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Research Article

Effectiveness of a Medical Device Based on Ectoine, Propolis, Grapefruit Extract with Glycerol for the Treatment of Uncomplicated Acute Pharyngitis

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Abstract

The pharynx is often exposed to infectious and non-infectious factors that can lead to an inflammatory reaction referred to as pharyngitis or sore throat. Even if viral pharyngitis is a self-limiting disease, the related acute sore throat can be very annoying; therefore, rapid pain relief, obtained effectively and safely, must be the primary therapeutic goal. Moreover, an effective pain alleviation can result in the reduction of drug abuse. A medical device based on a compound made up of ectoine, propolis, grapefruit extract and glycerol (VG), to be sprayed directly into the oral cavity by means of a special nozzle, was compared with an oral spray based on isotonic saline solution (IS). The study is a prospective, controlled, monocentric, single-blind clinical trial. 49 patients were enrolled in the VG group and 52 patients were enrolled in the IS group. The investigators measured the patients' pharyngeal redness, their pharyngeal edema and their mucous secretion on an 11-point numerical rating scale (NRS) and compiled the relevant 3 questionnaires. Patients graded their sore throat, difficulty swallowing and swelling of the throat with the same 11-point NRS and compiled the relevant 3 questionnaires. The first application of VG or IS was made by patients with 4 sprays directly onto the pharynx and they compiled the relevant NRSs questionnaires within 3 hours from the first application, at predefined intervals. The patients then left the clinic and applied VG or IS 4 times throughout the first day and 5 times per day in the following 2 days, each time with 4 sprays directly onto the pharynx. Patients compiled the 3 NRS questionnaires at the end of the first, of the second and of the third day of therapy. At the end of the third day of application of the oral sprays, the patients evaluated the effectiveness of the spray based on a 5-point Likert scale. In the morning of the fourth day, the patients were visited again in the clinic by the investigators. The reduction of the characteristic signs and symptoms of uncomplicated acute pharyngitis resulted significantly more pronounced on patients treated with VG versus those treated with IS. Both investigators and patients evaluated VG significantly more effective than IS. Both the tolerability and the safety of VG have proven to be equivalent to those of IS. In conclusion, the oral spray containing ectoine, propolis, grapefruit extract and glycerol can be considered a valid alternative for the treatment of signs and symptoms of uncomplicated acute pharyngitis.

Keywords: Acute Pharyngitis; Sore Throat; Difficulty Swallowing; Swelling of the Throat; Medical Device; Ectoine; Propolis; Grapefruit Extract; *Citrus paradisi*; Glycerol

Abbreviations

VG: Viscoflu Gola; IS: Isotonic Saline Solution; NRS: Numerical Rating Scale

Introduction

The respiratory tract and, particularly, the pharynx are often exposed to infectious and non-infectious factors that can lead to an

inflammatory reaction referred to as pharyngitis or sore throat. According to a survey conducted in Europe and Asia, sore throats are extremely common, and it is estimated that around 54% of people experience this type of condition every year [1]. Characteristic signs and symptoms of uncomplicated acute pharyngitis can last for 3 up to 7 consecutive days. In most of the cases the symptoms disappear spontaneously without the need of drugs. Up to the 80% of pharyngitis has viral etiology [2,3] and, even if viral pharyngitis is a self-limiting disease, the related acute sore throat is very annoying; therefore, rapid pain relief, obtained effectively and safely, must be a primary therapeutic goal. Moreover, an effective pain alleviation can result in the reduction of antibiotics abuse, thus avoiding the spread of antibiotic resistance. As a matter of fact, many reports have evidenced that the inappropriate use of antibiotics is related to the belief that this treatment can provide rapid relief of sore throat [4,5].

