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COMMENTARY

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Essential oils: what is the clinical tolerance in asthmatic patients?

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ABSTRACT

Essential oils in air-spray form are being more and more used for several purposes, even by allergic and asthmatic patients. Available data on the potentially dangerous effects of volatile organic compounds and terpenes contained in essential oils are scarce, and sometimes difficult to compare. Through the present work, we evaluated the clinical tolerance of asthmatic patients exposed to compounds emitted by an essential oils spray, and compared previous and new data available in the scientific literature, focusing on the aspects that may influence clinical results.

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Essential oils; asthma; volatile organic compounds; terpenes; limonene; review

Introduction

Highly valued for ecological reasons, essential oils (EOs) in air-spray form are being more and more used to purify indoor air, because of their antiviral, antibacterial, acaricidal and fungicidal properties, which have been demonstrated *in vitro*. An increasing number of allergic and asthmatic patients use them to eliminate or reduce the concentrations of allergens (mites, molds), virus, or bacteria that might be present in indoors areas (1). Health-care professionals are therefore more and more widely confronted with increasing demands from their patients for « natural medicine » and for the use of EOs. There is little data in the literature concerning the potentially dangerous effects of volatile organic compounds (VOCs) and terpenes contained in EOs, focusing on human airways especially in sensitive subjects (allergic and asthmatic patients). The aim of the present report was to ascertain the clinical tolerance of asthmatic patients when exposed to terpene VOCs, and specifically to limonene, emitted by an EO spray, and to compare previous and new data available in the scientific literature.

Previous studies with puressentiel® spray containing 41 EOs (SPA41)

The various EO sprays available on the market contain VOCs, and, specifically, terpenes, which are emitted at variable concentrations in indoor air during the utilization of these sprays. A recent meta-analysis of the effects of VOCs measured in indoor air concluded that VOC exposure was unlikely to be a major risk factor for the development of asthma/allergy in the general population (2).

Assessment by photo-ionization and spectrophotometry

Delmas et al. (3) provided results from two methodological different assessment (Katrem ppbRAE3000 photo-ionization, and spectrophotometry on TENAX TA cartridges), under different exposure conditions, to measure airborne concentrations of terpene VOCs (especially limonene), released during pulverization of SPA41. Analysis of VOC concentrations was performed by TERA Environnement (Crolles, France). VOC measurements were obtained in a 9 m^3 exposure chamber with an average air renewal of 30.5 m^3/h and in a 42 m^3 room without specification of the precise level of air renewal.

Measurements were performed after one, four or eight pulverizations, per different experimental conditions. In a 9 m^3 exposure chamber, the maximal limonene concentration, 30 s after one pulverization of SPA41 in the center of the room, was 73.6 mg/m^3; after 20 min, it was 2 mg/m^3. After 4 pulverizations from the four corners of the room, limonene concentrations

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measured by photo-ionization were 57.3 mg/m^3 at peak and 3 mg/m^3 after 30 min. In a 42 m^3 room, one pulverization liberated an average concentration of 2 mg/m^3; over a 30-min period, and after 8 pulverizations, the average limonene concentration was 15 mg/m^3. These concentrations were measured by photo-ionization. Under the same conditions, the measurements performed by spectrophotometry showed lower concentrations: 4.9 mg/m^3 after the first 30 min, in the 42 m^3 room. The sum of the terpene VOCs was 39 mg/m^3 for the first 30 min and 20.9 mg/m^3, when assessed after the following 30 min, in the same 42 m^3 room.

The high concentrations of limonene and VOCs reported in this study led the authors to conclude that there was a possibility of deleterious effects in sensitive populations (allergic and/or asthmatic patients) when this EO spray was used indoors.

Assessment without air removal

In a study performed by TERA Environnement (4), measurements were performed in a 7.5 m^3 exposure chamber without renewal of the air, using GAS cartridges installed outside of the room, after one pulverization with SPA41. The measurements were made before (T0), 30 min (T30), and 60 min (T60) after pulverization.

Measurements were performed in March 2018. Limonene concentrations were undetectable at T0, ranged from 0.690 to 3.272 mg/m^3 at T 30, from 0.525 to 2.498 mg/m^3 at T60. The average values of total VOCs were 1.252 mg/m^3, 13.04 mg/m^3, and 11.026 mg/m^3, at T0, T30, and T60, respectively.

