

## ***Myrtus communis* Essential Oil for The Treatment of Hemorrhoids: A Randomized Double-Blind Double-Dummy Parallel-Group Comparative Study**

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### **Abstract**

The aim of this study was to evaluate the efficacy of a topical lotion prepared from *M. communis* essential oil of in the alleviation of hemorrhoids symptoms, and compare its effects with those of anti-hemorrhoid ointment in a randomized double-blind double-dummy trial. A total of 106 patients with hemorrhoids symptoms were recruited and randomized to receive either *M. communis* lotion and placebo ointment (n=50; age: 36.2±10.8) or anti-hemorrhoid ointment (containing hydrocortisone, lidocaine, aluminium subacetate and zinc oxide) and placebo lotion (n=56; age: 40.6±11.1) for a period of two weeks. The severity and frequency of hemorrhoids symptoms were evaluated at baseline and at the end of trial. All evaluated symptoms (bleeding, permanent pain, pain during defecation, anal itching and irritation, heaviness and tenesmus) were significantly decreased by the end of trial in either of the study groups (p<0.001). There was no significant difference in the improvement rate for any of the assessed symptoms between *M. communis* lotion and anti-hemorrhoid ointment (p>0.05). The results of this research provide the first clinical evidence on the efficacy of *M. communis* essential oil in the alleviation of hemorrhoids symptoms and further support the application of this plant as an anti-hemorrhoid agent in traditional medicine.

**Key words:** Myrtle, Myrtaceae, Hemorrhoids, Randomized controlled trial, Human, Volatile oil.

### **Hemoroid Tedavisi İçin *Myrtus communis* Uçucu Yağı: Randomize Çift-kör Çift-plasebo Paralel Grup Karşılaştırmalı Bir Çalışma**

Bu çalışmanın amacı, *Myrtus communis*'den elde edilen uçucu yağdan hazırlanan topikal losyonun hemoroid belirtilerinin hafifletilmesindeki klinik etkinliğinin değerlendirilmesi ve etkinin randomize olarak seçilmiş anti-hemoroid merhemlerin çift kör ve çift-plasebo denemeleri ile karşılaştırılmasıdır. Hemoroid belirtisi gösteren 106 hastanın 50'si (yaş: 36.2 ± 10.8) *M. communis* losyonu ve plasebo merhem ile 56'sı (yaş: 40.6 ± 11) da hidrokortizon, lidokain, alüminyum subasetat ve çinko oksit içeren antihemoroid merhem ve plasebo losyon ile 2 haftalık süreçte tedavi edilmiştir. Hemoroid belirtilerinin şiddeti ve sıklığı hem başlangıçta hem de denemelerin sonunda değerlendirilmiştir. Değerlendirilen tüm semptomlar (kanama, sürekli ağrı, defekasyon sırasında ağrı, anal kaşıntı ve tahriş, şiddetli ve ağrılı işeme) çalışmanın sonunda her iki çalışma grubunda da önemli oranda azalmıştır (p<0.001). *M. communis* losyonu ve antihemoroid merhem arasında, değerlendirilen semptomların hiçbirisinin artış hızında belirgin bir farklılık görülmemiştir (p>0.05). Elde edilen verilere göre bu araştırma, *M. communis*'den elde edilen uçucu yağın hemoroid semptomlarını hafifletmede etkili olmasına dair ilk klinik kanıttır ve geleneksel tıpta bu bitkinin antihemoroid etkili ajan olarak kullanılması da bu bilgiyi desteklemektedir.