Topical spray formulations are particularly suitable for the treatment of inflammatory conditions of the oropharyngeal cavity as they guarantee a more direct access to the interested area. In clinical studies, the local application of sprays containing anesthetic or non-steroidal anti-inflammatory drugs has shown to induce relief from acute pharyngitis symptoms [6,7]. However, drugs that belong to these groups have been shown to have contraindications, drug interactions and potential side effects. Indeed, it has been demonstrated that an inappropriate use of topical corticosteroids causes side effects including dry mouth, taste disorders and cough [8]. With the goal to evaluate the effectiveness, the safety, and the tolerability of a new spray product classified as medical device, we performed a clinical study to assess its effectiveness in reducing signs and symptoms of uncomplicated acute pharyngitis. Patients, who received the treatment with the new spray product classified as medical device or with a spray containing isotonic salt solution, were observed for 3 consecutive days starting 3 hours prior the first application. An additional goal of the trial was the comparison between the evaluation of the effectiveness made by the investigators and that made by the patients. Finally, our aim was also to compare the tolerability and the safety of the products.

Materials and Methods

Tested spray devices

Viscoflu Gola (VG - Pharma Line S.r.l. Milano) is a medical device based on Ectociclina-ProG®. The product was placed on the market on 12 May 2021 and was included in the list of medical devices on 13 May 2021 with registration number 2105212.

Ectociclina-ProG® is compound made up of ectoine, propolis extract, grapefruit (*Citrus paradisi* Macfad., 1830) seeds and juice extract, glycerol and with controlled pH. The compound is applied directly into the oral cavity by means of a special spray nozzle able to nebulize it in droplets of diameter (> 25 µm) sufficiently big not to bypass the oropharyngeal district, thus remaining localized in that area.

This medical device is indicated as adjuvant treatment of oral and throat diseases associated with inflammatory phenomena of infectious (viral or bacterial) or irritative nature (cigarette smoke, environmental pollutants, or allergens), both acute and chronic. It is also indicated as adjuvant treatment of inflammatory irritations of the oral cavity such as stomatitis and gingivitis and in case of extraesophageal manifestations of gastroesophageal reflux.

VG was compared with an oral spray based on an isotonic saline solution (IS), an aqueous solution containing 0.9% (m/m) of sodium chloride (NaCl). The isotonic saline solution thanks to its wetting action and its cleansing activity on the oropharyngeal mucosa, actively carries out a symptomatic action, as already highlighted in the literature [9].

The packaging materials of the two sprays were identical, so patients could not determine whether they were treated with VG or IS. The investigator instead could distinguish the two products thanks to the lot number printed on the package.

Enrolled patients

Patients of both genders, aged between 18 and 75 years, not suffering from allergic symptoms, with acute uncomplicated pharyngitis onset ≤1 day before the visit were included in the study. Enrolled patients had to perceive pain with an intensity of at least 6 points of score on the numerical scale of pain intensity (NRS). The NRS is a pain screening tool, commonly used to assess pain severity at that moment in time using a 0–10 scale, with 0 meaning "no pain", 5 meaning "moderate pain" and 10 meaning "the worst pain imaginable" [10].

Patients excluded from the study were those with infections requiring antibiotic therapy, suffering from pharyngitis of proven

non-viral etiology, with sensitivity to one or more components of VG, with malignant pathologies, who had already taken medications, supplements or medical devices for the treatment of pharyngitis in the two weeks prior to the start of the use of the two sprays, pregnant or breastfeeding, presenting medical or psychiatric conditions, that in the investigators' opinion, could have exposed the patient to risks or could have had a negative impact on the compliance with the study protocol.

Patients from the two groups were forbidden to take other medications, sweet melts or tablets for sore throats during the study. In addition, they were forbidden to use toothpaste or mouthwash, smoke, chew gum, eat or drink immediately after application of the product.

Study design and results evaluations

The study was a prospective, controlled, monocentric, single-blind clinical trial, in which the comparison was made between patients treated with VG and patients treated with IS. Patients, who received any of the two treatments, were examined twice by the investigators: at the time of enrollment (T0), which coincided with the start of the spray application, and by the morning of the fourth day after enrollment. Each patient received an identification number and signed a regular informed consent to the proposed therapy and for processing personal data.

