DOI: 10.35845/kmuj.2019.18883

EFFECTIVENESS OF HERBAL COMBINATION OF IVY, THYME AND CISTI EXTRACTS IN MANAGEMENT OF ACUTE COUGH IN CHILDREN AND ADULTS

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Date Submitted: December 26, 2018
Date Revised: July 28, 2019
Date Accepted: July 30, 2019

ABSTRACT

OBJECTIVE: To determine the efficacy of herbal combination of Ivy, Thyme, and Cisti extracts in management of acute cough in children and adults.

METHODS: An open label study was conducted to assess the efficacy of herbal combination of Ivy, Thyme and Cisti extracts in relieving acute cough. It was conducted from 1st December 2017 till 28th February 2018 in Children's Hospital and Services Institute of Medical Sciences, Lahore and Saifee Hospital, Karachi, Pakistan. It was completed by 157 participants of age 2-75 years who reported their cough frequency, severity, and bothersomeness score on a Likert scale of 0 (not at all) to 6 (extremely). Data was entered and analyzed using SPSS v.21.

RESULTS: There were 53.5% males and 46.5% females with mean age of 20.1±19.1 years. The most common clinical features with cough were sputum (70%) and fever (70%). The age group 2-12 years included 53.5% patients who showed significant improvement in frequency (from 4.33±1.13 to 0.69±0.97 in night time and 3.98±1.00 to 0.58±0.88 in daytime), severity (from 4.19±0.99 to 0.65±0.91 in night time and 3.99±1.13 to 0.44±0.84 in daytime), and bothersomeness (from 4.04±1.08 to 0.46±0.83 in night time and 3.86±1.15 to 0.48±0.85 in daytime) with three days of therapy with of Ivy, Thyme and Cisti extracts syrup. No side effect was reported with three days of therapy.

CONCLUSION: Our study concluded that herbal combination of Ivy, Thyme, and Cisti extracts is an efficacious natural cough suppressant in terms of frequency, severity and bothersomeness of cough.

KEY WORDS: Herbal Medicines (MeSH); Cough suppression (Non-MeSH); Phytomedicine (Non-MeSH); Ivy extract (Non-MeSH); Thyme extract (Non-MeSH); Cisti extract (Non-MeSH); Thymus Plant (MeSH); Cistus (MeSH); Hedera (MeSH); Children (MeSH).

THIS ARTICLE MAY BE CITED AS: Rana MN, Masood MK, Fahim U, Siddiqui AS. Effectiveness of herbal combination of Ivy, Thyme and Cisti extracts in management of acute cough in children and adults. Khyber Med Univ J 2019;11(3):165-9. DOI: 10.35845/kmuj.2019.18883

INTRODUCTION

Cough is one of the most common reasons for seeking medical attention and also a very troublesome and persistent symptom.[1] Cough is frequently caused by exposure to environmental allergens or acute viral URTIs and its course is self-limiting, however, bacterial super-infection is frequently seen.[2] Acute cough is usually short-lived and resolve with removal of allergic agent or medication. However, chronic cough has various underlying causes. The prevalence of chronic cough in general population is found to be around 2.5% according to a Korean study.[3]

Classic mucolytics, including N-acetyl cysteine (NAC), have shown little or no evidence in alleviating cough by helping in mucus expectoration. Over the counter (OTC) cough syrups and cough suppressants have also shown little consistency in cough alleviation.[4] Herbal medicines, including phytotherapy and hydrotherapy, have long been utilized in various cultures for cough and other upper respiratory tract symptoms. Although, randomized controlled studies (RCTs) are being conducted to assess the effects of herbal medicines in alleviating cough, the data is still generally lacking.[5] A number of other medicinal plants are in use for cough suppression since decades. Some of these include Adhatoda zeylanica, Viola odorata, Malva sylvestris and hundreds of others.[6]

