

**The effect of mucoadhesive gel containing
satureja hortensis extract of 1% on severity
of chemotherapy-induced mucositis pain in
children: A double-blind clinical trial study**

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Background and objective:

- Mucositis is one of the common complications of chemotherapy, and one of its symptoms is severe pain.
- The mucositis management is initiated by assessment of oral hygiene, as well as by changes of diet and management of pain.
- Many uses have been mentioned for *satureja hortensis* in traditional medicine.
- *The present study was carried out with the aim of determining the effect of satureja hortensis extract mucoadhesive gel of 1% on severity of mucositis-induced pain in children under chemotherapy.*

Satureja Hortensis

(summer savory)

- Satureja is a genus of aromatic plants of the family Lamiaceae, related to rosemary and thyme. It is native to North Africa, southern and southeastern Europe, the Middle East, and Central Asia.
- *In Azerbaijan, savory is often incorporated as a flavoring in black tea.*



- Summer savory with the scientific name of *Satureja hortensis* is an annual, gramineous semi-woody plant.
- It is one of higher flowering plants and dicotyledons often spread in Mediterranean areas.
- The ingredients of *Satureja hortensis* include materials such as Carvacrol, Thymol, Beta-Pinene, Paracemenu, Lemothen, Camphene, minerals, and vitamins.
- *Carvacrol has antimicrobial, analgesic, anti-inflammatory and antioxidant effects.*



■ Abbasloo E, Dehghan F, Khaksari M, Najafipour H, Vahidi R, Dabiri S, et al. The anti-inflammatory properties of *Satureja khuzistanica* Jamzad essential oil attenuate the effects of traumatic brain injuries in rats. *Scientific reports*. 2016;6: DOI: 10.1038/srep33769.

■ Sharifzadeh A, Khosravi AR, Ahmadian S. Chemical composition and antifungal activity of *Satureja hortensis* L. essential oil against planktonic and biofilm growth of *Candida albicans* isolates from buccal lesions of HIV+ individuals. *Microbial pathogenesis*. 2016;96:1-9.

■ Moradian H, Bazargani A, Rafiee A, Nazari Alam A. In vitro comparison of antimicrobial activity of aqueous decoction of *Coriandrum sativum*, and Dentol Drop with chlorhexidine on *Streptococcus mutans*. *Iranian journal of microbiology*. 2013;5(3):239.

■ Landa P, Kokoska L, Pribylova M, Vanek T, Marsik P. In vitro anti-inflammatory activity of carvacrol: Inhibitory effect on COX-2 catalyzed prostaglandin E₂ biosynthesis. *Archives of pharmacological research*. 2009;32(1):75-8.

- In traditional medicine, this herb has therapeutic uses such as antispasmodic, anti-diarrhea, stimulation of reproduction and treatment of digestive disorders.
- Anti-bacterial, anti-inflammatory, anti-fungal and antioxidant properties have been also mentioned for *Satureja hortensis*.
- Considering the prevalence of mucositis in children under chemotherapy,

■Shahab A, Haghighati F, Baeeri M, Jamalifar H, Abdollahi M. A clinical, microbiological and immunological comparison between subgingival irrigation with Dentol and chlorhexidine in advanced periodontitis. Arch Med Sci. 2011;7(1):15460.

■Zolfagharian F, Razavi BM, Hosseinzadeh H. Anticonvulsant effect of *Satureja hortensis* aerial parts extracts in mice. Avicenna Journal of Phytomedicine. 2016;6(3):305.

■Vosough-Ghanbari S, Rahimi R, Kharabaf S, Zeinali S, Mohammadirad A, Amini S, et al. Effects of *Satureja khuzestanica* on serum glucose, lipids and markers of oxidative stress in patients with type 2 diabetes mellitus: a double-blind randomized controlled trial. Evidence-Based Complementary and Alternative Medicine. 2010;7(4):465-70.

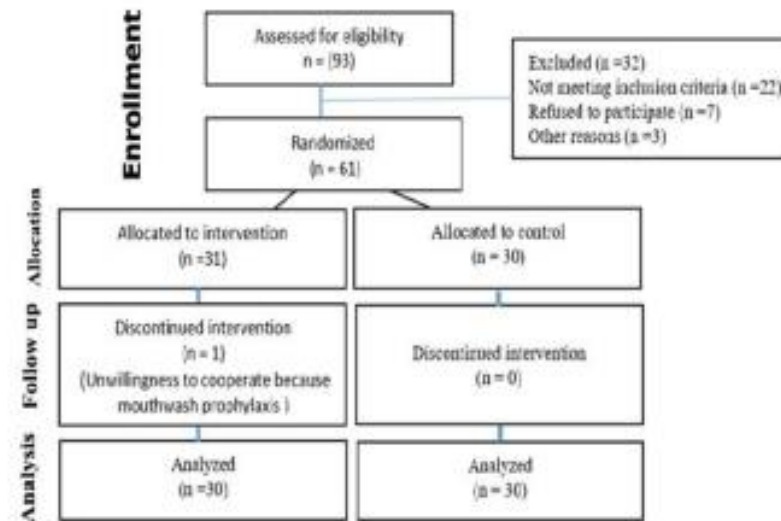
This study was carried out with the aim of determining the effect of *Satureja hortensis* extract 1% on severity of mucositis-induced pain and it's healing in children under chemotherapy.

