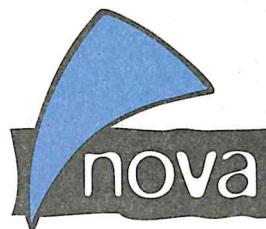


EINGEGANGEN

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Slus



**Institut**  
für Ökologie und Innovation \*

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

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

**nova-Institut GmbH**

Chemiepark Kapsack  
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



Bio-basierte Ökonomie  
Bio-based Economy

August 22, 2017

## 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 August 15, 2016 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 Medic, the Mighty Medic or other vaporizers for the administration of cannabinoids in humans. The primary focus was studies on safety issues. One study compared the preferred modes of administration of cannabis, the second compared cannabinoids in oral fluid after cannabis use by a vaporizer and other modes of administration, and the third compared modes of administration of cannabis in different regions of the world.

### 1. Preferred modes of administration for cannabis

Scientists of the Centre for Cardiovascular and Chronic Care, Faculty of Health, University of Technology Sydney, Australia, and other Australian research facilities conducted a cross-sectional anonymous survey online and in eight adult outpatient palliative care and/or cancer services (Luckett et al. 2016). Respondents were eligible if they were  $\geq 18$  years, had advanced cancer and poor appetite/taste problems/weight loss and might consider participating in a medicinal cannabis trial. There were 204 survey respondents, of whom 26 (13%) reported prior medicinal cannabis use. Tablets/capsules were the preferred delivery mode ( $n = 144$ , 71%), followed by mouth spray ( $n = 84$ , 42%) and vaporiser ( $n = 83$ , 41%). Thus, a high number of patients preferred the use of a vaporizer for the intake of cannabis.

### 2. Comparison of cannabinoids in oral fluid after cannabis use by a vaporizer and other modes of administration

Scientists of Chemistry and Drug Metabolism Section, Clinical Pharmacology and Therapeutics Branch, National Institute on Drug Abuse Intramural Research Program, National Institutes of Health,

Geschäftsführer:  
Michael Carus, Dirk Schubert

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

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Kölner Bank  
Konto 528 684 009, BLZ 371 600 87

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in Baltimore, USA, compared cannabinoid concentrations in oral fluid after administration of cannabis in a cookie, by smoking and by vaporising (Swortwood et al. 2017). Significantly greater THC C<sub>max</sub> and significantly later THCV, CBD, and CBG t<sub>last</sub> were observed after smoked and vaporized cannabis compared to oral cannabis in frequent smokers only. No significant differences in THC, 11-OH-THC, THCV, CBD, or CBG t<sub>max</sub> between routes were observed for either group. For occasional smokers, more 11-OH-THC and THCCOOH-positive specimens were observed after oral dosing than after inhaled routes, increasing % positive cannabinoid results and widening metabolite detection windows after oral cannabis consumption.

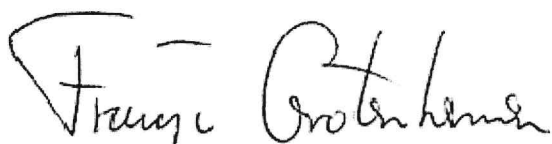
### 3. Comparison of mode of administration of cannabis in different regions of the world

Scientists from the Clinical Psychopharmacology Unit, University College London, UK, and other research institutions conducted a cross-sectional online survey, which was completed by 33,687 respondents (mean age = 27.9; % female = 25.9) who smoked cannabis at least once in the last 12 months (Hindocha et al. 2016). Tobacco-based routes of administration were used by 65.6% of respondents. These were most common in Europe (77.2-90.9%) and Australasia (20.7-51.6%) and uncommon in the Americas (4.4-16.0%). Vaporizer use was most common in Canada (13.2%) and the United States (11.2%).

#### Summary:

The Volcano Medic continues to be used for research with cannabinoids, and cannabis users increasingly use this mode of administration. Preferred ways of intake vary considerably between different regions of the world. Patients, who are unfamiliar with cannabis use, favor vaporization as their preferred mode of use to a large degree.

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

- Hindocha C, Freeman TP, Ferris JA, Lynskey MT, Winstock AR. No Smoke without Tobacco: A Global Overview of Cannabis and Tobacco Routes of Administration and Their Association with Intention to Quit. *Front Psychiatry*. 2016 Jul 5;7:104.
- Luckett T, Phillips J, Lintzeris N, Allsop D, Lee J, Solowij N, Martin J, Lam L, Aggarwal R, McCaffrey N, Currow D, Chye R, Lovell M, McGregor I, Agar M. Clinical trials of medicinal cannabis for appetite-related symptoms from advanced cancer: a survey of preferences, attitudes and beliefs among patients willing to consider participation. *Intern Med J*. 2016 Nov;46(11):1269-1275.
- Swortwood MJ, Newmeyer MN, Andersson M, Abulseoud OA, Scheidweiler KB, Huestis MA. Cannabinoid disposition in oral fluid after controlled smoked, vaporized, and oral cannabis administration. *Drug Test Anal*. 2017 Jun;9(6):905-915.

