EINGEGANGEN

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Certification

I confirm that I follow the issue of the medical use of cannabis and cannabinoids since 1994 and am aware of all relevant publications concerning vaporization of cannabis and cannabinoids since this time. Since the preparation of my review for Storz & Bickel and my last certification of 31 July 2012 no relevant new data on this issue came to my attention. The objective of my literature review was to detect new data on the use of the Volcano vaporizer for the administration of cannabinoids in humans. The primary focus were studies on safety issues. No studies on safety issues have been published since my last certification.
Instead, the Volcano vaporizer is increasingly used for clinical studies and other research areas on cannabinoids in humans due to the favorable safety of this way of administration. Three examples are presented below.

1. Clinical study on the use of vaporized cannabis with the Volcano vaporizer in patients with neuropathic pain

Researchers at the VA Northern California Health Care System, and Department of Physical Medicine and Rehabilitation of the University of California in Sacramento, USA, conducted a double-blind, placebo-controlled, crossover study evaluating the analgesic efficacy of vaporized cannabis by using the Volcano vaporizer in subjects, the majority of whom were experiencing neuropathic pain despite traditional treatment (Wilsey et al. 2013). Thirty-nine patients with central and peripheral neuropathic pain underwent a standardized procedure for inhaling medium-dose (3.53%), low-dose (1.29%), or placebo cannabis with the primary outcome being visual analog scale pain intensity.

2. Clinical study on the use of vaporized cannabis with the Volcano vaporizer in pain patients already receiving opioids

Researchers of the Division of Hematology-Oncology of the San Francisco General Hospital of the University of California in San Francisco, USA, investigated the potential pharmacokinetics and the safety of the combination of cannabinoids and opioids in humans (Abrams et al. 2011). Twenty-one individuals with chronic pain, on a regimen of twice-daily doses of sustained-release morphine or oxycodone were enrolled in the study and admitted for a 5-day inpatient stay. Participants were

asked to inhale vaporized cannabis with the Volcano vaporizer in the evening of day 1, three times a day on days 2-4, and in the morning of day 5. Scientists concluded from their results that vaporized cannabis augments the analgesic effects of opioids without significantly altering plasma opioid levels.

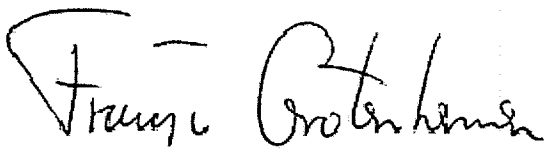
3. Clinical investigation on the involvement of the endocannabinoid system in cognitive brain function by administering THC with the Volcano vaporizer

In the so-called Pharmacological Imaging of the Cannabinoid System (PhICS) study, researchers of the Department of Neurology and Neurosurgery of the Rudolf Magnus Institute of Neuroscience at the University Medical Center Utrecht, The Netherlands, the involvement of the endocannabinoid system in cognitive brain function was assessed by comparing acute effects of THC on brain function between healthy controls and groups of psychiatric patients showing cognitive dysfunction (van Hell et al. 2011). THC in this study was administered by the Volcano vaporizer.

Summary:

Clinical and basic research with cannabinoids in humans is increasingly performed by using the Volcano Medic since this way of administration is regarded as safe and effective by the scientists working in this area.

I declare that literature quoted in this review reflects current state-of-the-art, that references in this review are taken from recognized scientific publications, and that this review is outcome of a study according to scientific principles.



Dr. F. Grotenhermen

Literature

Abrams DI, Couey P, Shade SB, Kelly ME, Benowitz NL. Cannabinoid-opioid interaction in chronic pain. Clin Pharmacol Ther 2011;90(6):844-51.

van Hell HH, Bossong MG, Jager G, Kahn RS, Ramsey NF. Methods of the pharmacological imaging of the cannabinoid system (PhICS) study: towards understanding the role of the brain endocannabinoid system in human cognition. Int J Methods Psychiatr Res 2011;20(1):10-27.

Wilsey B, Marcotte T, Deutsch R, Gouaux B, Sakai S, Donaghe H. Low-dose vaporized cannabis significantly improves neuropathic pain. J Pain 2013;14(2):136-48.

Abstracts of the cited literature, which are all available in the database PubMed

Wilsey B, Marcotte T, Deutsch R, Gouaux B, Sakai S, Donaghe H. Low-dose vaporized cannabis significantly improves neuropathic pain. J Pain. 2013 Feb;14(2):136-48. doi: 10.1016/j.jpain.2012.10.009. Epub 2012 Dec 11.