Three herbal extracts – Ivy leaf extracts (*Hedera helix*), Thyme extracts (*Thymus vulgaris*), and Cisti extracts (*Cistus creticus*) – have shown considerable benefits in alleviating acute cough and have also attracted researchers to dig out more about their therapeutic uses.[7] Ivy leaf extracts contains saponins which have mucolytic, spasmolytic, bronchodilatory and antibacterial properties. Its component alfa hederin acts as an inhibitor of the β_2 receptors endocytosis, resulting in indirect β_2 sympathomimetic action.[8] Thyme is a bronchial antispasmodic, antitussive, and expectorant with mucolytic and macrophage-inhibiting effects on upper respiratory tract.[9] Cisti is an immunostimulant for common cold and cough. Its active constituents are polyphenolic compounds. They exhibit

TABLE I: CHANGE IN COUGH SCORE AFTER 3 DAYS OF THERAPY WITH IVY, THYME AND CISTI LEAVES EXTRACTS (n=157)

Cough Score		Mean ± SD	95% CI	p value*
Night Cough Frequency	Start of therapy	4.83±1.23	3.69-4.23	< 0.001
	After 3 days of therapy	0.87±1.16		
Night Cough Severity	Start of therapy	4.68±1.22	3.57-4.11	< 0.001
	After 3 days of therapy	0.84±1.14		
Night Cough Bothersome	Start of therapy	4.64±1.30	3.63-4.17	< 0.001
	After 3 days of therapy	0.74±1.12		
Day Cough Frequency	Start of therapy	4.58±1.27	3.58-4.13	< 0.001
	After 3 days of therapy	0.72±1.10		
Day Cough Severity	Start of therapy	4.57±1.32	3.65-4.19	< 0.001
	After 3 days of therapy	0.65±1.06		
Day Cough Bothersome	Start of therapy	4.50±1.37	3.54-4.12	< 0.001
	After 3 days of therapy	0.66±1.10		

*Paired sample t-Test applied

TABLE II: CHANGE IN COUGH SCORE AFTER THERAPY WITH IVY, THYME AND CISTI LEAVES EXTRACTS (POPULATION AGE 2-12 YEARS)

Cough Score		Mean ± SD	95% CI	p value*
Night Cough Frequency	Start of therapy	4.33±1.13	3.32–3.95	< 0.001
	After 3 days of therapy	0.69±0.97		
Night Cough Severity	Start of therapy	4.19±0.99	3.23–3.83	< 0.001
	After 3 days of therapy	0.65±0.91		
Night Cough Bothersome	Start of therapy	4.04±1.08	3.26–3.88	< 0.001
	After 3 days of therapy	0.46±0.83		
Day Cough Frequency	Start of therapy	3.98±1.00	3.13–3.66	< 0.001
	After 3 days of therapy	0.58±0.88		
Day Cough Severity	Start of therapy	3.99 ±1.13	3.25–3.83	< 0.001
	After 3 days of therapy	0.44±0.84		
Day Cough Bothersome	Start of therapy	3.86±1.15	3.08–3.69	< 0.001
	After 3 days of therapy	0.48±0.85		

*Paired sample t-Test applied

TABLE III: CHANGE IN COUGH SCORE AFTER THERAPY WITH IVY, THYME AND CISTI LEAVES EXTRACTS (POPULATION AGE > 12 YEARS)

Cough Score		Mean ± SD	95% CI	p value*
Night Cough Frequency	Start of therapy	5.46±1.04	3.93–4.80	< 0.001
	After 3 days of therapy	1.09±1.33		
Night Cough Severity	Start of therapy	5.29±1.20	3.74–4.68	< 0.001
	After 3 days of therapy	1.08±1.33		
Night Cough Bothersome	Start of therapy	5.37±1.18	3.83–4.74	< 0.001
	After 3 days of therapy	1.08±1.32		
Day Cough Frequency	Start of therapy	5.33±1.16	3.94–4.92	< 0.001
	After 3 days of therapy	0.89±1.32		
Day Cough Severity	Start of therapy	5.28±1.19	3.91–4.85	< 0.001
	After 3 days of therapy	0.89±1.25		
Day Cough Bothersome	Start of therapy	5.28±1.21	3.88–4.88	< 0.001
	After 3 days of therapy	0.89±1.32		

*Paired sample t-Test applied

a range of antibacterial, antifungal, anti-inflammatory, antioxidant and immunostimulatory effects.[10-12] The antiviral activity of a specific Cistus incanus plant extract (CYSTUS052) has been demonstrated against influenza A virus infections.[13]

Herbal medicines for acute cold, cough, and flu have been a key interest of manufacturers as well as the general practitioners in the recent years due to their obvious benefits over synthetic, chemical-based cough syrups including minimal to no side effect profile – especially no drowsiness – over the counter availability and significant cost affectivity with herbal products. Despite the economic and epidemiological significance of herbal cough syrups, methodically strong and compact clinical studies are scarce.

