



Scholars Research Library

Der Pharmacia Lettre, 2016, 8 (13):75-79
(<http://scholarsresearchlibrary.com/archive.html>)



***Zingiber Officinalis* and *Althea Officinalis* in treatment of acute bronchitis-induced cough**

Hojjat Rouhi – Boroujeni¹, Forouzan Ganji², Parnian Rouhi – Boroujeni³, Minasadat Khoddami⁴ and Hamid Rouhi – Boroujeni^{5*}

¹ Student Research Committee, Medical Plants Research Center, Shahrekord University of Medical Sciences, Shahrekord, Iran

² Medical Plants Research Center, Shahrekord University of Medical Sciences, Shahrekord, Iran

³ Faculty of pharmacy, Isfahan University of Medical Sciences, Isfahan, Iran

⁴ Clinical Biochemistry Research Center, Shahrekord University of Medical Sciences, Shahrekord, Iran

^{5*} Pulmonologist, Clinical Biochemistry Research Center, Shahrekord University of Medical Sciences, Shahrekord, Iran

ABSTRACT

Cough is a natural mechanism of respiratory tract. However, if cough is exacerbated, it may cause discomfort and disturbance of social activities. Cough may be due to acute bronchitis which causes inflammation of airway, which may persist for weeks. This study was conducted to investigate the effect of combined Marshmallow and *Zingiber officinalis* on acute bronchitis-induced cough. In this double-blind clinical trial, 60 patients, presenting acute bronchitis symptoms following respiratory infections, were selected by convenience sampling and randomly assigned to two groups of 30 each, case and control. In addition to routine treatment, case group were administered with 15 drops of hydroalcoholic *Z. officinalis* (40 mg) and Marshmallow (300 mg) extract and control group with 15 drops of placebo every six hours. After 10 days of treatment, coughing, coughing attacks at night, awakening, and chest pain of the patients were examined by a researcher-developed questionnaire and the data were analyzed by chi-square and McNemar's test. After 10 days of treatment, coughing decreased in 80% and 60% of the patients of the case and control groups, respectively ($P < 0.05$), and only 2.7% and 50% of the patients of the case and control groups, respectively, presented chest pain ($P < 0.05$). In patients with acute bronchitis, herbal drop of combined Marshmallow and *Z. officinalis* caused decrease in coughing attacks and relief of trachite-induced chest pain by decreasing inflammation, and decreased gastrointestinal symptoms due to side effects of bronchodilators and synthetic, anti-inflammatory drugs.

Key words: Acute bronchitis, cough, chest pain, *Zingiber officinalis*, Marshmallow, herbal drop.

INTRODUCTION

Cough refers to a rapid exhalation in order to clear the tracheobronchial tree of foreign bodies and mucus. However, severe and persistent cough is a very common reason for referring to physicians, causes discomfort and disturbance of quality of life and sleep, and is constantly associated with carcinophobia [1, 2].

Coughing may be reflex or voluntary with involvement of efferent and afferent nerves. The afferent nerves consist of sensory (trigeminal, glossopharyngeal, upper laryngeal, and vagus) nerves and the efferent nerves are recurrent laryngeal and spinal nerves. Cough can accelerate air flow up to 2.3 of the speed of sound and therefore clear the airway of mucus [3].

Acute bronchitis is one the 10 diseases requiring medical attention [4]. Patients with acute bronchitis require to refer to physicians at least twice and may be absent from work for 2-3 days [5]. Diagnosis is made by the onset of acute symptoms, or mucus, fever, and chest pain may be absent and the patients present wheezing. However, these patients are also likely to present rhonchi and chronic cough [6].

In these patients, yellow or green mucus is not due to airway inflammation, and is not necessarily indicative of microbial infections, because peroxidase can discolor mucus. However, stiffening-induced symptoms are not observed in the X-ray pictures of these patients [7].

Regarding treatment, if patients with acute bronchitis smoke, they should immediately quit smoking. Besides that, vaporizer, analgesics, refrigerants, and anti-cough drugs may be prescribed. In addition, inhaled bronchodilators can relieve the symptoms.