Ethical issues, an approval with the number IR.TBZMED.REC.1395.282 was obtained from the ethics committee of Tabriz University of Medical Sciences.

The study was registered in Iranian Registry of Clinical Trial site with the number (IRCT- code) IRCT2016061813691N7.

Materials and method:

- This double–blind clinical trial study was carried out on 60 children who were affected by mucositis following chemotherapy at the Tabriz Children's Hospital from August to November, 2016.
- Tabriz Children's Hospital is pediatric education center is one the referee center in the North West of Iran.
- The samples were randomly assigned into two groups of intervention and control.
- *The intervention group applied satureja hortensis extract gel of 1% and the control group applied the placebo gel twice daily for 5 days after the onset of mucositis along with routine treatment.*



Consort diagram showed the flow of participants in the study

- Agricultural *Satureja hortensis* was used for preparing and extracting the cohesive gel.
- first completely cleaned and washed and then soaked in 70% hydro alcoholic solution and put on the shaker for 72 hours to extract the gel.
- Sodium carboxymethyl cellulose at a concentration of 4% was added to the solution and after stirring of the solution, it could stay at the same state until 24 hours to become fully hydrated.
- The whole obtained gel was passed from the threecylinder mill, filled in tubes of 40gr by a filling machine in aseptic conditions and packed by the machine.
- The placebo gel was also prepared from the materials used in preparation of *Satureja hortensis* extract gel, except for *Satureja hortensis* extract, and was packed in the tubes with the same shape and color.



Variables		Intervention group Number (Percent) n = 30	Control group Number (Percent) n = 30	P-value
Gender	Female	12 (40.0)	8 (26.8)	0.273
	Male	18 (60.0)	22 (73.3)	
Mother's education	Illiterate elementary	11 (36.7)	6 (20.7)	0.139
	Intermediate high school	13 (43.3)	20 (69.0)	
	University education	6 (20.0)	3 (10.3)	
Father's job	Employee	4 (13.8)	5 (16.7)	0.916
	Self-employed	13 (44.8)	11 (36.7)	
	Worker	7 (26.1)	9 (30.0)	
	Other	5 (16.7)	6 (16.7)	
Diagnosis	ALL	12 (40.0)	17 (56.7)	0.409
	Neuroblastoma	4 (13.3)	2 (6.7)	
	Connective tissue sarcoma	7 (23.3)	3 (10.0)	
	Other	2 (6.6)	3 (9.9)	
	Lymphoma	5 (16.7)	5 (16.7)	
Diet	Normal	15 (50.0)	19 (63.3)	0.297
	Low-salt	15 (50.0)	11 (36.7)	
Prophylaxis mouthwash	Yes	4 (13.3)	2 (6.7)	0.389
	No	26 (86.7)	28 (93.3)	
Variables		Mean (SD) n = 30	Mean (SD) n = 30	P-value
Times of hospitalization (month)		14.0 ± 10.8	15.2 ± 9.9	0.434
Duration of chemotherapy (day)		4.6 ± 2.2	4.0 ± 1.6	1.11
Absolute count of neutrophil *1000		1.5 ± 1.8	2.2 ± 1.6	1.49
Weight (kg)		25.5 ± 12.6	23.1 ± 10.5	0.814