In this prospective open study a powerful and natural combination of all three herbal extracts (Ivy leaf, Thyme and Cisti extracts) was investigated for the clinical efficacy in management of acute cough.

METHODS

Patients of age two years till seventy-five years of age presenting with the primary complaint of cough were recruited in this open label study. It was conducted from 1st December 2017 till 28th February 2018 in Children's Hospital and Services Institute of Medical Sciences, Lahore and Saifee Hospital, Karachi Pakistan. The total duration of study was 3 months. It was approved by the ethics and review committee of Dow University of Health Sciences Karachi, Pakistan. This open label study was also registered at https://clinicaltrials.gov/ with identifier no: NCT02981147.

Acute cough was defined as cough lasting for less than eight weeks.[14,15] Cough may or may not be associated with sputum, nasal discharge, sore throat, fever and body aches. Patients presenting with one of the above complaints without complaint of cough were not included. Furthermore, patients with cough along with lower respiratory tract infections, croupy cough and sub-acute and chronic cough were also excluded from the study. The treatment of cough associated with lower respiratory tract infections involves identifying the causative agent along with cough suppressants; hence we excluded its use which could

TABLE IV: COMPARISON OF COUGH SCORE OF AGE LESS THAN AND MORE THAN TWELVE YEARS AFTER THERAPY WITH IVY, THYME AND CISTI LEAVES EXTRACTS

Cough Score		N	Mean ± SD	95% CI	p value*
Night Cough Frequency	< 12 years	80	0.69±0.97	0.01- 0.75	0.04
	> 12 years	68	1.07±1.30		
Night Cough Severity	< 12 years	80	0.65±0.91	0.04- 0.77	0.02
	> 12 years	68	1.06±1.31		
Night Cough Bothersome	< 12 years	78	0.46±0.83	0.24 – 0.95	0.001
	> 12 years	68	1.06±1.30		
Day Cough Frequency	< 12 years	80	0.58±0.88	0.05 – 0.66	0.09
	>12 years	67	0.88±1.29		
Day Cough Severity	< 12 years	79	0.44±0.84	0.10 – 0.77	0.01
	> 12 years	68	0.88±1.22		
Day Cough Bothersome	< 12 years	80	0.48±0.85	0.05 – 0.76	0.02
	> 12 years	68	0.88±1.29		

*Independent sample t-Test applied

possibly bias the results. Patients having chest examination findings such as wheezing or crepitations or any sign of heart failure, respiratory failure, asthma exacerbation or chronic cough were excluded from the study.

The sample size calculated via OpenEpi was 139. Two hundred and twenty patients were invited to participate, one hundred and fifty-seven patients were responded and remaining patients were lost to follow up. During the study period complete therapy to the patients were provided free of cost. Patients were called to follow up using their phone numbers.

After collecting sociodemographic details of the participants, all the patients were prescribed a Thyme-Ivy-Cisti extract in syrup form, for three days, according to their age adjusted daily dose as below:

Children of age 2 to 6 years; 2.5ml twice daily

Children of age 6 to 12 years: 5ml twice daily

Adolescents, adults and elderly: 5ml thrice daily

A validated cough questionnaire measuring 3 aspects of daytime and nighttime cough (frequency, severity, bothersomeness) on a 7 point Likert scale was used each evening, for three days and nights, to rate for the past day, as regards these aspects. The scale rates each parameter from 0 to 6. The Likert scale can be used in many different conditions. It is an individual based analysis of his qualitative condition into quantity with zero being the least and 6 being the highest variable.[16]

Data was entered and analyzed using SPSS v.21. Frequency and percentage were deduced for independent variables such as age, gender and clinical symptoms. Paired sample t test was applied to deduce p value of the frequency, severity and bothersomeness of day and night cough on start of therapy and after three days of therapy. Independent sample t test was applied to compare the score of frequency, severity and bothersomeness of day and night cough after three days of therapy of participants 2-12 years of age and those of more than 12 years of age.

