

## DOES INHALATION SATUREJA MONTANA OIL PRODUCED BRONHODILATOR RESPONSE IN ASTHMA PATIENTS

Emilija Nikolić

Faculty of Medicine, Podgorica, University of Montenegro, Montenegro, [ema.med@t-com.me](mailto:ema.med@t-com.me)

Aleksandar Nikolić

NCG Engineering Podgorica, Montenegro, [tipotek@t-com.me](mailto:tipotek@t-com.me)

**Abstract:** Previous research have shown that the tested essential oils of Satureja species had a different chemical composition of pharmacologically active compounds. Apply of Satureja montana oil for bronchospasm in humans is rare. The purpose of this study was to investigate the chemical composition of Satureja montana L oil collected in Montenegro and the possible bronchodilator response in patients with asthma after inhalation of this oil. The chemical analysis of the essential oil, performed by Gas chromatography method. S. montana oil was plentiful in monoterpenes with thymol (54.09%), p-cymene (11.05%),  $\alpha$ -pinene (6.1%), carvacol (4.87%) and borneol (2.76%) were present in a high percentage. In total 90 asthma patients divided in three groups. Control groups 1,2 had conventional, physical therapy. Experimental group used to inhale 5% Satureja m.oil at 10 days protocol and conventional therapy. Lung function test was performed in all group. Experimental group had a significant improvement on PEF ( 7.10%), FEV1 ( 9%), FVC ( 7.6%).Conversely, both control groups had relative mean improvement: PEF( 2.7%; 2.8%), FEV1 (3.6%; 4.5%), FVC (4.7%;5.3%).The results indicated that inhalation of Satureja Montana oil provided bronchodilator response in asthma patients, and produced better lung function test results than conventional therapy.

**Keywords:** Satureja montana oil, asthma, bronchodilator response

### 1. INTRODUCTION

Essential oils represent a complex different compounds, mainly terpenoids and phenolics (Karapinar & Aktung,1987), (e.g. thymol, carvacrol, eugenol) (Fliou at all,&2020), which are known for their strong antimicrobial activity and antioxidant activity in addition to activity of alcohols (e.g. geraniol, linalool and menthol),( Aleksić, & Knežević,2014), aldehydes (e.g. neral, geranials and cuminal), ketones (e.g. carvone, menthone, piperitone) and ethers (e.g. oestragole and anethole).(Albayrak,& Silaharhoğlu, 2020) The genus Satureja L. of the family Lamiaceae appertain to subfamily Nepetoideae, tribe Menthae (Batool , &Khan,2016).There are different approaches relating the total number of species within the Satureja,(Milenkovic at all, 2009), ranging from about 30, mainly restricted to the eastern part of the Mediterranean (Tošić at all,2019), to more than 200 spread in the Mediterranean, Asia and boreal America. Satureja montana L. subsp. montana (Lamiaceae), winter savory, is a well-known aromatic and medicinal herb.(Bakhtiarpoor , Setorki , & Kaffashian ,2018)This plant grows wild on rocky, barren and sunny places, along the Adriatic coast of Croatia, Albania and Montenegro.(Milenković , Stošović , & Slavkovska ,2018). Generally, *Satureja* spp. have been used since ancient times as flavorings for food and for the treatment of various diseases; their essential oils have been documented for antimicrobial, antiviral, antidiarrheal, fungicidal, anti- depressive, anti- hypertensive , spasmolytic and antioxidant activities. (Hedayat, & Lapraz, 2019).

However, specific applications Satureja m. oil for bronchospasm treatment and for lung function test examination in humans are particularly uncommon and to our knowledge have never been reported before.The aim of the study was to establish the chemical composition of the Satureja montana oil on Montenegrin area, and possible bronchodilator response in the asthma patients. We showed scientific confirmation by measuring the parameters of pulmonary function before and after inhalation Satureja montana oil. The results obtained were also compared with spirometry parameters in the asthma patients treated with conventional medicine.