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

Intern Med J. 2016 Nov;46(11):1269-1275. doi: 10.1111/imj.13224.

Clinical trials of medicinal cannabis for appetite-related symptoms from advanced cancer: a survey of preferences, attitudes and beliefs among patients willing to consider participation.

Luckett T(1), Phillips J(2), Lintzeris N(3)(4), Allsop D(5), Lee J(6), Solowij N(7), Martin J(8), Lam L(2), Aggarwal R(9), McCaffrey N(10), Currow D(10), Chye R(11), Lovell M(12)(13), McGregor I(14), Agar M(2)(15)(16).

Author information: (1)Centre for Cardiovascular and Chronic Care, Faculty of Health, University of Technology Sydney, Sydney, New South Wales, Australia. tim.luckett@uts.edu.au. (2)Centre for Cardiovascular and Chronic Care, Faculty of Health, University of Technology Sydney, Sydney, New South Wales, Australia. (3)Discipline of Addiction Medicine, Central Clinical School, Sydney Medical School, Sydney, New South Wales, Australia. (4)Drug and Alcohol Services, South East Sydney Local Health District, NSW Health, Sydney, New South Wales, Australia. (5)School of Psychology, The University of Sydney, Sydney, New South Wales, Australia. (6)Palliative Care, Concord Repatriation General Hospital, Sydney, New South Wales, Australia. (7)School of Psychology, University of Wollongong, Wollongong, New South Wales, Australia. (8)Department of Clinical Pharmacology, School of Medicine and Public Health, University of Newcastle, Newcastle, New South Wales, Australia. (9)Palliative Care, Liverpool Cancer Therapy Centre, Liverpool Hospital, Sydney, New South Wales, Australia. (10)Palliative and Supportive Services, Flinders University, Adelaide, South Australia, Australia. (11)Sacred Heart Supportive and Palliative Care, St Vincent's Hospital, Sydney, New South Wales, Australia. (12)Palliative Care, Greenwich Hospital, HammondCare, Sydney, New South Wales, Australia. (13)Northern Clinical School, Sydney Medical School, HammondCare, Sydney, New South Wales, Australia. (14)Department of Psychopharmacology, Faculty of Science, The University of Sydney, Sydney, New South Wales, Australia. (15)The Ingham Institute of Applied Medical Research, Sydney, New South Wales, Australia. (16)South Western Sydney Clinical School, University of New South Wales, Sydney, New South Wales, Australia.

**BACKGROUND:** Australian clinical trials are planned to evaluate medicinal cannabis in a range of clinical contexts. **AIMS:** To explore the preferences, attitudes and beliefs of patients eligible and willing to consider participation in a clinical trial of medicinal cannabis for poor appetite and appetite-related symptoms from advanced cancer. **METHODS:** A cross-sectional anonymous survey was administered from July to December 2015 online and in eight adult outpatient palliative care and/or cancer services. Respondents were eligible if they were  $\geq 18$  years, had advanced cancer and poor appetite/taste problems/weight loss and might consider participating in a medicinal cannabis trial. Survey items focused on medicinal rather than recreational cannabis use and did not specify botanical or pharmaceutical products. Items asked about previous medicinal cannabis use and preferences for delivery route and invited comments and concerns. **RESULTS:** There were 204 survey respondents, of whom 26 (13%) reported prior medicinal cannabis use. Tablets/capsules were the preferred delivery mode ( $n = 144$ , 71%), followed by mouth spray ( $n = 84$ , 42%) and vaporiser ( $n = 83$ , 41%). Explanations for preferences ( $n = 134$ ) most commonly cited convenience ( $n = 66$ ; 49%). A total of 82% ( $n = 168$ ) of respondents indicated that they had no trial-related concerns, but a small number volunteered concerns about adverse effects ( $n = 14$ ) or wanted more information/advice ( $n = 8$ ). Six respondents volunteered a belief that cannabis might cure cancer, while two wanted assurance of efficacy before participating in a trial. **CONCLUSION:** Justification of modes other than tablets/capsules and variable understanding about cannabis and trials will need addressing in trial-related information to optimise recruitment and ensure that consent is properly informed.

Drug Test Anal. 2017 Jun;9(6):905-915. doi: 10.1002/dta.2092. Epub 2016 Oct 13.

Cannabinoid disposition in oral fluid after controlled smoked, vaporized, and oral cannabis administration.

Swortwood MJ(1), Newmeyer MN(1)(2), Andersson M(1), Abulseoud OA(1), Scheidweiler KB(1), Huestis MA(1)(3).