At the time of enrollment, the investigator collected the following information for each patient who was suffering from uncomplicated acute or subacute pharyngitis: an accurate medical history, and demographic data, with record of date of birth, gender, height, weight, date of onset of the first symptoms (the same day or the day before enrollment), smoking, known allergies, familiarity with throat disease, comorbidity, medications taken, and job.

After the assessment of compliance with the inclusion and exclusion criteria, the pain perceived was assessed by completing the NRS questionnaire. Once confirmed that these criteria met the parameters established for the inclusion in the study (T0), the investigators compiled three 11-point NRS questionnaires (0 = undetectable; 5 = moderate; 10 = extremely severe) concerning the pharyngeal redness, pharyngeal edema and mucous secretions. Patients then filled the 11-point NRS questionnaires for: sore throat (0 = no pain; 5 = moderate pain; 10 = the worst pain they experienced), difficulty swallowing (0 = no difficulty; 5 = moderate difficulty; 10 = the worst difficulty they experienced) and swelling of the throat (0 = no sensation; 5 = moderate sensation; 10 = worst sensation). The enrolled patients were then given one of the two sprays by lot.

The first application of the two sprays was carried out in the clinic of the investigator. The patients made the first application of VG or IS with 4 sprays directly onto the pharynx. Patients remained in the clinic and filled the NRSs questionnaires within 3 hours after the first application, at predefined intervals: after 15 minutes (T1), 30 minutes (T2), 45 minutes (T3), 60 minutes (T4), 1 hour and 30 minutes (T5), 2 hours (T6), 3 hours (T7) without repeating the spray application.

The patients then left the clinic and applied again VG or IS 4 times throughout the first day and 5 times per day in the following 2 days, each time with 4 sprays directly onto the pharynx. Patients completed the three NRS questionnaires at the end of the first day (T8), of the second day (T9) and of the third day of therapy (T10).

At the end of the third day of application of the assigned oral spray (T10), patients completed a 5-point Likert scale questionnaire for the evaluation of the effectiveness of the assigned spray. The patient was asked: "Please indicate with a cross on the scale below how satisfied you are with the effectiveness of the therapy implemented by the spray applied". The possible opinions, with the relative possible scores were as follows: no satisfaction for the effectiveness of the therapy (0 points), poor (1 point), satisfactory (2 points), good (3 points), excellent (4 points).

By the morning of the fourth day from the start of the application of the assigned oral spray (T11), so after 3 days of treatment, the investigator visited again the patients in the clinic. The NRS questionnaire was filled again by the investigator with his evaluation of the pharyngeal redness, the pharyngeal edema and the mucous secretions. In addition, a record of any adverse effects was done together with the filling of a 5-point Likert scale questionnaire for the assessment of the effectiveness of the therapy. In particular, the investigator was asked: "Please indicate with a cross on the scale below what is your opinion on the effectiveness of the spray applied". The possible answers, with the relative scores, were no effectiveness (0 points), poor (1 point), satisfactory (2 points), good (3 points), excellent (4 points).

All the data, recorded in appropriate paper forms, were subsequently collected for processing.

Statistical analysis

Descriptive statistics have been used to synthesize the characteristics of patient groups in terms of mean and standard deviation or frequencies, when appropriate. The effects of the treatments with VG and IS have been assessed in terms of variation in the outcomes. The significance of the differences was determined by applying the non-parametric Mann-Whitney test for paired data in the comparison between data of the same patient group at different times (T) and for unmatched data in the comparison between the two groups. In all the analyses, the results were considered statistically significant with $P < 0.05$. The data analysis was carried out using the program GraphPad Prism version 8.0.0 for Windows, GraphPad Software, San Diego, California USA, www.graphpad.com

Results and Discussion

Results

The study was conducted between 1 November 2021 and 31 March 2022. 101 patients were enrolled as follows: 49 patients in the VG group and 52 patients in the IS group. Demographic and medical records of the enrolled patients are presented in Table 1. There were no statistically significant differences between the two groups at the time of enrollment (T0).