### 2. MATERIALS AND METHODS

2.1. Material and methods Satureja montana L.Tranding essential oil of the Satureja montana L. was obtained from local supplier in Montenegro „Herbal Montenegro DOO“, known and acknowledged for high quality products. Chemical composition of the oil was investigated by GC and GC-MS

2.2. Participants and Setting

In total, 90 consecutive patients with mild, moderate or severe asthma, which was diagnosed and classified according to the Global Initiative for Asthma (GINA) standard (2018) at the Mediterranean Health Center for Physical Therapy and Rehabilitation, Igalo-Montenegro between June 1, 2019 and September 31, 2019 were enrolled. Patients with coexisting respiratory, cardiac, or other medical conditions and those with a smoking history

of <1 year before enrollment were excluded. The sample selection was purposive, and the participants sited in regular follow-up visits lasting 16 weeks, for routine treatment of their asthma. The group of 30 patients had medication, physical therapy in Health Centre Herceg Novi and constituted the control group 1. A group of 30 patients who treated with medication and physical therapy (abdominal breathing exercises, autogenic training, kinesitherapy) in Mediterranean Centre, constituted the control group 2. Finally, the group of 30 patients had medication, physical therapy, and inhalation with Satureja Montana oil and formed experimental group. All groups were nearly homogenous, with similar anthropometric characteristics and a body mass index of <35 kg/m<sup>2</sup>.

2.3. Experimental Measures: Asthma patients were invited to complete review medical questionnaire, and pulmonary function test results, at 10-daily intervals. The experimental group patients used to inhale 5% Satureja montana essential oil mixed in distilled water, a dose of 0.05-0.1mL (1-2 drops) after dilution with 3-4 mL of saline, ten minute, one time per day. Lung function test was performed before and after oil inhalation.

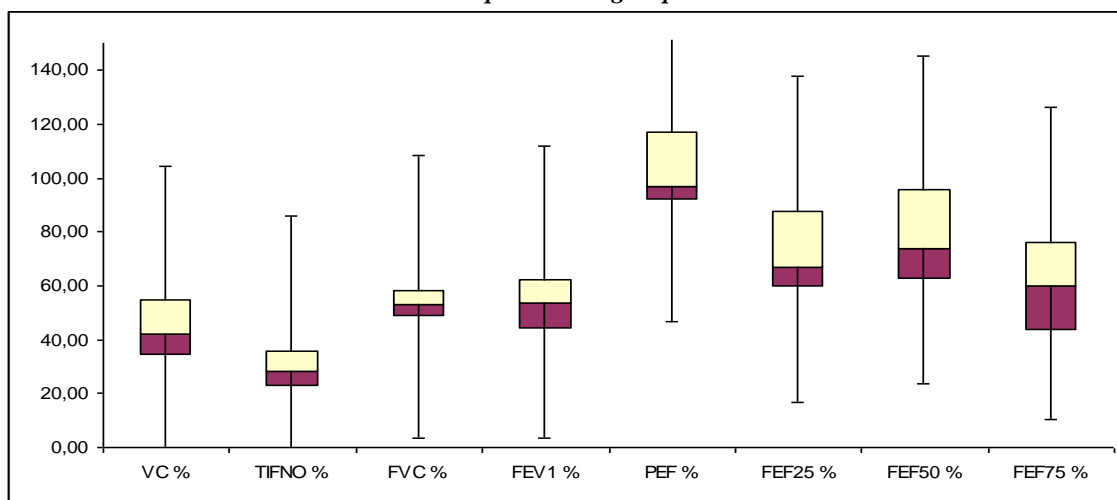
2.4. Ethical Approval: The study was conducted in accordance with the ethical standards of the Committee of Human Experimentation published by the Montenegreins Association of Physiotherapy (No. 29/2/2017), and was performed in accordance with the Declaration of Helsinki. All patients protected written informed consent.

