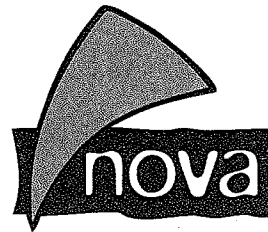


EINGEGANGEN

15. Sep. 2014



nova Institut
für Ökologie und Innovation *

nova-Institut GmbH • Chemiepark Knapsack • Industriestraße 300 • 50354 Hürth

nova-Institut GmbH
Chemiepark Knapsack
Industriestraße 300, 50354 Hürth
Deutschland
Tel.: +49 (0) 2233 48 14 40
Fax: +49 (0) 2233 48 14 50
contact@nova-institut.de
www.nova-institut.eu
www.bio-based.eu

STORZ & BICKEL GmbH & Co. KG
Rote Strasse 1
78532 Tuttlingen



Bio-basierte Ökonomie
Bio-based Economy

September 2, 2014

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 3 August 2013 three relevant new studies 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 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. Survey on the experience with a cannabis vaporizer in cannabis users

Researches of the Department of Psychology, University of New England in Armidale, Australia, conducted a study with individuals using a vaporizer on their own initiative. In a first study 96 adults anonymously answered questions about their experiences with a vaporizer and their use of marijuana with tobacco. Users identified 4 advantages to using a vaporizer over smoking marijuana: perceived health benefits, better taste, no smoke smell, and more effect from the same amount of marijuana. Users identified 2 disadvantages: inconvenience of setup and cleaning and the time it takes to get the device operating for each use. Only 2 individuals combined tobacco in the vaporizer mix, whereas 15 combined tobacco with marijuana when they smoked marijuana. Almost all participants intended to continue using a vaporizer. Authors concluded that "vaporizers seem to have appeal to marijuana users, who perceive them as having harm-reduction and other benefits. Vaporizers are worthy of experimental research evaluating health-related effects of using them".

Geschäftsführer:
Michael Carus, Dirk Schubert

Sitz der Gesellschaft: Hürth
Amtsgericht Köln, HRB Nr. 44144

USt-IdNr. DE811827699
Umsatzsteuer-Nr. 224/5731/0281

Kölner Bank
Konto 528 684 009, BLZ 371 600 87

S.W.I.F.T.-Code GENODE33
IBAN-Code: DE 74371600870528684009

* Eine Dienstleistung der nova-Institut für politische und ökologische Innovation GmbH

Gedruckt auf umweltfreundlichem und zu 100% recyceltem Papier

2. Two studies on the use of vaporised cannabinoids in rodents

Two studies with rats were conducted by researchers of the Department of Psychology of Wilfrid Laurier University in Waterloo, Ontario, Canada, to develop and validate a pulmonary cannabinoid route of exposure for experimental pharmacology studies in rodents and in a second step to compare behavioural effects of inhaled versus parenteral cannabinoids exposure in rodents.

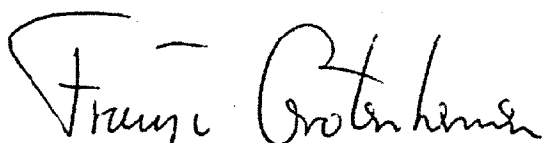
In the first study the animals were exposed to pulmonary THC delivered by the Volcano Medic at different doses (1, 5, and 10 mg) as well as to injected THC at different, but lower doses (0.25, 0.5, 1.0, and 1.5 mg/kg of bodyweight). THC produced some qualitatively different effects on behaviour depending upon the route of administration.

In the second study the same doses were administered to rats by the Volcano Medic and by injection of THC and effects on locomotor activity, food and water consumption were measured. Again some behavioural effects different in dependency of route of administration.

Summary:

The Volcano Medic continues to be used for clinical and basic research with cannabinoids. Recently Volcano was also reduced for THC administration in animals .