Routine use of antibiotics is not recommended for patients with bronchitis because the cause of bronchitis is mainly respiratory viral infections. However, some investigations reported that antibiotics were prescribed for 65%-80% of the patients [8].

In a study of treatment of patients with acute bronchitis, cough persisted in 26% of the patients. Although cough lasting for 30 days can be secondary to respiratory infections, it is recommended for these patients. In radiological investigations and lung function test, mucus culture is performed and antibiotics are prescribed. In some studies, procalcitonin test is performed and if the procalcitonin concentration is lower than 50µg/L, a course of antibiotics is not started.

According to the American College of Chest Physicians criteria, routine treatments, such as antibiotics and inhaled bronchodilators and anticholinergic agents are not recommended, unless the patients have a history of chronic obstructive airway diseases [9, 10]

Today, several herbal drugs have been used to treat many disorders such as cough and respiratory diseases. For example, *Pelargonium sidoides* root was investigated on 486 patients, but it needs further investigation [11- 14].

Barberry can improve immune system function and prevent repeated infections. In some studies, eucalyptus vaporizer declined the mucus density and enhanced its discharge. Moreover, a study demonstrated that peppermint was a potent anti-obstructive agent and relieved dry coughs by exerting sedative effects on throat and larynx [15].

Furthermore, slippery elm essential oil was demonstrated to be effective in reducing respiratory symptoms and relieving sore throat. The effective substances of stinging nettle have been used as expectorant. This plant has also antiviral effects. Moreover, *Allium sativum*, *Glycyrrhizaglabra*, Marshmallow, and *Zingiber officinalis* have been reported to be effective in reducing bronchitis-induced symptoms [16].

Ginger, scientifically called *Zingiber officinalis* Rosce, has played a significant role in Chinese, Japanese, and Indian traditional medicines since 1500 P.M. The root of *Z. officinalis* relieved nausea and vomiting due to pregnancy and chemotherapy, with cumulative effect with perchloroprazine. It also inhibited plaque aggregation [17].

Z. officinalis caused improvement of bronchitis-induced asthma although there has been no strong evidence to confirm this finding. However, in a study conducted in Shahrekord, Iran, *Z. officinalis* drop (150 mg/mL) was administered to patients with asthma three times a day. Wheezing relieved in 19.5% of the patients and chest pain relieved in 52% of them. Furthermore, asthma stage reduced in 8.7% of the patients. Coughing at night reduced considerably and the frequency of dyspnea decreased from 3.4 per week to 2.4 per week [18].

Recent investigations have demonstrated that *Z. officinalis* has antioxidant effects and is able to inhibit inflammatory compounds. Therefore, this plant has anti-inflammatory properties because of containing gingerols, and has been used to treat rheumatoid arthritis and osteoarthritis [19,20].

Marshmallow is a plant of family Althaeaceae. Marshmallow leaves can improve stimulated tissues and different types of inflammations, especially in mucus membranes. Because of having much emollient and adhesion, marshmallow is able to relieve mucus membranes [21].

Marshmallow is used as an anti-cough agent and to relieve dry and short coughs in laryngitis (I cough), cough, and whooping cough. Furthermore, it can enhance the immunity system function because it improves phagocytosis and macrophage. The daily use of Marshmallow is 5-6 g a day [22].

The anti-cough property of marshmallow was investigated on an Angiotensin converting enzyme inhibitor (ACEi) - induced cough in a double-blind study of 60 patients with hypertension under treatment with ACEi, and Marshmallow was demonstrated to relieve cough intensity in 75% of the patients and to improve cough in 25% of them.

In a study on the properties of *Z. officinalis*, this plant, combined with bitter kala, exerted antibacterial effects.

Regarding the anti-cough effects of *Z. officinalis* and Marshmallow demonstrated in previous studies with different mechanisms, this study was conducted to investigate the effect of combined *Z. officinalis* and Marshmallow on cough.

MATERIALS AND METHODS

First, 5000 mg/kg of drop was gavaged in rats and all toxic symptoms were investigated in the first 24 h and then once an hour. Regarding no death, previous findings about the two plants, drop standardization, AOT 425 software, and investigation of chronic, 28-day toxicity, we decided to administer 15 drops of hydroalcoholic extract, containing 40 mg/mL *Z. officinalis* and 300 mg/mL Marshmallow, each six hours.