### 3. RESULTS

3.1. Chemical composition of *Satureja montana*: The GC/MS analyses detected 26 compounds: the monoterpenes being the major fraction. The oxygen-containing phenolic monoterpene carvacrol (4.87%), thymol (54.76%), borneol (2.76%) were found to be the main constituents. The group of monoterpene hydrocarbons constituted (29.77%) of the oil. Within this group aromatic monoterpene *p*-cymene 11.05%, limonene 0.64%,  $\alpha$ -pinene 1.21% were detected to be in significant amounts. In the group of sesquiterpenes hydrocarbons (9.66%): trans-(E)-caryophyllene (5.19%) and  $\beta$ -Bisabolene (4.47%).

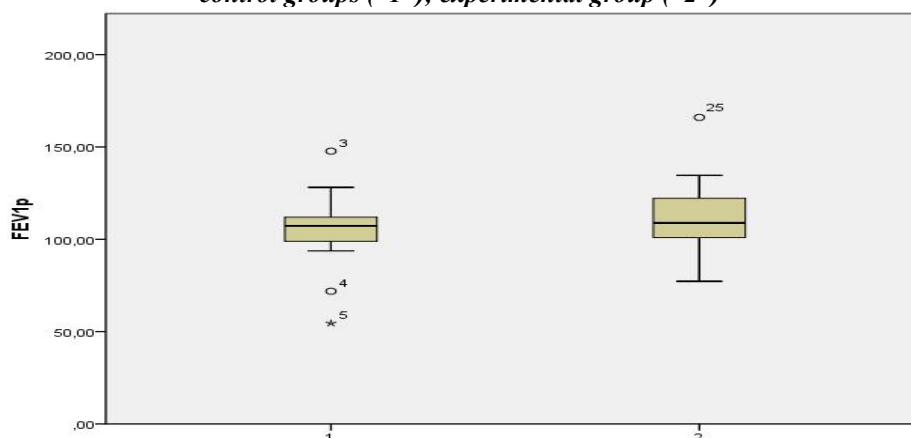
3.2. Results lung function test: In total, 16 men and 14 women in each group: no significant differences between the three groups with regard to sex and age ( $t = .36754$ ,  $df = 118$ ,  $P = .7139$ ); the mean ages in all groups were 47.1 and 46.4 years, respectively. Aromatherapy improved all spirometry parameters in the experimental group.

**Figure 1. Improvement in the: Vital capacity (VC), Tiffno index, forced expiratory volume in the first second (FEV1), forced vital capacity (FVC), peak expiratory flow (PEF), forced expiratory flow 25–75% (FEF 25–75) experimental group**



The improvement in the control group (represented by “1”) and experimental group (represented by “2”) is shown in the boxplots in Figure 2.

**Figure 2: Improvement in the forced expiratory volume in the first second (FEV1) after aromatherapy for control groups (“1”); experimental group (“2”)**



#### 4. DISCUSSION

The inhalation therapy of essential oils has been used to cure acute and chronic bronchitis and acute sinusitis. Inhalation of essential oil vapors increased the secretion of respiratory tract fluid and reduced asthma. (Seifi, 2018) Chemical composition of the oil *S. montana* collected at National park Lovćen, Montenegro, (Bojovic, Soskic, & Tadic, 2018) demonstrated that the group of monoterpene hydrocarbons (46.6%) were the prevalent group of compounds. The most flush compound in the group was p-cymene representing 16.6%. Limonene (10.8%) and  $\alpha$ -pinene (6.1%) were present in a high percentage.

In our study the cluster of oxygenated monoterpenes (60.85%) were dominant group (thymol (54.09%), carvacol (4.00%), borneol (2.76%) of compounds.

The group of monoterpene hydrocarbons constituted (29.77%) of the oil. Within this group aromatic monoterpenes p-cymene 11.05%, limonene 0.64%,  $\alpha$ -pinene 1.21% were determined to be in significant amounts.