RESULTS

One hundred and fifty-seven participants completed the study, out of which 86 (54.7%) were males 71 (45.2%) were females. The mean age of the sample was 20.1±19.1 years. Eighty four (53.5%) patients were aging less than 12 years and 73 (46.5%) were more than 12 years of age. The most common clinical features recorded along with cough were sputum (70.7%) and fever (70.7%), followed by sore throat (66.9%), nasal discharge (54.8%) and body aches (51.0%).

The nighttime and daytime cough score of the study population at baseline and after three days of therapy were assessed. Both daytime and nighttime cough was significantly improved in all three parameters – frequency, severity and bothersomeness. The nighttime frequency improved from a mean ± SD of 4.83±1.23 to 0.87±1.16, and daytime frequency improved from a mean±SD of 4.58±1.27 to 0.72±1.10. All scores are shown in Table I.

Paired sample t test was applied to deduce the improvement in cough score at baseline and after three days of therapy with Ivy, Thyme, and Cisti extracts combination in participants of both the age groups.

The younger age group showed remarkable improvement in all three parameters. The nighttime frequency improved from a mean±SD of 4.33±1.13 to 0.69±0.97, and the daytime frequency improved from a mean±SD of 3.98±1.00 to 0.58±0.88. All score are shown in Table II. The older group of age twelve years and more also showed significant improvement in cough in all three parameters. The nighttime frequency improved from a mean±SD of 5.46±1.04 to 1.09±1.33 and daytime frequency improved from a mean±SD of 5.33±1.16 to 0.89±1.32. All scores are shown in Table III.

Both age groups have shown significant improvement in symptoms (Table II and III). However, when the improvement after three days of therapy was compared between the two groups; it was seen that the younger age groups has more significant improvement in few parameters (Table IV). No side effect was reported with three days of therapy.

DISCUSSION

Natural combination of three herbal extracts (Ivy leaf, Thyme, and Cisti extracts) – also called as a "nutraceuticals product" – in the form of a cough syrup has shown significant improvement in acute cough over three days, more in children but also in adults too. Although these herbal extracts have been studied either as mono-preparations or a combination of two, to our knowledge, a combined effect of Ivy, Thyme and Cisti as herbal medicine

has not been studied before this trial.

As far as the role of traditional OTC chemical combinations for cough suppressants are concerned; studies have shown conflicting evidences. There is no good evidence for or against the effectiveness of OTC medicines in acute cough.[4] In another study, conducted on children with acute cough, the best score was seen in children to which the group prescribed "honey," while the "dextromethorphan" group was not any better than "no treatment" group.[17] In another pediatric study, neither diphenhydramine nor dextromethorphan produced any superior outcomes than the placebo group.[18]

The role of a nutraceutical polyherbal cough syrup was evaluated for its antihistaminic properties by the inhibition of histamine induced contractions on the guinea pig ileum. The results were supportive and the effect of the formulated cough syrup was well comparable with the standard diphenhydramine syrup.[19] Previously, open trials, as post marketing surveillance-studies sponsored by the manufacturers, have been conducted to investigate Ivy mono-preparations as well as Ivy/Thyme combinations as potential nutraceutical cough syrups.[20-22] Improvement or cure after treatment has been observed in almost 90%. Global efficacy has been rated as "good" or "very good" by physicians in 77–86%.[23,24]

Where in the previous open studies, the duration of treatment ranged from 7-12 days, our study of a combination regimen showed significant improvement in three days only.[22,23] The role of Cisti extracts is crucial in early alleviation of cough as it boosts the immune system and helps revert to the norm promptly. Cisti extracts as monotherapy or in combination with other herbal extracts has been minimally studied for benefits in upper respiratory tract infections (URTIs). In its first prospective, placebo controlled clinical study, Cistus incanus was found to be more effective than placebo in reducing the average duration and severity of symptoms in patients with URTIs with viral etiology.[25]

This first open label study with a combination of Ivy, Thyme and Cisti extracts has shown remarkable efficacy in shorter period of time over an extensive age range of patients. However, there is still a need of further detailed controlled studies with special populations to have a comprehensive profile of the efficacy, tolerability and safety of this herbal combination. Future studies should approach specific issues concerning concomitant therapy and baseline conditions.

