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24. Juli 2018  
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July 18, 2018

## 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 22, 2017 two 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 investigated the question whether the perceived lower risks following vaporization may increase the intake of cannabis. The second compared the physiological and subjective effects of cannabis after different modes of intake.

### 1. Investigation into the use of vape-pens, small vaporizers

Scientists of several universities in the US, including the (1) University of Florida, Department of Health Education and Behavior, College of Health and Human Performance, Gainesville, (2) Yale School of Medicine, Department of Psychiatry, New Haven, (3) Arizona State University, Department of Psychology, Tempe, investigated the proliferation of electronic devices for the intake of cannabis for recreational use (Frohe et al. 2017).

In a secondary data analysis they utilized surveys at multiple colleges in the U.S. (N = 270). Alcohol use, social anxiety, cannabis expectancies, injunctive and descriptive norms and facets of impulsivity were examined as correlates of vape-pen use and knowledge using bivariate correlations and logistic regressions. Vape-pens, also referred to as vaporizer pens, vapor pens or vape pen mods are tiny pen-shaped vaporizers. They found that alcohol use was correlated with cannabis vape-pen use and knowledge. Frequency of cannabis use, peer injunctive norms, and positive expectancies were associated with increased likelihood of vape-pen use. Lack of premeditation, a facet of impulsivity, was associated with cannabis vape-pen knowledge. Researchers concluded that "given the unknown nature and consequences of cannabis vape-pens, the present findings offer valuable information on correlates of this behavior. Further, correlates of knowledge of vape-pens may point to areas for education and clinical intervention to prevent heavy cannabis vape-pen use." It has to be noted that

it is unclear if these results are relevant for larger vaporizers such as those from Storz & Bickel and to what extent.

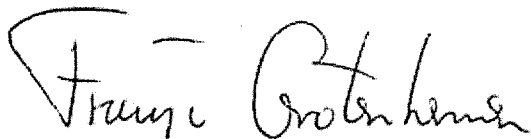
## **2. Comparison of physiological and subjective effects following different routes of administration including vaporization**

Scientists of the National Institute on Drug Abuse National Institutes of Health in Baltimore, USA, compared cannabis' subjective and physiological effects following multiple administration routes, including vaporization (Newmeyer et al. 2017). Subjective and physiological effects, and expired carbon monoxide (CO) were evaluated in frequent and occasional cannabis users following placebo, smoked, vaporized, and oral cannabis (6.9% THC, ~54mg). Participants' subjective ratings were significantly elevated compared to placebo after smoking and vaporization, while only occasional smokers' ratings were significantly elevated compared to placebo after oral dosing. Frequent smokers' maximum ratings were significantly different between inhaled and oral routes, while no differences in occasional smokers' maximum ratings between active routes were observed. Additionally, heart rate increases above baseline 0.5h after smoking (mean 12.2bpm) and vaporization (10.7bpm), and at 1.5h (13.0bpm) and 3h (10.2bpm) after oral dosing were significantly greater than changes after placebo, with no differences between frequent and occasional smokers. Finally, smoking produced significantly increased expired CO concentrations 0.25-6h post-dose compared to vaporization. Researchers concluded that "vaporized cannabis is an attractive alternative for medicinal administrations over smoking or oral routes; effects occur quickly and doses can be titrated with minimal CO exposure. These results have strong implications for safety and abuse liability assessments."

### **Summary:**

The study by Newmeyer et al. (2017) confirms previous research that the administration of cannabis by vaporizers has advantages over smoking and oral intake and call it "an attractive alternative for medicinal administrations over smoking or oral routes." The study by Frohe et al. (2017) found, that the use of small pen-like vaporizers, so-called vape-pens, is associated with an increased frequency of use.

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**

- Frohe T, Leeman RF, Patock-Peckham J, Ecker A, Kraus S, Foster DW. Correlates of cannabis vape-pen use and knowledge among U.S. college students. *Addict Behav Rep.* 2017 Nov 21;7:32-39.
- Newmeyer MN, Swortwood MJ, Abulseoud OA, Huestis MA. Subjective and physiological effects, and expired carbon monoxide concentrations in frequent and occasional cannabis smokers following smoked, vaporized, and oral cannabis administration. *Drug Alcohol Depend.* 2017 Jun 1;175:67-76.