Parameter	VG Group (n = 49)	IS Group (n = 52)
Gender, % W (n)	40.8 (20)	44.2 (23)
Age (years, mean ± SD; min; max)	37.9 ± 16.5; 18; 73	40.1 ± 16.4; 19; 75
Height (cm, mean ± SD)	172.3 ± 6.19	171.3 ± 7.12
Weight (kg, mean ± SD)	69.8 ± 9.16	68.8 ± 10.7
BMI (kg/m^2, mean ± SD)	23.3 ± 2.12	23.2 ± 2.39
Smoke, % yes (n)	46.9 (23)	46.1 (24)
Allergies, % yes (n)	22.4 (11)	17.3 (9)
Family history of upper respiratory tract infections, % yes (n)	48.9 (24)	36.5 (19)

Table 1: Demographic and medical records of enrolled patients. At T0 the two groups are homogeneous from the demographic and the clinical points of view.

The NRS questionnaires were administered to the enrolled patients to evaluate signs of acute pharyngitis. Specifically, the considered signs were the pharyngeal redness, the pharyngeal edema, and the mucosal secretions. As it is shown in Table 2, the parameters considered were significantly reduced in both groups: VG group ($P < 0.0001$ for the three parameters considered) and IS group ($P < 0.0001$ for the three parameters considered). Interestingly, the average percentage reductions in the NRS scores referring to the three signs of acute pharyngitis observed as results of the treatment with VG was significantly greater than the reduction obtained with the treatment with IS (Table 2, Figure 1; $P < 0.0001$ for the three parameters).

Parameter	Mean change in NRS score (%) from T0 to T11 (3 days of treatment) and statistical comparison between the two treated groups	
Pharyngeal redness	VG	-61.60 ± 9.42
	IS	-22.62 ± 13.85
	P-value	< 0.0001
Pharyngeal edema	VG	-70.36 ± 14.81
	IS	-21.63 ± 20.80
	P-value	< 0.0001
Mucus secretion	VG	-74.16 ± 9.25
	IS	-28.53 ± 18.79
	P-value	< 0.0001

Table 2: Mean change in NRS scores (expressed as percentage) from T0 to T11 (3 days of treatment) and statistical comparison between the two treated groups. After 3 days of treatment the signs of acute pharyngitis significantly decreased in both the groups ($P < 0.0001$ for the three parameters considered in both groups). The average percentage reduction in the NRS score resulting from treatment with VG was significantly greater than the reduction obtained upon treatment with IS ($P < 0.0001$ for the three parameters considered).

Figure 1: Graphical representation of the NRS scores. The average percentage change in the NRS score for pharyngeal redness, pharyngeal edema and mucus secretion was negative in both groups. The scores were significantly lower in the VG group than in the IS group (**** P < 0.0001).

The average percentage changes in the NRS scores for sore throat, difficulty swallowing and swelling of the throat were negative in both groups, confirming a progressive reduction in symptoms (Table 3, Figure 2). It is worth mentioning that in relation to the parameter "sore throat" the NRS score of the VG treatment decreases in a significantly manner (T1 vs T0, P = 0.0005) right after 15 minutes from the first application, While IS treatment does not. Indeed, in the IS group the statistical significance is reached after 30 minutes (T2 vs T0, P <0.0001). Notably, the other two parameters "difficulty swallowing" and "swelling of the throat" presented the same trend in both groups. Specifically, the statistical significance is already reached after 15 minutes from the first application of both VG and IS sprays (difficulty swallowing: VG, P = 0.0156; IS, P = 0.0313; swelling of the throat: VG, P = 0.0020; IS, P = 0.0039).

However, considering the trend of the average percentage change in the NRS scores, the three symptoms decreased much more with VG treatment than with IS (Table 3, Figure 2). The difference between the results obtained in the VG group compared to those obtained in the IS group is already statistically significant at T1 for sore throat (P = 0.0320), while both for difficulty swallowing and for swelling of the throat it becomes statistically significant from T2 (respectively P = 0.0133 and P = 0.0141).