Bojovic, Soskic, & Tadic, 2018) showed that oxygenated sesquiterpenes (15.2%) and hydrocarbon sesquiterpenes (5.5%) represented in a lower percentage, which was confirmed by our study. Furthermore, the most flush compounds in the group of sesquiterpenes hydrocarbons were trans-(E)-caryophyllene (5.19%) and  $\beta$ -Bisabolene (4.47%).

Previous studies have presented terpenes (Johnson, 2017) and their biological properties after application: thymol, bisabolene (Koyama, & Heinbockel, 2020), antibacterial and antiviral activity, while p-cymene, carvacol have anti-apoptotic, analgesic, anti-inflammatory, anti-nociceptive and caryophyllene (Ngo, & Vo, 2019) improved re-epithelialization of cutaneous wound, stimulated cell proliferation and migration, anti-inflammatory effect. (Wang, & Heinbockel, 2018)

We used *Satureja m.* by inhaling. The mechanism of oil action means the integration of essential oils into the biological signal of receptor cells in the nose, during inhalation. (Maßberg, & Hatt, 2018) The signal is transmitted to the limbic and hypothalamic parts of the brain via the olfactory bulb, cause the brain to release neuro messengers such as serotonin, endorphins, etc. (Ngo, & Vo, 2019). Subsequently, there are non-olfactory receptors in the skin and the gastro-intestinal system that are activated by odorous chemical compounds [Dey, et al., 2015].

Previous studies confirmed that it is highly likely that the GABA (Gamma amino butyric acid) system and TRP (Transient receptor potential) channels have crucial roles in the mechanisms that mediate the effects of chemical compounds in essential oils. (Wang, & Heinbockel, 2018) In addition, some monoterpenes such as thymol, thymoquinone, and borneol, are known as positive modulators for GABAA receptors. (Wang, & Heinbockel, 2018) This suggests that some constituents of oils activate olfactory signaling with a different enclosure of neuromodulators. (Johnson, 2017)

Our study in the asthma patients, we achieved a satisfactory bronchodilator response by applying oil inhalation *Satureja m.* Also, unexpectedly, we did not have side effects in patients, such as an allergic reaction, odor intolerance when inhaling the solution, spasm of the upper respiratory tract. In addition, the results of all spirometry parameters after inhalation of oil *Satureja m.* compared with the lung function test in those treated with conventional methods, were significantly better.

We hope that our work will advance a wider exploration of inhalation this oil for obstructive syndrome patients. Future research should focus on symptoms, the number of asthma attacks patients who will be use inhalation of *Satureja m.* oil.

The limitations of our study are: 1) this study had a small number of patients; 2) the use of an ultrasonic nebulizer for Omron 23 inhalation often caused occlude of the mesh during oil evaporation.

## 5. CONCLUSION

We tested the chemical composition of the Satureja m. oil from „Herba Life“ Montenegro manufacturers and found that thymol (54.09%) was the major constituent of the oil. Inhalation of Satureja montana oils in the asthma patients has resulted in bronchodilator effect. Compared with conventional therapy, inhalation of 5% oil solution Satureja montana produced better lung function test results. We believe that inhalation this oil can be improved the clinical picture of asthma patients and consequently will enable its acceptability in conventional treatment.