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

- Malouff JM(1), Rooke SE, Copeland J. Experiences of marijuana-vaporizer users. *Subst Abus.* 2014;35(2):127-8. doi: 10.1080/08897077.2013.823902.
- Manwell LA(1), Charchoglyan A(2), Brewer D(2), Matthews BA(3), Heipel H(3), Mallet PE(3). A vaporized $\Delta(9)$ -tetrahydrocannabinol ($\Delta(9)$ -THC) delivery system part I: Development and validation of a pulmonary cannabinoid route of exposure for experimental pharmacology studies in rodents. *J Pharmacol Toxicol Methods.* 2014 Jun 25. [Epub ahead of print]
- Manwell LA(1), Ford B(2), Matthews BA(2), Heipel H(2), Mallet PE(2). A vapourized $\Delta(9)$ -tetrahydrocannabinol ($\Delta(9)$ -THC) delivery system part II: Comparison of behavioural effects of pulmonary versus parenteral cannabinoid exposure in rodents. *J Pharmacol Toxicol Methods.* 2014 Jun 21. [Epub ahead of print]



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

J Pharmacol Toxicol Methods. 2014 Jun 25. pii: S1056-8719(14)00223-8. doi: 10.1016/j.vascn.2014.06.006. [Epub ahead of print]

A vaporized $\Delta(9)$ -tetrahydrocannabinol ($\Delta(9)$ -THC) delivery system part I: Development and validation of a pulmonary cannabinoid route of exposure for experimental pharmacology studies in rodents.

Manwell LA(1), Charchoglyan A(2), Brewer D(2), Matthews BA(3), Heipel H(3), Mallet PE(3).

Author information: (1)Department of Psychology, Wilfrid Laurier University, Waterloo, ON N2L3C5, Canada; Department of Psychology, University of Guelph, Guelph, ON N1G2W1, Canada; Mass Spectrometry Facility, University of Guelph, Guelph, ON N1G2W1, Canada; Centre for Addiction and Mental Health, Social Aetiology of Mental Illness Program, University of Toronto, ON M5T1R8, Canada. Electronic address: laurie.manwell@camh.ca. (2)Mass Spectrometry Facility, University of Guelph, Guelph, ON N1G2W1, Canada. (3)Department of Psychology, Wilfrid Laurier University, Waterloo, ON N2L3C5, Canada.

INTRODUCTION: Most studies evaluating the effects of $\Delta(9)$ -tetrahydrocannabinol ($\Delta(9)$ -THC) in animal models administer it via a parenteral route (e.g., intraperitoneal (IP) or intravenous injection (IV)), however, the common route of administration for human users is pulmonary (e.g., smoking or vaporizing marijuana). A vaporized $\Delta(9)$ -THC delivery system for rodents was developed and used to compare the effects of pulmonary and parenteral $\Delta(9)$ -THC administration on blood cannabinoid levels and behavior. **METHODS:** Sprague-Dawley rats were exposed to pulmonary $\Delta(9)$ -THC (1, 5, and 10mg of inhaled vapor) delivered via a Volcano[®] vaporizing device (Storz and Bickel, Germany) or to parenteral $\Delta(9)$ -THC (0.25, 0.5, 1.0, and 1.5mg/kg injected IP). Quantification of $\Delta(9)$ -THC and its psychoactive metabolite, 11-hydroxy- $\Delta(9)$ -THC (11-OH- $\Delta(9)$ -THC), in blood was determined by liquid chromatography/mass spectrometry (LC/MS). In order to verify the potential for the vaporization procedure to produce a robust conditioned place preference (CPP) or conditioned place avoidance CPA, classical conditioning procedures were systematically varied by altering the exposure time (10 or 20min) and number of exposed rats (1 or 2) while maintaining the same vaporization dose (10mg). **RESULTS:** Blood collected at 20min intervals showed similar dose-dependent and time-dependent changes in $\Delta(9)$ -THC and 11-OH- $\Delta(9)$ -THC for both pulmonary and parenteral administration of $\Delta(9)$ -THC. However, vaporized $\Delta(9)$ -THC induced CPP under certain conditions whereas IP-administered $\Delta(9)$ -THC induced CPA. **CONCLUSION:** These results support and extend the limited evidence (e.g., Naef et al., 2003, 2004; Niyuhire et al., 2007a) that $\Delta(9)$ -THC produces qualitatively different effects on behavior depending upon the route of administration.

Copyright © 2014 Elsevier Inc. All rights reserved.

PMID: 24973534 [PubMed - as supplied by publisher]

J Pharmacol Toxicol Methods. 2014 Jun 21. pii: S1056-8719(14)00221-4. doi: 10.1016/j.vascn.2014.06.004. [Epub ahead of print]

A vapourized $\Delta(9)$ -tetrahydrocannabinol ($\Delta(9)$ -THC) delivery system part II: Comparison of behavioural effects of pulmonary versus parenteral cannabinoid exposure in rodents.