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We conducted a double-blind, placebo-controlled, crossover study evaluating the analgesic efficacy of vaporized cannabis in subjects, the majority of whom were experiencing neuropathic pain despite traditional treatment. Thirty-nine patients with central and peripheral neuropathic pain underwent a standardized procedure for inhaling medium-dose (3.53%), low-dose (1.29%), or placebo cannabis with the primary outcome being visual analog scale pain intensity. Psychoactive side effects and neuropsychological performance were also evaluated. Mixed-effects regression models demonstrated an analgesic response to vaporized cannabis. There was no significant difference between the 2 active dose groups' results (P > .7). The number needed to treat (NNT) to achieve 30% pain reduction was 3.2 for placebo versus low-dose, 2.9 for placebo versus medium-dose, and 25 for medium- versus low-dose. As these NNTs are comparable to those of traditional neuropathic pain medications, cannabis has analgesic efficacy with the low dose being as effective a pain reliever as the medium dose. Psychoactive effects were minimal and well tolerated, and neuropsychological effects were of limited duration and readily reversible within 1 to 2 hours. Vaporized cannabis, even at low doses, may present an effective option for patients with treatment-resistant neuropathic pain.PERSPECTIVE: The analgesia obtained from a low dose of delta-9-tetrahydrocannabinol (1.29%) in patients, most of whom were experiencing neuropathic pain despite conventional treatments, is a clinically significant outcome. In general, the effect sizes on cognitive testing were consistent with this minimal dose. As a result, one might not anticipate a significant impact on daily functioning.

Abrams DI, Couey P, Shade SB, Kelly ME, Benowitz NL. Cannabinoid-opioid interaction in chronic pain. Clin Pharmacol Ther. 2011 Dec;90(6):844-51. doi: 10.1038/clpt.2011.188. Epub 2011 Nov 2.

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Comment in Clin Pharmacol Ther. 2012 Jun;91(6):972; author reply 972-3. Clin Pharmacol Ther. 2011 Dec;90(6):769-71.

Cannabinoids and opioids share several pharmacologic properties and may act synergistically. The potential pharmacokinetics and the safety of the combination in humans are unknown. We therefore undertook a study to answer these questions. Twenty-one individuals with chronic pain, on a regimen of twice-daily doses of sustained-release morphine or oxycodone were enrolled in the study and admitted for a 5-day inpatient stay. Participants were asked to inhale vaporized cannabis in the evening of day 1, three times a day on days 2-4, and in the morning of day 5. Blood sampling was performed at 12-h intervals on days 1 and 5. The extent of chronic pain was also assessed daily. Pharmacokinetic investigations revealed no significant change in the area under the plasma concentration-time curves for either morphine or oxycodone after exposure to cannabis. Pain was significantly decreased (average 27%, 95% confidence interval (CI) 9, 46) after the addition of vaporized cannabis. We therefore concluded that vaporized cannabis augments the analgesic effects of opioids without significantly altering plasma opioid levels. The combination may allow for opioid treatment at lower doses with fewer side effects.

van Hell HH, Bossong MG, Jager G, Kahn RS, Ramsey NF. Methods of the pharmacological imaging of the cannabinoid system (PhICS) study: towards understanding the role of the brain endocannabinoid system in human cognition. Int J Methods Psychiatr Res. 2011 Mar;20(1):10-27. doi: 10.1002/mpr.327.

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Various lines of (pre)clinical research indicate that cannabinoid agents carry the potential for therapeutic application to reduce symptoms in several psychiatric disorders. However, direct testing of the involvement of cannabinoid brain systems in psychiatric syndromes is essential for further development. In the Pharmacological Imaging of the Cannabinoid System (PhICS) study, the involvement of the endocannabinoid system in cognitive brain function is assessed by comparing acute effects of the cannabinoid agonist Δ9-tetrahydrocannabinol (THC) on brain function between healthy controls and groups of psychiatric patients showing cognitive dysfunction. This article describes the objectives and methods of the PhICS study and presents preliminary results of the administration procedure on subjective and neurophysiological parameters. Core elements in the methodology of PhICS are the administration method (THC is administered by inhalation using a vaporizing device) and a comprehensive use of pharmacological magnetic resonance imaging (phMRI) combining several types of MRI scans including functional MRI (fMRI), Arterial Spin Labeling (ASL) to measure brain perfusion, and resting-state fMRI. Additional methods like neuropsychological testing further specify the exact role of the endocannabinoid system in regulating cognition. Preliminary results presented in this paper indicate robust behavioral and subjective effects of THC. In addition, fMRI paradigms demonstrate activation of expected networks of brain regions in the cognitive domains of interest. The presented administration and assessment protocol provides a basis for further research on the involvement of the endocannabionoid systems in behavior and in psychopathology, which in turn may lead to development of therapeutic opportunities of cannabinoid ligands.