ISSN: 0976-3104
SUPPLEMENT ISSUE: Biological Science

ARTICLE

HERBAL MEDICINE AND PULMONARY DISORDERS: A SYSTEMATIC REVIEW AND META-ANALYSIS OF UPDATED CLINICAL TRIALS

Hamid Rouhi-Boroujeni[1], Soheila Mosharraf[2], Ehsan Bakhshian Dehkordi[3], Hojjat Rouhi-Boroujeni[4*]

[1]*Pulmonologist, Associate professor of Clinical Biochemistry, Shahrekord University of Medical Sciences, Shahrekord, IRAN*

[2]*General Practitioner, Isfahan University of Medical Sciences, Isfahan, IRAN*

[4*]*Student Research Committee, Medical plants Research Center, Shahrekord University of Medical Sciences, Shahrekord, IRAN*

[4] *Cellular and Molecular Research Center, Shahrekord University of Medical Sciences, Shahrekord, IRAN*

ABSTRACT

Background: Recently, particular attentions have been focused the effective role of herbal drugs in chronic disease conditions, malignancies, and also allergic and inflammatory diseases. The current systematic review and meta-analysis attempted to summate recent evidences on the use of herbal drugs to treat various types of lung diseases in different nations. Methods: Studies were identified by searching electronic databases including Cochrane Library, Medline, Embase and Cinahl databases, and the Social Sciences Citation Index, scanning reference lists of included articles and consultations with experts in the field. Our sample is based on data published during recent five years from 2009 to 2014. Among 215 studies reviewed based on the included keywords, 48 med the study criteria and finally reviewed. Results: Overall, 15061 patients included into the analysis that among those, 11852 had COPD, 1324 were diagnosed to have non-small-cell lung cancer (NSCLC), 1012 suffered asthma, 492 had pneumonia, 172 had ARDS, 146 had radiation-induced pneumonitis, and 63 had lung contusion. The used herbal drugs could affect by different mechanisms including increase of pulmonary functional parameters including FEV1/FVC, PaO2/FiO2, and peak expiration flow rate as well as lowering inflammatory biomarkers such as cytokines of interleukin-6 (IL-6), interleukin-8, tumor necrosis factor-alpha, and transformation growth factor-beta1 leading improvement of clinical manifestations (indicated by lowering symptom score), increase of survival rate (in malignant states), reduce of ICU stay, reduce of ventilation time, improvement of quality of life, and lowering level of depression and anxiety. Conclusion: According to the pointed beneficial effects of herbal therapy, this option can be a good alternative for treatment with chemical drugs in various types of malignant, inflammatory, obstructive, and sensitivity-based pulmonary disorders.

KEY WORDS
Herbal medicine, pulmonary, meta-analysis, clinical trials

Received: 31 Jan 2017
Accepted: 28 Feb 2017
Published: 16 March 2017

***Corresponding Author**
Email:
dr_rohib@yahoo.com

INTRODUCTION

A long history of herbal medicine has been recorded to treat various types of diseases. By developing drugs derived from medicinal plants, the use of chemical drugs has been relatively declining [1]. In any individual culture, the materials used were those that were available within the geographical location and addressed local health concerns; however with exposing cultural traditions as well as overwhelming traditional medicine by modern scientific concepts, the use of herbal remedies is global regardless of geographic, ethnic, or cultural aspects [2,3]. The developments of chemically synthesized drugs have revolutionized healthcare services in whole of the word, but large sections of the population in developing countries still rely on traditional and herbal medicines for their primary care [4]. In Africa, up to 90% and in India 70% of the population tend to use traditional medicine to achieve healthcare needs. Besides, in China, herbal medicine accounts for about half of healthcare delivered and more than 90% of general hospitals in this country have especial units for herbal medicine [5]. Most importantly, using traditional medicine is not limited to developing countries so that during the recent decades, the interest in applying natural medicine has greatly increased in developed countries [6, 7]. This tendency has also expanded remarkably even in American and European countries so that about one-third of Americans [8, 9] and approximately 20% of Europeans [10, 11] tend to use herbal therapy. The most frequent reasons for applying herbal medicine include more affordability, more closely corresponding to the individual's ideology, allaying concerns about the adverse effects of chemical synthetic drugs, satisfying a desire for more personalized healthcare, and allowing greater public access to health information [12]. However, the use of herbal medicines is mostly considered unfortunately when conventional medicine is ineffective in the treatment of disease.