**Anahtar kelimeler:** Mersin, Myrtaceae, Hemoroid, Randomize kontrollü çalışma, İnsan, Uçucu yağ.

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## INTRODUCTION

Hemorrhoids is the most common disease of anorectal area which has been shown to affect about 10 million people in the US equivalent to a prevalence of 4.4% (1,2). This disorder is caused by dilatation of upper or lower hemorrhoid veins network along with continuous increase of venous pressure (3). Hemorrhoids encircle the distal rectum and anus and the symptoms are manifested after inflammation and thrombosis (4,5). Usually, patients name any anal symptom, e.g. irritation, salient mass, pain and bleeding, as hemorrhoids (5). In general, several factors such as heredity, anatomy, nutrition, profession, climate, psychological status, age, endocrinal changes, drugs, infection, pregnancy and physical inactivity are involved in the pathophysiology of hemorrhoids (6). Categorization of hemorrhoids is often based on the area of emergence (inside, outside, both) or grading (first, second, third and forth) (7). Common symptoms of hemorrhoids include bleeding, salient mass, pain, irritation and pressure sensation along with hypertension of hemorrhoids. The most widespread symptom that hemorrhoid patients typically experience is bleeding during or after defecation which increases after continuous constipations (7,8). There are different medical, minimally invasive and surgical treatments for hemorrhoids that could be performed for outpatients or inpatients. The most widely used medications are topical lidocaine (gel and ointment) and topical anti-hemorrhoid formulations (ointment and suppository) which contain lidocaine, aluminium subacetate, zinc oxide and hydrocortisone. There is evidence indicating that patients with grades I-II hemorrhoids have favourable therapeutic response to topical anti-hemorrhoid medications (9). Further to the conventional treatments, herbal preparations have also been shown to be effective in relieving hemorrhoids symptoms especially in the early stages of disease (10). Besides, such botanical treatments could be of adjunctive utility in the management of more advanced disease stages where surgical intervention is deemed necessary. (myrtle) is a well-known medicinal plant in Iranian folk medicine. Modern scientific research has unveiled numerous pharmacological activities for this plant (11). Among these activities which are of especial importance for the treatment of hemorrhoids are anti-inflammatory, anti-nociceptive, wound healing, antibacterial, antifungal and astringent properties (8-14). Since *M. communis* has a reputation in folk medicine

for the treatment of hemorrhoids, the present study aimed to evaluate the clinical efficacy of a topical lotion prepared from the essential oil of this medicinal plant in the alleviation of disease severity and symptoms of patients with hemorrhoids. In addition the efficacy of the aforementioned oil was compared with that of anti-hemorrhoid ointment as the most widely used medication for this disorder.

## EXPERIMENTAL

### Subjects

This study was a randomized, double-blind, double-dummy, parallel-group and comparative trial performed between 2009 and 2011. Recruited subjects were those (n = 106; females: 41.5%) who referred to the Colorectal Clinic at the Baqiyatallah Hospital (Tehran, Iran) or Najmie Hospital (Tehran, Iran) and for whom a diagnosis of hemorrhoids had been made by a specialized physician. Exclusion criteria were the presence of thrombosed or strangulated external hemorrhoids, anal fistula, anal fissure, anal abscess, pregnancy, portal hypertension, renal dysfunction and any malignancy. For each patient a questionnaire containing information about age, gender, hemorrhoids grade, family history of hemorrhoids, history of laxative consumption, smoking, hemorrhoids therapy, dry and hard excrements, and straining during defecation was filled at baseline. Besides, frequency and severity of hemorrhoids symptoms (including bleeding, permanent pain, pain during defecation, anal itching, irritation, heaviness and tenesmus) were assessed at baseline as well as at the end of trial. Hemorrhoids grading of symptoms was from 0 (lack of symptom) to III (severe symptom) and each grade was defined as follows:

Score 0: no symptoms.

Score I (mild): symptoms are present but have no interference with usual jobs

Score II (moderate): symptoms are present and have interference with usual jobs but are not debilitating

Score III (severe): symptoms are present and debilitating

With respect to bleeding scoring, the following classification was applied:

Score 0: no bleeding

Score I (mild): bleeding is presented as a rake of blood in feces (light bleeding)

Score II (moderate): bleeding is presented discontinuously while relieving (average bleeding)

Score III (severe): bleeding is presented continuously while relieving (high bleeding)

### Study design

Recruited patients were randomly assigned to receive *M. communis* lotion (Barij Essence Pharmaceutical Co., Mashade Ardehal, Kashan, Iran) and placebo ointment (n = 50; age: 36.2 ± 10.8) or anti-hemorrhoid ointment (Behvazan Pharmaceutical Co., Rasht, Iran) and placebo lotion (n = 56; age: 40.6 ± 11.1) for a period of 2 weeks. *M. communis* lotion was standardized as having 30 mg 1, 8 cineole in each mL of product while anti-hemorrhoid ointment contained hydrocortisone acetate (35 mg/g ointment), lidocaine (50 mg/g), aluminium subacetate (35 mg/g) and zinc oxide (180 mg/g). Patients were instructed to apply 10-15 drops of lotion on the anal area (b.i.d.) followed by immediate application of placebo ointment with applicator. Placebo preparations were matched with their respective drugs and contained all ingredients except the active herbal constituents. The study protocol was approved by the Baqiyatallah University of Medical Sciences Ethics Committee and written informed consent was obtained from each participant.