CONCLUSION

This first of its kind, open study has shown significant improvement of cough with herbal combination of Ivy, Thyme and Cisti extracts in terms of frequency, severity and bothersomeness. No side effect were reported during the study period. Further randomized controlled clinical studies should be conducted to assess the efficacy, tolerance and safety of this combination in management of acute cough.

ACKNOWLEDGMENT

Authors acknowledge the facilitation by "Clinision" [www.clinision.com] and PharmEvo (Pvt) Ltd Pakistan for providing academic and financial grant for this research project.

REFERENCES

1. Irwin RS, French CT, Lewis SZ, Diekemper RL, Gold PM, Adams TM, et al. Overview of the management of cough: CHEST guideline and expert panel report. Chest 2014;146(4): 885-9. DOI: 10.1378/chest.14-1485.
2. Irwin RS, Madison JM. The diagnosis and treatment of cough. New Engl J Med 2000;343(23):1715-21. DOI: 10.1056/NEJM200012073432308.
3. Koo HK, Jeong I, Lee SW, Park J, Kim JH, Park SY, et al. Prevalence of chronic cough and possible causes in the general population based on the Korean National Health and Nutrition Examination Survey. Medicine (Baltimore) 2016 Sep;95(37):e4595. DOI: 10.1097/MD. 0000000000004595.
4. Smith SM, Schroeder K, Fahey T. Over-the-counter (OTC) medications for acute cough in children and adults in community settings. Cochrane Database Syst Rev 2014;(11): CD001831. DOI: 10.1002/14651858.CD001831.pub5.
5. Wagner L, Cramer H, Klose P, Lauche R, Gass F, Dobos G, Langhorst J. Herbal medicine for cough: a systematic review and meta-analysis. Forsch Komplementmed 2015;22(6):359-68. DOI: 10.1159/000442111.
6. Jahan Y, Mahmood T, Bagga P, Kumar A, Singh K, Mujahid M. Future prospects of cough treatment; herbal medicines v/s modern drugs. Int J Pharm Sci Res 2015 Sep 1;6(9):3689-97.
7. Schmidt S. Ivy leaf cough mixtures. SA Pharmacist's Assistant 2017 Apr 1;17(2):5-6.
8. Hegener O, Prenner L, Runkel F, Baader SL, Kappler J, Häberlein H. Dynamics of β2-adrenergic receptor− ligand complexes on living cells. Biochemistry 2004;43 (20):6190-9. DOI: 10.1021/bi035928t.
9. Hosseinzadeh S, Jafarikukhdan A, Hosseini A, Armand R. The application of medicinal plants in traditional and modern medicine: a review of Thymus vulgaris. Int J Clin Med 2015;6(9):635-42. DOI:10.4236/ijcm.2015.69084.
10. Cos P, Bruyne TD, Hermans N, Apers S, Berghe DV, Vlietinck AJ. Proanthocyanidins in health care: current and new trends. Curr Med Chem 2004;11(10):1345-59. DOI: 10.2174/0929867043365288.
11. Arts IC, Hollman PC. Polyphenols and disease risk in epidemiologic studies. Am J Clin Nutr 2005;81(1):317S-25S. DOI: 10.1093/ajcn/81.1.317S.
12. Halliwell B, Rafter J, Jenner A. Health promotion by flavonoids, tocopherols, tocotrienols, and other phenols: direct or indirect effects? Antioxidant or not? Am J Clin Nutr 2005;81(1):268S-76S. DOI: 10.1093/ajcn/81.1.268S.
13. Ehrhardt C, Hrincius ER, Korte V, Mazur I, Droebner K, Poetter A, et al. A polyphenol rich plant extract, CYSTUS052, exerts anti influenza virus activity in cell culture without

toxic side effects or the tendency to induce viral resistance. Antiviral Res 2007;76(1):38-47. Doi: 10.1016/j.antiviral.2007.05.002.