Assessment by the french institut national de la consommation

This study was performed in a 1 m^3 essay chamber with injection of SPA41 in liquid form (ISO 16000–9 emission essay chamber method) (5). The results are extrapolated for a 30 m^3 reference room with air renewal at 0.5 m^3/h and the equivalent of 4 pulverizations of SPA41. Measured under these conditions, limonene concentration was 2.9 mg/m^3.

Comments on previous studies

The 3 studies differ on several points, and it is difficult to compare the measurement techniques and the conditions of use of SPA41 (number of pulverizations and volume of the area). Nevertheless, the concentrations of limonene or total VOC are roughly the same in the 3 studies when compared at 30 min after pulverization (between 2 and 3 mg/m^3 for limonene and between 12 and 15 mg/m^3 for total VOCs). These values would correspond to those obtained for 4 pulverizations in a 30 m^3 room.

In the study by Delmas et al. (3), for a 42 m^3 room, and after 8 pulverizations, limonene concentrations at 30 min were higher (15 mg/m^3 by photo-ionization and 4.87 mg/m^3 by TENAX spectrophotometry cartridges). Similarly, total VOC concentrations in the same study were 39 mg/m^3, 30 min after pulverization.

It should be noted, however, that the study recorded these concentrations after 8 pulverizations (3), while, in case of a prolonged use of SPA41, instructions suggest the use of 2 daily pulverizations only. The 8 pulverizations are meant to be a one-time-only attack dosage, after which it is advised to aerate the room and exit it for at least 30 min.

Also, it is important to underline that these 3 studies measured limonene and VOC concentrations emitted by SPA41, but not their clinical consequences in normal or potentially sensitive subjects, such as allergic and/or asthmatic patients.

Discussion

No threshold exists for the effects of limonene on health in nonprofessional use in indoor air; in case of professional exposure, threshold levels are 110 mg/m^3 (6). Nevertheless, there are data in the literature that constitute a body of evidence of undesirable effects, appearing from a concentration of 4.5 mg/m^3 for limonene (7,8).

A few studies focusing on human exposure to limonene showed no effects on respiratory functions, after 2 h of exposure at 10 mg/m^3 and 225 mg/m^3; and only weak effects, after 2 h of exposure at a concentration of 450 mg/m^3 in healthy subjects (9,10). Also, these studies showed no ocular irritation after limonene exposure up to a concentration of 450 mg/m^3.

Two controlled studies (11,12), run in healthy subjects, who were exposed for 2 h to mixtures of terpenes dominated by α-pinene (2–6-mg/m^3), with total VOCs concentration of 9–13 mg/m^3, showed no change in FeNO, a marker of bronchial inflammation, nor in respiratory function, in exposed participants.

Little data concerning asthmatic patients may be found in the literature. One study (13), conducted on 11 mild-to-moderate asthmatic patients exposed to a mixture of VOCs, including α-pinene, at concentrations of 2.5 et 25 mg/m^3 for 90 min in a 9 m^3 room, showed a minimal decrease in FEV_1, when patients were exposed at the highest concentrations.

This weak decrease in FEV_1 wasn't clinically significant and was identical to that observed after exposure to saline solution in the same subjects.

A recent study (14) evaluated the tolerance to SPA41 in 25 patients with mild-to-moderate persistent asthma, under the same conditions that are recommended for the product home use (2 pulverizations per day in a 9 to 12 m^3 room). Respiratory functions and bronchial reactivity were assessed through objective measurements, including provocation methacholine test and bronchial FeNO measurement, and asthma control was evaluated as well. The study found no significant effects on the different parameters after a prolonged exposure to two daily pulverizations of SPA41, over 30 days.

These findings might be explained by the fact that reactions to limonene are usually due to derivatives formed by the auto-oxidation of the pure substance (dipentene hydroperoxide and carvone) (15). It is therefore important, when drawing any clinical conclusion from experimental studies or clinical trials, to measure the oxidation status of limonene.

Declaration of interest

The authors have no financial nor personal relationships with other people or organizations that could inappropriately influence (bias) their work. The funding source (Puressentiel) had no role in the design, conduct, or analysis of the study or the decision to submit the manuscript for publication.

Authors' contribution

Conception and design: DC, CN, PD; Drafting or revising the manuscript for important intellectual content: DC, CN, PD; Final approval of the version to be published: DC, CN, PD; Agreement to be accountable for all aspects of the work: DC, CN, PD.

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