### Statistical analysis

Statistical analyses were performed using SPSS software. Values were expressed as number (%) (for categorical data) and mean ± SD (for numerical variables). Group comparisons were performed using independent samples t-test, paired samples t-test, Wilcoxon signed-rank test or Mann-Whitney U test. Categorical data were compared using chi-square or McNemar's test. A two-sided p-value of < 0.05 was considered as statistically significant.

## RESULTS

The groups were comparable in their baseline characteristics including age, gender disease duration, frequency of hemorrhoids symptoms (straining during defecation, dry and hard excrements, bleeding, permanent pain, pain during defecation, anal itching, anal irritation, anal heaviness and tenesmus), history of smoking, dry and hard excrements, straining during defecation and family history of hemorrhoids (p > 0.05). However, history of hemorrhoids therapy (p = 0.023) and laxative consumption (p = 0.03) was higher in the group receiving *M. communis* lotion. Demographic

characteristics of study groups are summarized in Table 1.

Baseline severities of hemorrhoids symptom,0s (including bleeding, permanent pain, pain during defecation and anal irritation) did not significantly differ between the groups (p > 0.05) except for anal itching (p = 0.015), anal heaviness (p = 0.030) and tenesmus (p = 0.090). In the same manner, comparison of post-trial frequencies did not reveal any significant difference between *M. communis* lotion and anti-hemorrhoid ointment (p > 0.05). However, all evaluated symptoms were significantly and effectively decreased by the end of trial in either of the study groups (p < 0.001) (Table 2).

The rate of improvement for each symptom was also compared between the study groups. The results revealed no statistically significant difference in the improvement rate (defined as the number of patients with moderate to severe symptom at baseline whose post-trial evaluation showed a regression to a less severe category) for any of the assessed symptoms between the groups (p > 0.05) (Figure 1)

## DISCUSSION

The present study was designed to determine the effects of topical *M. communis* essential oil in comparison with the widely administered medication, anti-hemorrhoid ointment, in the alleviation of hemorrhoids symptoms. The results implied that *M. communis* oil is as effective as anti-hemorrhoid ointment and could reduce the frequency of hemorrhoids symptoms including bleeding, pain, itching, irritation, heaviness and tenesmus. Current anti-hemorrhoid medications that are routinely used for the alleviation of symptoms generally contain a corticosteroidal component. On the other hand, chronic application of corticosteroids is usually associated with several adverse effects including skin atrophy, stretch marks, telangiectasia, rosacea, increased susceptibility to infections and so forth (19, 20).

Hence, it would be desirable to find safe and effective agents from natural sources. Some of the most important medicinal plants which have been used for the treatment of hemorrhoids include *Ruscus aculeatus*, *Aesculus hippocastanum*, *Collinsonia canadensis* and *Hammamelis virginiana* (10).

**Table 1.** Demographic characteristics of study groups

Group		<i>M. communis</i>	Anti-hemorrhoid	<i>p</i> -value
<i>n</i>		50	56	-
Gender	Male	27 (54)	35 (62.5)	0.375
	Female	23 (46)	21 (37.5)	
Age (years)	30 ≤	21 (44.7)	11 (20.4)	0.07
	30-39	11 (23.4)	19 (35.2)	
	40-49	9 (91.1)	16 (29.6)	
	≥ 50	6 (12.8)	8 (14.8)	
	Overall	36.2 ± 10.8	40.6 ± 11.13	
Disease duration (months)	≤ 6	24 (48)	25 (44.6)	0.941
	7-12	20 (40)	24 (42.9)	
	≥ 13	6 (12)	7 (12.5)	
	Overall	9.6 ± 7.7	9.23 ± 5.8	
Straining during defecation		37(74)	48(85.5)	0.131
Dry and hard stool		39 (78)	49 (87.5)	0.193
Family history of hemorrhoids		25 (50)	31 (55.4)	0.581
History of	Hemorrhoids therapy	36 (72)	50 (89.3)	0.023
	Laxative consumption	34 (68)	48 (85.7)	0.030
	Dry and hard excrements	39 (78)	49 (87.5)	0.193
	Straining during defecation	37 (74)	48 (85.5)	0.131
	Smoking	17 (34)	15 (26.8)	0.419