Figure 2: Graphical representation of the three evaluated symptoms. The mean percentage change in the NRS score for sore throat, difficulty swallowing, and swelling of the throat was negative in both groups. Score decreased much more in the VG group compared with the IS group.

Parameter	Mean percentage change in score and statistical comparison between the two treated groups											
		T0	T1	T2	T3	T4	T5	T6	T7	T8	T9	T10
Sore throat	VG	0.0	-3.02 ± 5.39	-10.96 ± 9.06	-15.69 ± 11.08	-25.24 ± 12.94	-29.49 ± 14.08	-36.10 ± 13.27	-39.70 ± 14.76	-46.47 ± 12.99	-55.49 ± 9.30	-73.21 ± 8.03
	IS	0.0	-1.18 ± 4.17	-5.82 ± 7.55	-8.43 ± 8.12	-12.86 ± 10.13	-14.65 ± 11.49	-18.59 ± 13.58	-19.64 ± 13.94	-23.49 ± 13.82	-35.79 ± 8.13	-48.15 ± 17.62
	P value	-	0.0320	0.0343	0.0328	<0.0001	<0.0001	<0.0001	<0.0001	<0.0001	<0.0001	<0.0001
Difficulty swollowing	VG	0.0	-1.89 ± 4.72	-8.54 ± 11.77	-12.60 ± 11.54	-20.35 ± 16.41	-27.01 ± 18.25	-34.81 ± 18.87	-37.48 ± 18.77	-42.56 ± 16.65	-52.55 ± 12.91	-81.56 ± 9.47
	IS	0.0	-1.72 ± 4.87	-3.92 ± 8.64	-6.92 ± 10.02	-8.07 ± 11.65	-10.73 ± 11.86	-14.26 ± 14.06	-15.19 ± 13.63	-18.14 ± 15.58	-31.49 ± 13.36	-46.64 ± 21.14
	P value	-	0.7774	0.0133	0.0144	0.0002	<0.0001	<0.0001	<0.0001	<0.0001	<0.0001	<0.0001
Swelling of the throat	VG	0.0	-3.47 ± 8.14	-11.45 ± 11.62	-18.32 ± 11.95	-27.61 ± 12.45	-35.69 ± 13.14	-40.39 ± 13.57	-44.71 ± 15.44	-48.75 ± 12.86	-60.73 ± 10.73	-82.49 ± 10.08
	IS	0.0	-2.73 ± 6.08	-4.92 ± 9.61	-8.46 ± 11.56	-11.60 ± 13.80	-14.63 ± 15.25	-15.85 ± 16.22	-17.18 ± 16.41	-21.69 ± 18.22	-36.69 ± 10.97	-52.48 ± 16.98
	P value	-	0.8309	0.0141	0.0039	<0.0001	<0.0001	<0.0001	<0.0001	<0.0001	<0.0001	<0.0001

Table 3: Mean percentage changes in symptoms and statistical comparison between the two treated groups. Comparing the trend of the average percentage variation of the scores, it is noted that for the three symptoms considered the score has decreased more markedly in the VG group compared with the IS group.

At the end of the treatment, the investigators and patients gave an overall assessment of the effectiveness of the treatment using 5-point Likert scales. The average scores of these assessments and the statistical comparison are given in table 4.

Parameter	Mean scores of the efficacy and statistical comparison	
Efficacy (Investigators)	VG	3,92 ± 0,28
	IS	1,40 ± 0,87
	P value	< 0,0001
Efficacy (Patients)	VG	3,94 ± 0,24
	IS	1,25 ± 0,44
	P value	< 0,0001

Table 4: Efficacy of the treatment according to investigators and patients' evaluation. Both acute pharyngitis patients and investigators have evaluated the treatment with VG more effective in relieving the considered signs and symptoms.