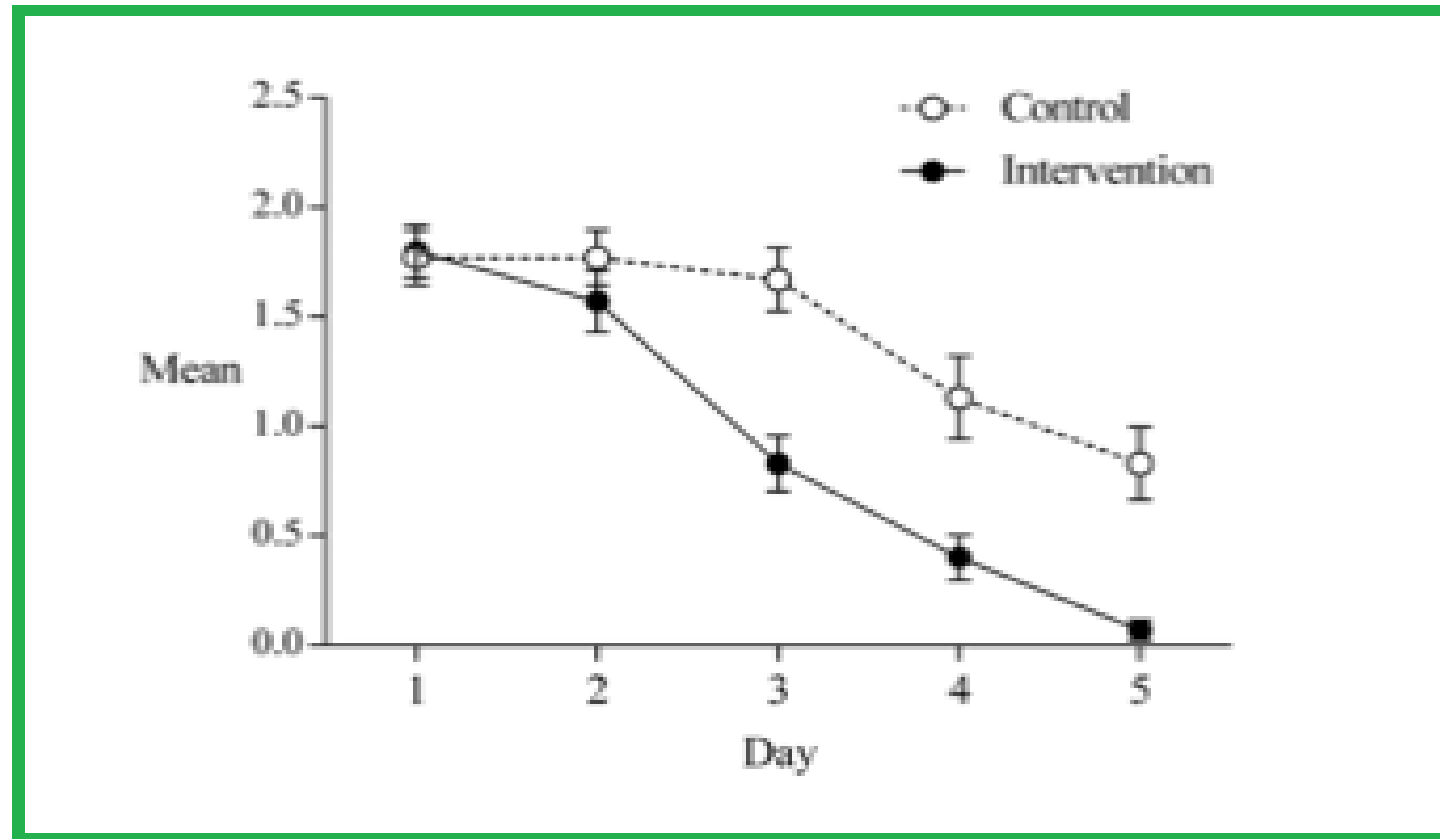
SD: Standard deviation; ALL: Acute lymphoblastic leukemia.

The demographic and clinical characteristics of the patients in the two groups of control and intervention

Time	Intervention group	Control group	P- value*
	Mean (SD), n = 30	Mean (SD), n =30	
First day	3.5 ± 2.1	3.1 ± 1.8	P<0.001
Second day	1.8 ± 1.4	2.5 ± 2.0	
Third day	0.2 ± 0.5	1.9 ± 1.6	
Fourth day	0.0 ± 0.0	1.1 ± 1.4	
Fifth day	0.0 ± 0.0	0.4 ± 1.0	

*: Repeated measures ANOVA; SD: Standard deviation.

The comparison of the severity of mucositis-induced pain in 5 days between the two groups of intervention and control



The diagram of the severity mucositis pain in 5 day between two groups (intervention and control)

Conclusion:

- Based on the findings obtained from the present study, it seems that *Satureja hortensis* extract mucoadhesive gel of 1% can be effective in treatment of chemotherapy-induced mucositis pain.
- Especially that the preparation of this herb is less costly for the patient compared to the other chemical mouthwashes.
- One of limitation of this study is a small number of patients, and it is recommended that a study be conducted with a larger sample size and in several different treatment centers, as well as the individual and physiological characteristics of the patients as another limitation of the study.

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CONFLICT OF INTEREST: None.