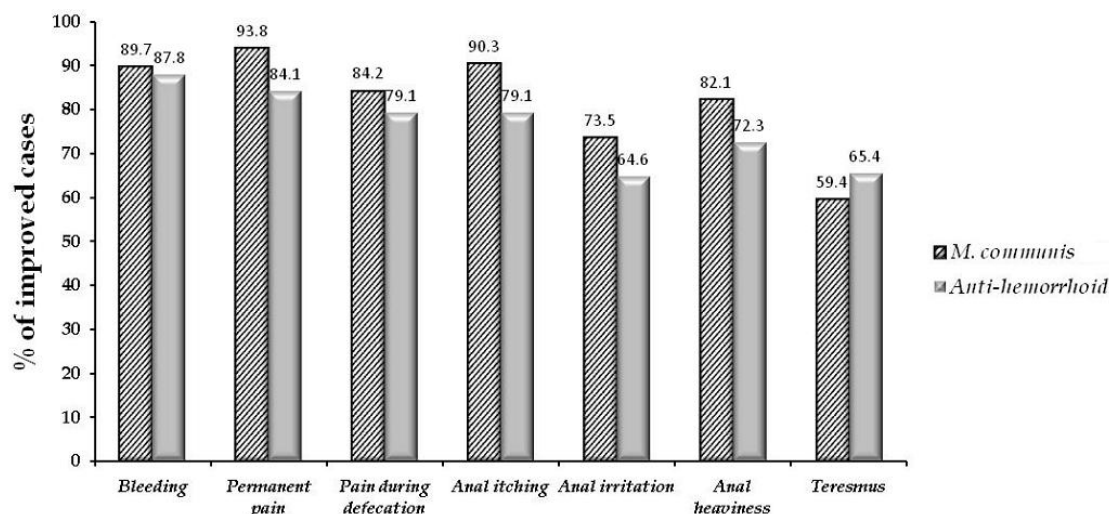
In an open-label trial by Bennani et al., oral administration of *Ruscus aculeatus* (600-900 mg/day) for 7 days was associated with a good or excellent therapeutic response as rated by both patients and physicians. Besides, this herbal remedy was reported to be safe and well-tolerated (21). In another double-blind survey, Pirard et al. reported that oral administration of aescin (a natural mixture of triterpene saponins from *Aesculus hippocastanum*; 120 mg/day) to patients with acute symptomatic hemorrhoids for two months effectively reduced disease symptoms (22). Essential oils are another important class of natural products which have diverse biological properties important for human health (23-25). *M. communis* is a medicinal plant with wide application in traditional medicine and numerous biological activities (11, 26). An important characteristic of *M. communis* is its flavour which is due to the essential oil being present in the leaves (amounting 1.5-2%). Chemical composition of *M. communis* oil is well documented and previous studies have reported oxygenated monoterpenes as the most frequent class of components. The major volatile ingredients have been noted to be  $\alpha$ -pinene, limonene, 1,8-cineole,  $\alpha$ -terpinolene, linalyl acetate and myrtenyl acetate (26-29).

An example of the beneficial activities of *M. communis* is the anti-inflammatory effect which is well-documented (15, 16). Since inflammation has a key role in the pathogenesis of chronic venous insufficiency (30), the observed protective effects of *M. communis* (such as decreasing the rate of irritation) are, at least in part, due to the mitigation of inflammation. One of the main constituents of *M. communis* oil is 1,8 cineole which is an oxygenated monoterpene with established anti-inflammatory effects (31, 32). *M. communis* extract has also been shown to possess anti-nociceptive properties which are deemed to be exerted both centrally and peripherally (16). Findings of the present study on the alleviation of pain and itching further confirm these antinociceptive effects and extrapolates these properties to the essential oil. Compounds with astringent properties represent another class of medications for hemorrhoids (33). Interestingly, *M. communis* is reputed in folk medicine for its astringent and antiseptic characteristics which are both required for an effective anti-hemorrhoid agent. This astringent effect was noted in our results as the severity of bleeding was reduced by around 90% using either of the tested formulations.