The effectiveness of the treatment was evaluated by the investigators as optimal in the 91.8% of VG patients and in the 3.8% of IS patients. The effectiveness of the treatment was evaluated as excellent by the 93.9% of patients in the VG group, while the 25.0% of patients in the IS group judged it satisfactory and the 75.0% of patients in the IS group considered it poor.

No adverse effects were found in relation to the application of oral sprays both in the VG group and in the IS group.

Discussion

Although self-limiting, sore throats can be extremely irritating and uncomfortable. Therefore, offering a rapid, efficient, and safe relief from symptoms must be the first aim in managing uncomplicated acute pharyngitis.

This prospective, controlled, monocentric, single-blind clinical study evaluated the effectiveness, safety and liking of the use in the oropharyngeal cavity of a spray product classified as medical device to relieve symptoms and reduce the signs of uncomplicated acute pharyngitis.

The application of the VG spray as well as the application of the IS spray have been associated with a significant reduction in the intensity of sore throat, difficulty swallowing, and swelling of the throat (Table 2 and 3; Figure 1 and 2). In addition, a significant reduction observed by the investigators in the signs of acute pharyngitis was reported. The improvement obtained by applying VG was significantly greater than that obtained by applying IS. This observation was confirmed by the judgment of the effectiveness expressed both by the investigators and the patients (Table 4). However, since upon the use of both VG and IS treatments a significant improvement in signs and symptoms was achieved, further considerations must be made to highlight the additional benefits obtained using VG. For this purpose, it is worth referring to some published studies where, scoring "sore throat" parameter on NRSs from 0 to 10, a 30% reduction is identified as the limit for a clinically important relief from acute pain, a condition that is associated with the perception of being "much better" [10,11].

In the VG group the 30% average reduction in the perceived pain was manifested between T5 (90 minutes after the first application), when the average reduction was equal to -29,49 ± 14,08%, and T6 (120 minutes after the first application), when the average reduction was equal to -36,10 ± 13,27%. At T5, 30.61% of patients in the VG group perceived a reduction in sore throat by more than 30%, while at T6 61.22% of patients in the same group perceived a reduction in sore throat by more than 30%.

In the IS group the 30% average reduction in the pain perceived was observed between T8 (at the end of the first day of treatment), when the average reduction was equal to -23,49 ± 13,82%, and T9 (at the end of the second day of treatment), when the average reduction was equal to -35,78 ± 8,13%. At T8, 48.08% of patients in the IS group perceived a reduction in sore throat by more than 30%, while at T9 86.54% of patients in this group perceived a reduction in sore throat by more than 30%. A very similar trend was observed for the difficulty swallowing and for the swelling of the throat. At the same time, in the VG group there was a significantly greater reduction than in the IS group in the signs of pharyngeal redness, of pharyngeal edema and of mucous secretions observed by the investigators (for all $P < 0.0001$).

The medical device VG contains Ectociclina-ProG®, a compound made up of ectoine, propolis, grapefruit seeds and juice extract, and glycerol.

Ectoine (2-methyl-3,4,5,6-tetrahydropyrimidine-4-carboxyl acid) is a low molecular weight cyclic amino acid and is a compatible solute produced by halophilic bacteria [12]. With the term compatible solutes, we refer to a class of low molecular weight, mostly neutral or zwitterionic, cytoprotective compounds produced by cells under stress conditions [13]. The reduction of cellular stress by compatible solutes is a highly conserved evolutionary biological process that occurs in living organisms from bacteria up to the highest classes of vertebrates. These molecules strongly bind water molecules and stabilize macromolecules without interfering with cellular processes [14].

Ectoine behaves as an osmoregulator molecule, attracting water to form a hydrating capsule around the main biological macromolecules, such as lipids and proteins. This mechanism of action is believed to promote the formation of biological macromolecules more thermodynamically stable, thus protecting individual cells and their components from insults mediated by external agents [14]. The ability of ectoine to reduce redness has been demonstrated in several preclinical studies [15-17]. Ectoine increases both the stability and the fluidity of the cell membranes, as demonstrated in biophysics experiments [18-20], leading to a greater stabilization of the epithelial barrier, to an increased protection against stressors and to the consequent reduction of redness [21].