14. Shields MD, Thavagnanam S. The difficult coughing child: prolonged acute cough in children. Cough 2013;9(1):11. DOI: 10.1186/1745-9974-9-11.
15. Holzinger F, Beck S, Dini L, Stöter C, Heintze C. The diagnosis and treatment of acute cough in adults. Dtsch Ärztebl Int 2014;111(20):356. DOI: 10.3238/arztebl.2014.0356.
16. Herman AC, Clalit HS. Comparison of Efficacy and Tolerability of Two Cough Syrups in Cough Due to Cold in Children. 2015. In: ClinicalTrials.gov Bethesda (MD): National Library of Medicine (US). [Cited on: Dec 24, 2018]. Available from URL: https://clinicaltrials.gov/ct2/show/NCT02486835. NLM Identifier:NCT02486835.
17. Paul IM, Beiler J, McMonagle A, Shaffer ML, Duda L, Berlin CM. Effect of honey, dextromethorphan, and no treatment on nocturnal cough and sleep quality for coughing children and their parents. Arch Pediatr Adolesc Med 2007;161(12):1140-46. DOI: 10.1001/archpedi.161.12.1140.
18. Paul IM, Yoder KE, Crowell KR, Shaffer ML, McMillan HS, Carlson LC, et al. Effect of dextromethorphan, diphenhydramine, and placebo on nocturnal cough and sleep quality for coughing children and their parents. Pediatrics 2004;114(1):e85-e90. DOI: 10.1542/peds.114.1.e85.
19. Sunilson JAJ, Anandarajagopal K, Khan A, Pasha K, Hassan QB, Raja PVK. Antihistaminic evaluation of formulated polyherbal cough syrup. J Med Plant Res 2013;4(14):1482-85. DOI: 10.5897/JMPR09.234.
20. Santoro M Jr. Evaluation of Hedera helix as an expectorant in patients with productive cough. A multicenter study over 5850 patients. Rev Bras Med 2011;62(1):47-52.
21. Fazio S, Pouso J, Dolinsky D, Fernandez A, Hernandez M, Clavier G, et al. Tolerance, safety and efficacy of Hedera helix1 extract in inflammatory bronchial diseases under clinical practice conditions: A prospective, open, multicentre postmarketing study in 9657 patients. Phytomed 2009;16(1):17-24. DOI: 10.1016/j.phymed.2006.05.003.
22. Hecker M. Efficacy and tolerance of Ivy extract (Prospan®) in patients suffering from respiratory tract diseases. Nat Med 1999;14:28–33.
23. Büechi S, Vögelin R, von Eiff MM, Ramos M, Melzer J. Open trials to assess aspects of safety and efficacy of a combined herbal cough syrup with Ivy and Thyme. Complement Med Res 2005;12(6):328-32. DOI: 10.1159/000088934.
24. Marzian O. Treatment of acute bronchitis in children and adolescents. Non-interventional postmarketing surveillance study confirms the benefit and safety of a syrup made of extracts from Thyme and Ivy leaves. MMW Fortschr Med 2007;149(27-28 Suppl):69-74.
25. Kalus U, Grigorov A, Kadecki O, Jansen JP, Kiesewetter H, Radtke H. Cistus incanus (CYSTUS052) for treating patients with infection of the upper respiratory tract: a prospective, randomised, placebo-controlled clinical study. Antiviral Res 2009;84(3):267-71. DOI: 10.1016/j.antiviral.2009.10.001.

AUTHORS' CONTRIBUTIONS

Following authors have made substantial contributions to the manuscript as under:

MNR: Concept and study design, providing data, drafting the manuscript, final approval of the version to be published

MKM & UZ: Providing data, review the manuscript, final approval of the version to be published

ASS: Analysis & interpretation of data, drafting and the manuscript, critical review, final approval of the version to be published

Authors agree to be accountable for all aspects of the work in ensuring that questions related to the accuracy or integrity of any part of the work are appropriately investigated and resolved.

CONFLICT OF INTEREST

Authors declared no conflict of interest

GRANT SUPPORT AND FINANCIAL DISCLOSURE

Financial support by PharmEvo (Pvt) Ltd. Pakistan

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