For the protocol of this clinical trial, the ethical approval was provided by the Ethics Committee of the Shahrekord University of Medical Sciences. The plants used in this study were provided from the Iranian Medicinal Plants Preparation and Distribution Co. (no. 870737). The hydroalcoholic extract which contained 40 mg/mL Marshmallow and 300 mg/mL *Z. officinalis* was prepared by percolation. The dry extract was prepared by evaporation in an oven at 37°C,

The patients were enrolled in this study if they were 10-50 years, had no history of systemic diseases, did not take any medications on a chronic basis, had recently developed respiratory infection, had clinical symptoms of acute bronchitis, referred to the Pulmonary Diseases Clinic of the Shahrekord University of Medical Sciences and physicians' offices in Shahrekord, and provided consent to use the medicinal plant under study alongside routine treatments for acute bronchitis.

In this double-blind study, 60 patients that met the inclusion criteria were randomly assigned to two groups. The case group was administered with 15 *Z. officinalis* and Marshmallow herbal drops and the control group with 15 placebo drops each six hours for 10 h.

In this study, inhaled bronchodilator (combivent) and oral antihistamine (cetirizine) were used. The patients' symptoms, cough, coughing attacks at night, chest pain, and muscular pain were recorded in a researcher-developed questionnaire before and 10 days after treatment.

After 10 days of treatment, the patients were examined for the previous symptoms of coughing attacks and the results of examinations were compared with the data gathered from the questionnaires by independent t-test, chi-square, and McNemar's test.

RESULTS

The mean age of the patients was 34.6 ± 5.1 and 32.2 ± 6.5 years in the case and control groups, respectively. In the case and control groups, 18 (60%) and 16 (52%) patients were men, respectively ($P > 0.05$).

McNemar's test indicated that the clinical symptoms, cough, bone pain, and muscular pain, relieved significantly in the case group compared to the control group after the treatment ($P < 0.05$) (Table 1).

Case		Control				Group		Variable
After		Before		After		Before		
%	No.	%	No.	%	No.	%	No.	
60	18	100	30	20	6	100	30	Cough
23.3	7	48	14	3.3	1	42.3	13	Retrosternal pain
3.3	1	66.6	20	3.3	1	76.3	23	Bone pain
10	3	76.3	23	0	0	76.3	23	Muscular pain

Case group was administered with hydroalcoholic Zingiber officinalis root (40 mg) and Marshmallow (300 mg) combined extract for 10 days.
Control group was administered with placebo.
 $P < 0.05$
after treatment compared to before treatment

Chi-square indicated a significant difference in cough and retrosternal pain between the case and control groups ($P > 0.05$), but bone pain and muscular pain were not significantly different between the two groups after the treatment ($P > 0.05$) (Table 1).

DISCUSSION

This study indicated that the combined *Z. officinalis* and Marshmallow caused the improvement of patients' cough 10 days after development of acute bronchitis and early treatment of chest pain, trachite, and cough due to respiratory infection.

In a study of *Z. officinalis* anti-cough effect on relief of asthma symptoms, in addition to relatively weak improvement of forced expiratory volume in first second, the severity of asthma reduced by one stage through relief of reflex and asthma [13]. These findings are consistent with the present study.

In a study on the anti-cough effect of Marshmallow in reducing angiotensin inhibitors-induced cough in Shahrekord, Marshmallow improved dry cough and reduced cough intensity and degree through reducing inflammation and emollient property because of inhibiting the receptors in tracheobronchial tree. Consistently, in our study, cough improved and the cough intensity reduced within 10 days of treatment.

The exclusive use of beta-agonist drugs with prolonged effect failed to improve cough and acute bronchitis symptoms, and is not prescribed as a routine treatment [13,16]. The effects of *Z. officinalis* and Marshmallow have already been investigated separately. However, this study considered other mechanisms of cough and was conducted to investigate the synergistic effects of these two plants in relieving bronchitis symptoms.

