success in recruiting this population. A further impediment to participation in CMCR studies, particularly in cancer patients, was the inability of CMCR to continue to provide study drug beyond the study period to patients who find active treatment beneficial. Additionally, some individuals already were using cannabis to treat pain or other symptoms, and so had less incentive to participate in research.

The CMCR portfolio also included basic science studies in animals and in human cells (pre-clinical research). This research was supported because it had the potential to provide insights into therapeutic use of cannabinoids in human disease. One study provided evidence, by way of recordings of nerve cell activity and in awake animals, of analgesic effects of cannabis-like compounds on head and facial pain, suggesting that clinical trials of cannabis might be warranted in patients with headache or other facial pain. Another study reported that cannabis did not interfere with the function of blood cells involved with immunity, an important finding considering potential therapeutic use of cannabis compounds will be in persons with chronic illnesses.

Other CMCR Activities

In addition to the research, CMCR has also functioned as a catalyst for discussion and examination of the potential development of cannabis as medicine. In July, 2002, CMCR sponsored a workshop "Future Directions in Cannabinoid Therapeutics" featuring presentations by intellectual and scientific leaders in the field of cannabinoid science from around the world. CMCR hosted a second meeting in summer 2004 to address recent progress in science that would be likely to lead to clinical trials of new cannabinoid compounds. "Future Directions in Cannabinoid Therapeutics II: From the Bench to the Clinic" brought together the major stakeholders in the development of cannabinoid therapeutics in order to survey laboratory compounds that are most promising for testing in human trials and to confront potential stumbling blocks to testing and development of these compounds. A special issue of the journal *Neuropharmacology* (2005) was dedicated to publishing the research presented at this meeting. CMCR researchers have also published two literature reviews on the neuropsychological effects of cannabis use in order to better understand the potential hazards of cannabis use in short and long-term treatment settings (Grant, et al., 2003 & Gonzalez, et. al, 2002 – see reference list).

Conclusion

As a result of the vision and foresight of the California State Legislature Medical Marijuana Research Act (SB847), the CMCR has successfully conducted the first clinical trials of smoked cannabis in the United States in more than 20 years. As a result of this program of systematic research, we now have reasonable evidence that cannabis is a promising treatment in selected pain syndromes caused by injury or diseases of the nervous system, and possibly for painful muscle spasticity due to multiple sclerosis.

Obviously more research will be necessary to elucidate the mechanisms of action and the full therapeutic potential of cannabinoid compounds. Meanwhile, the knowledge and new findings from the CMCR provide a strong science-based context in which policy makers and the public can discuss the place of these compounds in medical care.

Mission Statement

“The Center for Medicinal Cannabis Research (CMCR) will conduct high quality scientific studies intended to ascertain the general medical safety and efficacy of cannabis products and examine alternative forms of cannabis administration. The Center will be seen as a model resource for health policy planning by virtue of its close collaboration with federal, state, and academic entities.”