## REFERENCE

- Albayrak, S., & Silaharhoğlu, N. (2020). Determination of biological activities of essential oil and extract obtained from *Achillea coarctata* Poir. *Advances in Traditional Medicine*, 20, 77–88.
- Aleksić, V., & Knežević, P. (2014). Antimicrobial and antioxidative activity of extracts and essential oils of *Myrtus communis* L. *Microbiol Res*, 169, 240.
- Batool, Z., N., & Khan, S.Z. (2016). What is done and what has to be done in Lamiaceae. *Phylogenetics PeerJ*, 12, 35.
- Bakhtiarpoor, M., Setorki, M., & Kaffashian, M. (2018). *Effects of Essential Oil of Satureja bachtiarica* Bunge in a Rat Model of Reserpine-Induced Depression. *Iran J Med Sci*, 43(4), 409–415.
- Bojovic, D., Soskic, M., & Tadic, V. (2018). Comparative study of chemical composition of the essential oils from *Satureja Cuneifolia* Ten. and *Satureja Montana* L., Lamiaceae collected at National park Lovcen, Montenegro. *Studia universitatis babes-bolzai chemia*, 63(4), 167–180.
- Dey, S., Chamero, P., Pru, J.K., Chien, M.S., Ibarra-Soria, X., Spencer, K.R., Logan, D.W., Matsunami, H., Peluso, J.J. & Stowers, L. (2015). Cyclic Regulation of Sensory Perception by a Female Hormone Alters Behavior. *Cell*, 161, 1334–1344.
- Fliou, J., Riffi, O., Ghouati, Y., & Ali, A. (2020). *Comparative study of the chemical composition of the essential oil of origanum compactum from the seven regions of morocco and their antimicrobial activity*. *Journal of Microbiology, Biotechnology and Food Sciences*, 2(3), 22–25.
- Hedayat, K.M., & Lapraz, J.K. (2019). Infectious diseases of the ear, nose, throat, and bronchus. *The Theory of Endobiogeny*. 129–143.
- Johnson, S. A. (2017). *Supercritical Essential Oils. A Companion Resource to Medicinal Essential Oils*. Orem, UH, USA: Scott A Johnson Professional Writing Services, LLC.
- Karapinar, M., & Aktung, S. E. (1987). Inhibition of foodborne pathogens by thymol, eugenol, menthol and anethole. *Int. J. Food Microb.* 4; 161–166.
- Koyama, S., & Heinbockel, T. (2020). The Effects of Essential Oils and Terpenes in Relation to Their Routes of Intake and Application. *International Journal of Molecular Sciences*, 21( 1558), 25–36.
- Milenković, M., Stošović, J. & Slavkowska, V. (2018). Synergy between essential oils of *Calamintha* species (Lamiaceae) and antibiotics. *Nat Prod Commun*, 13, 371–374.
- Maßberg, D., & Hatt, H. (2018). Human Olfactory Receptors: Novel Cellular Functions Outside of the Nose. *Physiol. Rev.*, 98, 1739–1763.
- Menkovic, N.R., Savikin, K.P., Zdunic, G.M., & Gojgic-Cvijovic, G. (2009). Chemical composition and antimicrobial activity of essential oil of *Physocaulis nodosus* (L.) W. D. J. Koch. *Journal of Essential Oil Research*, 21, 89–90.
- Ngo, D.H., & Vo, T. S. (2019). An Updated Review on Pharmaceutical Properties of Gamma-Aminobutyric Acid. *Molecules*, 24, 2678.
- Seifi, Z., Bikmoradi, A., Bazrafshan, M., & Jokar, M. (2018). The Effect of Inhalation Aromatherapy with Lavender Essential oil on Pain Severity of Patients After Coronary Artery Bypass Surgery: A Single-blind Randomised Clinical Trial. *Journal of Clinical and Diagnostic Research*, 12 (7).
- Tošić, S., Stojičić, D., Stojičić, D., Slavkowska, V., Mihailov-Krstev, T., Zlatković, B., Budimir, S., & Uzelac, B. (2019). Phytochemical composition and biological activities of native and in vitro-propagated *Micromeria croatica* (Pers.) Schott (Lamiaceae) Planta, 249, 1365–1377.
- Wang, Z.J., & Heinbockel, T. (2018). Essential oils and Their constituents Targeting the GABAergic System and Sodium Channels as treatment of neurological disease. *Molecules*, 23, 1061.