Manwell LA(1), Ford B(2), Matthews BA(2), Heipel H(2), Mallet PE(2).

Author information: (1)Department of Psychology, Wilfrid Laurier University, Waterloo, ON N2L3C5, Canada; Department of Psychology, University of Guelph, Guelph, ON N1G2W1, Canada; Centre for Addiction and Mental Health, Social Aetiology of Mental Illness Program, University of Toronto, ON M5T1R8, Canada. Electronic address: laurie.manwell@camh.ca. (2)Department of Psychology, Wilfrid Laurier University, Waterloo, ON N2L3C5, Canada.

INTRODUCTION: Studies of the rewarding and addictive properties of cannabinoids using rodents as animal models of human behaviour often fail to replicate findings from human studies. Animal studies typically employ parenteral routes of administration, whereas humans typically smoke cannabis, thus discrepancies may be related to different pharmacokinetics of parenteral and pulmonary routes of administration. Accordingly, a novel delivery system of vapourized $\Delta(9)$ -tetrahydrocannabinol ($\Delta(9)$ -THC) was developed and assessed for its pharmacokinetic, pharmacodynamic, and behavioural effects in rodents. A commercially available vapourizer was used to assess the effects of pulmonary (vapourized) administration of $\Delta(9)$ -THC and directly compared to parenteral (intraperitoneal, IP) administration of $\Delta(9)$ -THC. **METHODS:** Sprague-Dawley rats were exposed to pure $\Delta(9)$ -THC vapour (1, 2, 5, 10, and 20mg/pad), using a Volcano[®] vapourizing device (Storz and Bickel, Germany) or IP-administered $\Delta(9)$ -THC (0.1, 0.3, 0.5, 1.0mg/kg), and drug effects on locomotor activity, food and water consumption, and cross-sensitization to morphine (5mg/kg) were measured. **RESULTS:** Vapourized $\Delta(9)$ -THC significantly increased feeding during the first hour following exposure, whereas IP-administered $\Delta(9)$ -THC failed to produce a reliable increase in feeding at all doses tested. Acute administration of 10mg of vapourized $\Delta(9)$ -THC induced a short-lasting stimulation in locomotor activity compared to control in the first of four hours of testing over 7 days of repeated exposure; this chronic exposure to 10mg of vapourized $\Delta(9)$ -THC did not induce behavioural sensitization to morphine. **DISCUSSION:** These results suggest vapourized $\Delta(9)$ -THC administration produces behavioural effects qualitatively different from those induced by IP administration in rodents. Furthermore, vapourized $\Delta(9)$ -THC delivery in rodents may produce behavioural effects more comparable to those observed in humans. We conclude that some of the conflicting findings in animal and human cannabinoid studies may be related to pharmacokinetic differences associated with route of administration.

Copyright © 2014 Elsevier Inc. All rights reserved.

PMID: 24956154 [PubMed - as supplied by publisher]

Subst Abus. 2014;35(2):127-8. doi: 10.1080/08897077.2013.823902.

Experiences of marijuana-vaporizer users.

Malouff JM(1), Rooke SE, Copeland J.

Author information: (1)a Department of Psychology, University of New England, Armidale, New South Wales, Australia.

BACKGROUND: Using a marijuana vaporizer may have potential harm-reduction advantages on smoking marijuana, in that the user does not inhale smoke. Little research has been published on use of vaporizers. **METHODS:** In the first study of individuals using a vaporizer on their own initiative, 96 adults anonymously answered questions about their experiences with a vaporizer and their use of marijuana with tobacco. **RESULTS:** Users identified 4 advantages to using a vaporizer over smoking marijuana: perceived health benefits, better taste, no smoke smell, and more effect from the same amount of marijuana. Users identified 2 disadvantages: inconvenience of setup and cleaning and the time it takes to get the device operating for each use. Only 2 individuals combined tobacco in the vaporizer mix, whereas 15 combined tobacco with marijuana when they smoked marijuana. Almost



Bio-basierte Ökonomie
Bio-based Economy

all participants intended to continue using a vaporizer. CONCLUSIONS: Vaporizers seem to have appeal to marijuana users, who perceive them as having harm-reduction and other benefits. Vaporizers are worthy of experimental research evaluating health-related effects of using them.

PMID: 24821347 [PubMed - in process]