Author information: (1)Chemistry and Drug Metabolism Section, Clinical Pharmacology and Therapeutics Branch, National Institute on Drug Abuse Intramural Research Program, National Institutes of Health, Baltimore, MD, USA. (2)Program in Toxicology, University of Maryland Baltimore, Baltimore, MD, USA. (3)University of Maryland School of Medicine, Baltimore, MD, USA.

Oral fluid (OF) is an important matrix for monitoring drugs. Smoking cannabis is common, but vaporization and edible consumption also are popular. OF pharmacokinetics are available for controlled smoked cannabis, but few data exist for vaporized and oral routes. Frequent and occasional cannabis smokers were recruited as participants for four dosing sessions including one active (6.9%  $\Delta^9$ -tetrahydrocannabinol, THC) or placebo cannabis-containing brownie, followed by one active or placebo cigarette, or one active or placebo vaporized cannabis dose. Only one active dose was administered per session. OF was collected before and up to 54 (occasional) or 72 (frequent) h after dosing from cannabis smokers. THC, 11-hydroxy-THC (11-OH-THC), 11-nor-9-carboxy-THC (THCCOOH), tetrahydrocannabivarin (THCV), cannabidiol (CBD), and cannabigerol (CBG) were quantified by liquid chromatography-tandem mass spectrometry. OF cannabinoid C<sub>max</sub> occurred during or immediately after cannabis consumption due to oral mucosa contamination. Significantly greater THC C<sub>max</sub> and significantly later THCV, CBD, and CBG t<sub>last</sub> were observed after smoked and vaporized cannabis compared to oral cannabis in frequent smokers only. No significant differences in THC, 11-OH-THC, THCV, CBD, or CBG t<sub>max</sub> between routes were observed for either group. For occasional smokers, more 11-OH-THC and THCCOOH-positive specimens were observed after oral dosing than after inhaled routes, increasing % positive cannabinoid results and widening metabolite detection windows after oral cannabis consumption. Utilizing 0.3  $\mu\text{g/L}$  THCV and CBG cut-offs resulted in detection windows indicative of recent cannabis intake. OF pharmacokinetics after high potency CBD cannabis are not yet available precluding its use currently as a marker of recent use. Published 2016. This article is a U.S. Government work and is in the public domain in the USA.

Front Psychiatry. 2016 Jul 5;7:104. doi: 10.3389/fpsyt.2016.00104. eCollection 2016.

No Smoke without Tobacco: A Global Overview of Cannabis and Tobacco Routes of Administration and Their Association with Intention to Quit.

Hindocha C(1), Freeman TP(1), Ferris JA(2), Lynskey MT(3), Winstock AR(4).

Author information: (1)Clinical Psychopharmacology Unit, University College London, London, UK. (2)Institute for Social Science Research, University of Queensland, QLD, Australia. (3)Department of Addiction, Institute of Psychiatry, Psychology and Neuroscience, King's College London, London, UK. (4)Department of Addiction, Institute of Psychiatry, Psychology and Neuroscience, King's College London, London, UK; South London and the Maudsley NHS Trust, London, UK; Global Drugs Survey Ltd., London, UK.

Cannabis and tobacco are common drugs of abuse worldwide and are often used in combination through various routes of administration (ROAs). Here, we aimed to provide an overview of how

cannabis and tobacco routes varied across countries and assess the impact of tobacco-based ROAs on motivation to use less cannabis, and less tobacco, in different models. A cross-sectional online survey (Global Drugs Survey 2014) was completed by 33,687 respondents (mean age = 27.9; % female = 25.9) who smoked cannabis at least once in the last 12 months. Most common ROA, frequency of cannabis/tobacco use, and questions about motivation to use less cannabis/tobacco were recorded. Tobacco-based ROA were used by 65.6% of respondents. These were most common in Europe (77.2-90.9%) and Australasia (20.7-51.6%) and uncommon in the Americas (4.4-16.0%). Vaporizer use was most common in Canada (13.2%) and the United States (11.2%). Using a non-tobacco ROA was associated with a 10.7% increase in odds for "desire to use less" tobacco (OR: 1.107, 95% CI: 1.003, 1.221), 80.6% increase in odds for "like help to use less tobacco" (OR: 1.806, 95% CI: 1.556, 2.095), and a 103.9% increase in the odds for "planning to seek help to use less tobacco" (OR: 2.039, 95% CI: 1.638, 2.539), in comparison to using a tobacco-based ROA. Associations between ROA and intentions to use less cannabis were inconsistent. Results support considerable global variation in cannabis and tobacco ROA. Tobacco routes are common, especially "joints with tobacco," especially in Europe, but not in the Americas. Non-tobacco-based routes are associated with increased motivation to change tobacco use. Interventions addressing tobacco and cannabis need to accommodate this finding and encourage non-tobacco routes.