**Table 2.** Effect of *M. communis* vs. anti-hemorrhoid in the alleviation of hemorrhoids symptoms.

Symptom	Severity	<i>M. communis</i>			<i>Anti-hemorrhoid</i>			Pre-trial comparison	Post-trial comparison
		Pre-trial	Post-trial	<i>p</i> -value*	Pre-trial	Post-trial	<i>p</i> -value*	<i>p</i> -value	<i>p</i> -value
Bleeding	No	3 (6)	22 (44)	< 0.001	2 (3.6)	26 (46.6)	< 0.001	0.355	0.758
	Mild	18 (36)	25 (50)		13 (23.2)	25 (44.6)			
	Moderate	13 (26)	3 (6)		22 (39.3)	3 (5.4)			
	Severe	16 (22)	-		19 (33.9)	2 (3.6)			
Permanent pain	No	1 (2)	21 (42)	< 0.001	1 (1.8)	17 (30.4)	< 0.001	0.390	0.077
	Mild	17 (34)	27 (54)		11 (19.6)	32 (57.1)			
	Moderate	17 (34)	2 (4)		28 (50)	6 (10.7)			
	Severe	15 (30)	-		16 (28.6)	1 (1.8)			
Pain during defecation	No	1 (2)	22 (44)	< 0.001	1 (1.8)	23 (41.1)	< 0.001	0.702	0.533
	Mild	1 (22)	22 (44)		12 (21.4)	24 (42.9)			
	Moderate	26 (52)	6 (12)		27 (48.2)	8 (14.3)			
	Severe	12 (24)	-		16 (28.6)	1 (1.8)			
Anal itching	No	2 (12)	21 (42)	< 0.001	3 (5.4)	20 (35.7)	< 0.001	0.015	0.199
	Mild	13 (36)	26 (52)		10 (17.9)	27 (48.2)			
	Moderate	25 (50)	3 (6)		25 (44.6)	9 (16.1)			
	Severe	6 (12)	-		18 (32.1)	-			
Anal irritation	No	4 (8)	20 (40)	< 0.001	1 (1.8)	21 (37.5)	< 0.001	0.141	0.288
	Mild	12 (24)	21 (42)		7 (12.5)	18 (32.1)			
	Moderate	14 (28)	9 (18)		25 (44.6)	16 (28.6)			
	Severe	20 (40)	-		23 (41.1)	1 (1.8)			
Anal heaviness	No	7 (14.0)	26 (52.0)	< 0.001	3 (5.3)	22 (39.3)	< 0.001	0.003	0.062
	Mild	15 (30.0)	19 (39.0)		6 (10.7)	21 (37.5)			
	Moderate	17 (34.0)	5 (10.0)		24 (42.9)	12 (21.4)			
	Severe	11 (22.0)	-		23 (41.1)	1 (1.8)			
Tenesmus	No	9 (18)	22 (44)	< 0.001	-	19 (33.9)	< 0.001	0.009	0.217
	Mild	8 (16)	15 (30)		4 (7.1)	19 (33.9)			
	Moderate	12 (24)	12 (24)		27 (48.2)	11 (19.6)			
	Severe	21 (42)	1 (2)		25 (44.6)	7 (12.5)			

**Figure 1.** Number of patients with moderate to severe symptom whose disease regressed to a less severe category. No significant difference was found between the groups ( $p > 0.05$ ).



Moreover, the essential oil of *M. communis* has wound healing properties (18) which is another advantage of this herbal remedy in the treatment of hemorrhoids as well as acceleration of the recovery following hemorrhoidectomy surgery. Another Important finding to emerge from the current investigation is the equal efficacy of *M. communis* lotion and anti-hemorrhoid ointment in the mitigation of hemorrhoids symptoms. To conclude, the results of this research provide the first clinical evidence on the efficacy of *M. communis* essential oil in the alleviation of hemorrhoids symptoms and support the application of this plant as an anti-hemorrhoid agent in the traditional medicine. In light of the present findings, *M. communis* oil may be used as an effective drug for the treatment of early stages of hemorrhoids and as an adjunct to surgery in severe stages. Besides, regarding its equal efficacy to the anti-hemorrhoid ointment, *M. communis* lotion may be used as an effective alternative treatment for hemorrhoids patients who suffer from dermatologic side effects of corticosteroids. While these findings are promising, further investigations are warranted to compare the efficacy of *M. communis* oil with other commercially available anti-hemorrhoid preparations. Finally, the efficacy and safety of the oral administration of *M. communis* oil is another rissue that deserve to be clarified by future investigations, and possibly with additional efficacy measures including change in hemorrhoids size.

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