The hydroalcoholic extract of combined *Z. officinalis* and Marshmallow was able to improve cough and the symptoms of acute bronchitis. The effect of this combined drug can be explained partially by improving gastrointestinal symptoms and reflex, which causes relief of cough intensity. However, recent studies have considered this explanation to a lesser extent.

The main effect mechanism of this combined drug is to relieve inflammation and mucilage property. Given the findings of this study, these herbal drugs are recommended to be prescribed for acute bronchitis patients, at least as adjuvant treatments, instead of frequent use of different antibiotics and antihistamines about which inconsistent findings have been obtained in different studies till larger studies are conducted. Since antihistamines cause drying of mucus, further studies are recommended to compare the effects of herbal drugs and antihistamines.

REFERENCES

- [1] RS Irwin; MH Baumann; DC Bolser; LP Boulet; SS Braman; CE Brightling; *Chest*. 2006, 129 (1), 1-23.

-
- [2] AS Fauci; E Braunwald; DL Kasper; SL Hauser; DL Longo; JL Jameson; Harrison's principles of internal medicine, 17th ed., McGraw-Hill, London, **2008**, 225-227.
- [3] PG Gibson; M Fujimura; A Niimi; *Thorax*, **2002**, 57(2), 178-182.
- [4] RA Haque; OS Usmani; PJ Barnes; *Chest*, **2005**, 127(5), 1710-1713.
- [5] D Knutson; C Braun; *Am Fam Physician*, **2002**, 65(10), 2039-2044.
- [6] S Chodosh; *Am J Med*, **1987**, 82(4A), 154-163.
- [7] RP Wenzel; AA Fowler; *N Engl J Med.*, **2006**, 355(20), 2125-2130.
- [8] R Gonzales; JF Steiner; MA Sande; *JAMA*, **1997**, 278, 901-904.
- [9] MS Chesnutt; TJ Prendergast; IN Lung; LM Tierney; Current medical diagnosis and treatment, 41st ed, McGraw-Hill, New York, **2002**, 269-362.
- [10] M Rafieian-Kopaei; N Shahinfard; H Rouhi- Boroujeni; M Gharipour; P Darvishzadeh- Boroujeni; Evidence-Based Complementary and Alternative Medicine, **2014**, 1-4.
- [11] H Rouhi-Boroujeni; M Gharipour; M Asadi-Samani; Rouhi-Boroujeni HA; *Der Pharmacia Lettre*, **2016**, 8 (3), 105-109.
- [12] H Rouhi-Boroujeni; H Mosharraf; M Gharipour; M Asadi-Samani; HA Rouhi-Boroujeni; *Der Pharmacia Lettre*, **2016**, 8 (3), 143-147.
- [13] H Rouhi-Boroujeni; HA Rouhi-Boroujeni; E Heidarian; F Mohammadzadeh; M Rafieian-Kopaei; *ARYA Atheroscler*, **2015**, 11(4), 252-258.
- [14] H Rouhi-Boroujeni; HA Rouhi-Boroujeni; M Gharipour; F Mohammadzadeh; S Ahmadi; M Rafieian-Kopaei; *Acta Biomed*, **2015**, 14, 86(2), 130-136.
- [15] EA Bryer; *J Midwifery Women's Health*, **2005**, 50(1), 1-3.
- [16] LL Dupuis; PC Nathan; *Paediatr Drugs*, **2003**, 5(9), 597-613.
- [17] H Rouhi; F Ganji; H Nasri; *Pak J Nutr*, **2006**, 4, 373-376.
- [18] I Wigler; I Grotto; D Caspi; M Yaron; *Osteoarthritis Cartilage*, **2003**, 11(11), 783-789.
- [19] RD Altman; KC Marcussen; *Arthritis Rheum*, **2001**, 44(11), 2531-2538.
- [20] H Rouhi; F Ganji; *Pak J Nutr*, **2007**, 6(3), 256-258.
- [21] S MK Nourbakhsh; HA Rouhi-Boroujeni; M Kheiri; M Mobasheri; M Shirani; S Ahrani; J Karami; Z Keivani; *Journal of Clinical and Diagnostic Research*, **2016**, 10(1), WC04-WC06
- [22] H Matthys; R Eisebitt; B Seith; M Heger; *Phytomedicine*, **2003**, 4(10), 7-17