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

Addict Behav Rep. 2017 Nov 21;7:32-39. doi: 10.1016/j.abrep.2017.11.004. eCollection 2018 Jun.

Correlates of cannabis vape-pen use and knowledge among U.S. college students.

Frohe T(1), Leeman RF(1)(2), Patock-Peckham J(3), Ecker A(4)(5), Kraus S(6), Foster DW(2).

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Introduction: The proliferation of electronic devices, such as vape-pens, has provided alternative means for cannabis use. Research has found cannabis-vaping (i.e., vape-pen use) is associated with lower perceived risks and higher cannabis use. Knowledge of these products may increase likelihood of subsequent use. As policies for cannabis shift, beliefs that peers and family approve of this substance use (injunctive norms) increase and there has been an increase in vape-pen use among young adults (18-35 year olds); however, correlates thereof remain unknown. Young adults often engage in cross-substance use with cannabis and alcohol, making alcohol a potential correlate of cannabis vape-pen use and knowledge. Therefore, we examined alcohol use and other potential correlates of vape-pen use and knowledge among a sample of university students. Methods: This secondary data analysis utilized surveys at multiple colleges in the U.S. (N = 270). Alcohol use, social anxiety, cannabis expectancies, injunctive and descriptive norms and facets of impulsivity were examined as correlates of vape-pen use and knowledge using bivariate correlations and logistic regressions. Results: Alcohol use was correlated with cannabis vape-pen use and knowledge. Frequency of cannabis use, peer injunctive norms, and positive expectancies were associated with increased likelihood of vape-pen use. Lack of premeditation, a facet of impulsivity, was associated with cannabis vape-pen knowledge. Conclusions: Given the unknown nature and consequences of cannabis vape-pens, the present findings offer valuable information on correlates of this behavior. Further, correlates of knowledge of vape-pens may point to areas for education and clinical intervention to prevent heavy cannabis vape-pen use.

DOI: 10.1016/j.abrep.2017.11.004 PMID: 29450254

Drug Alcohol Depend. 2017 Jun 1;175:67-76. doi: 10.1016/j.drugalcdep.2017.02.003. Epub 2017 Mar 29.

Subjective and physiological effects, and expired carbon monoxide concentrations in frequent and occasional cannabis smokers following smoked, vaporized, and oral cannabis administration.

Newmeyer MN(1), Swortwood MJ(2), Abulseoud OA(3), Huestis MA(4).

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**BACKGROUND:** Although smoking is the most common cannabis administration route, vaporization and consumption of cannabis edibles are common. Few studies directly compare cannabis' subjective and physiological effects following multiple administration routes. **METHODS:** Subjective and physiological effects, and expired carbon monoxide (CO) were evaluated in frequent and occasional cannabis users following placebo (0.001%  $\Delta^9$ -tetrahydrocannabinol [THC]), smoked, vaporized, and oral cannabis (6.9% THC, ~54mg). **RESULTS:** Participants' subjective ratings were significantly elevated compared to placebo after smoking and vaporization, while only occasional smokers' ratings were significantly elevated compared to placebo after oral dosing. Frequent smokers' maximum ratings were significantly different between inhaled and oral routes, while no differences in occasional smokers' maximum ratings between active routes were observed. Additionally, heart rate increases above baseline 0.5h after smoking (mean 12.2bpm) and vaporization (10.7bpm), and at 1.5h (13.0bpm) and 3h (10.2bpm) after oral dosing were significantly greater than changes after placebo, with no differences between frequent and occasional smokers. Finally, smoking produced significantly increased expired CO concentrations 0.25-6h post-dose compared to vaporization. **CONCLUSIONS:** All participants had significant elevations in subjective effects after smoking and vaporization, but only occasional smokers after oral cannabis, indicating partial tolerance to subjective effects with frequent exposure. There were no differences in occasional smokers' maximum subjective ratings across the three active administration routes. Vaporized cannabis is an attractive alternative for medicinal administrations over smoking or oral routes; effects occur quickly and doses can be titrated with minimal CO exposure. These results have strong implications for safety and abuse liability assessments.

Published by Elsevier B.V.

DOI: 10.1016/j.drugalcdep.2017.02.003 PMID: 28407543 [Indexed for MEDLINE]