Over the past decade, topical application of ectoine has been tested as a treatment for allergic rhinitis, rhino-conjunctivitis, and other diseases [22-25]. In a clinical study the use of ectoine in acute rhinosinusitis patients showed positive results [23]. The stabilizing effect of the barrier function in the epithelial tissues mediated by ectoine has allowed us to hypothesize that this ingredient augments the resistance of the pharyngeal mucosa from external insults, thus

leading to its restoration. A clinical study compared the efficacy and the tolerability of the treatment of acute pharyngitis and/or laryngitis with a spray containing 1% ectoine and with salt tablets. The spray has shown to be more effective and safer than the salt tablets in relieving the symptoms [26].

Propolis has a variable composition that can affect its therapeutic effectiveness. To overcome this disadvantage a poplar propolis with a standardized polyphenol content, obtained by means of a patented extraction method, was included in the composition of VG [27]. This propolis is characterized by a standardized chemical composition especially for the six main flavonoids: galangin, chrysin, pinocembrine, apigenin, pinobanksin and quercetin [27] and has shown to possess antioxidant and anti-inflammatory activity [28,29]. Propolis itself was used in a clinical study where, contained in an oral spray, it showed, to be effective in treating symptoms and in accelerating the resolution of mild viral and bacterial upper respiratory tract infections [30].

Grapefruit is the fruit of the *Citrus paradisi* plant. Both the seeds and the juice extracts of this plant are rich in vitamins and antioxidant compounds, among which flavonoids such as naringin stand out [31]. Grapefruit is widely used in phytotherapy for the therapeutic properties that are attributed to it. Researchers have proven that the substances present in the extract have antioxidant, anti-inflammatory, antibacterial, antifungal, and antiviral effects [31].

Glycerol is strongly hygroscopic and perfectly soluble in water, is non-toxic and does not irritate the mucous membranes. Its effectiveness is related exclusively to its physical and chemical properties, as it does not possess any pharmacological action. It is believed that the wetting and emollient properties of glycerol significantly contribute to the symptomatic effectiveness of cough syrups. Moreover, since the pharynx and the tongue surfaces slip against each other during swallowing and phonation, and this mechanical stimulation can irritate the sensory nerves and induce coughing, the lubricating property of glycerol is useful for oiling the pharyngeal area providing an antitussive symptomatic action [32].

The results obtained in our clinical study suggest that the combination of the multiple actions mediated by the different ingredients of the VG are at the basis of the significant improvement of signs and symptoms of acute uncomplicated pharyngitis when compared to a general isotonic saline solution application.

Conclusion

The reduction of the characteristic signs of uncomplicated acute pharyngitis has shown to be significantly more pronounced in the treatment with VG versus that with IS. The reduction of symptoms perceived by patients with uncomplicated acute pharyngitis has also shown to be significantly more pronounced by applying VG rather than by applying IS.

Already after 90 minutes from the first application, 30.61% of the patients in the VG group experienced a reduction in sore throat higher than 30% and, after 120 minutes, the reduction in pain occurred in 61.22% of the patients. A 30% reduction on NRS from 0 to 10 is the limit for a clinically important relief from acute pain, a condition that is associated with the perception of being “much better”. On average, IS group patients obtained the same benefits between the first and the second day of treatment.

Both investigators and patients evaluated VG more effective than IS in a significant manner. The tolerability and safety of VG have proven to be equivalent to those of IS.

In conclusion, VG oral spray containing ectoine, propolis, grapefruit seeds and pulp extracts and glycerol, can be considered a valid alternative for the treatment of signs and symptoms of uncomplicated acute pharyngitis.

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Conflict of Interest

The authors declare that they have no business or other relationships that could pose a conflict of interest concerning the article presented.

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