Recently, particular attentions have been focused the effective role of herbal drugs in chronic disease conditions, malignancies, and also allergic and inflammatory diseases. Recent investigations have been demonstrated beneficial effects of herbal medicine in many types of pulmonary diseases such as obstructive pulmonary lung disease (COPD), lung cancer, asthma, and even pneumonia in both children and adults. The current systematic review attempted to summate recent evidences on the use of herbal drugs to treat various types of lung diseases in different nations.

MATERIALS AND METHODS

Study population & data collection

Methods of the systematic review were specified in advance and documented in a published protocol in the International Prospective Register of Systematic Reviews (PROSPERO). Studies were identified by searching electronic databases including Cochrane Library, Medline, Embase and Cinahl databases, and the Social Sciences Citation Index, scanning reference lists of included articles and consultations with experts in the field. Our sample is based on data published during recent five years from 2009 to 2014 because of large volumes of studies on selected keywords and also knowledge of the latest results of studies on effects of herbal therapy in lung diseases. Only English language manuscripts and the manuscript with the available full texts were reviewed. Controlled vocabulary and keywords focused on "herbal medicine", "pulmonary disease", "lung", "herb" and "clinical trial". The clinical trial study design was only imposed. Studies were included regardless of study quality. The following data were extracted from each paper: country, description of the sample, type of pulmonary disease, type of herbal drugs, age range of patients, date of data collection, criteria measured, and standards used to judge quality, and the results. Two reviewers independently assessed studies identified by the search for eligibility based on the title and abstract. Selected full text papers were then assessed independently by the two reviewers. Among 205 studies reviewed based on the included keywords, 47 med the study criteria and finally reviewed [13-59].

Quality assessment of studies:

The selected studies were heterogeneous in terms of studied pulmonary disease, country, and scientific rigor. It was therefore inappropriate to aggregate or conduct a detailed quantitative analysis of the data. Instead, we assessed the studies using the following criteria: type of disease, patient's age range, sampling strategy, and sample size. These criteria were applied in a structured way to each of the selected studies. As for the data extraction, the quality assessment of the study methodology was performed. The quality criteria were found to be easy to apply to the papers and no differences were found between assessors. The main reviewed endpoint was the effects of different types of herbal drugs on pulmonary function status, symptoms score, inflammatory biomarkers, survival rate, as well as quality of life and depression-anxiety status.

Statistical analysis:

In meta-analysis phase, the k statistic was used to assess the agreement between two reviewers for study selection. The pooled relative risk (RR) was calculated for each outcome using the inverse-variance method for random effect, as well as for fixed effects [14]. The data heterogeneity was assessed using the Cochrane Q test via a $\chi 2$ test and quantified with the I2 test [15]. We used the log RR as the dependent variable. The log RR standard error was used to measure the within-study variability, and the residual maximum likelihood method was used to estimate the between-study variance. All analyses were performed using STATA version 11.0 (Stata Corp; College Station, TX) and SPSS version 21.0 for windows (SPSS Inc., Chicago, IL).

RESULTS

Among 205 records retrieved from the initial search, 47 studies were reviewed in full-text that all included in the meta-analysis. The inter-reviewer agreement for the study selection was high with k= 0.93. Overall, 15061 patients included into the analysis that among those, 11852 had COPD, 1324 were diagnosed to have non-small-cell lung cancer (NSCLC), 1012 suffered asthma, 492 had pneumonia, 172 had RDS, 146 had radiation-induced pneumonitis, and 63 had lung contusion. Two studies were published in 2014, 9 in 2013, 12 in 2012, 16 in 2011, and 7 in 2010. No obvious heterogeneity was also identified among the included studies ($x2 = 6.55$, p for $x2 = 0.428$; $I2 = 6.6\%$). In 11 studies, a combination of traditional Chinese herbal drugs was used as the intervention protocol. In studies which assessed the efficacy of herbal medicine on improvement of COPD, the use of this treatment protocol resulted in increase of FEV1/FVC ratio, reduce of inflammatory biomarkers such as interleukin-6 (IL-6), interleukin-8, tumor necrosis factor-alpha, and transformation growth factor-beta1, reduce of acute exacerbation frequency, reduce of lung symptoms score, increase of 6-min walking diameter, as well as improvement of health-related quality of live and reduce of depression-anxiety score. In patients who suffered NSCLC, using herbal drugs could considerably increase survival rate, improve quality of life, reduce inflammatory markers, reduce bone marrow suppression, and also reduce tumor markers. Those who were diagnosed to have asthma faced improvement of FEV1/FVC ratio, reduce of symptoms score, reduce of inflammatory biomarkers, increase of peak expiration flow rate, reduce of recurrence rate, increase of IgG immunoglobulin, and also increase the asthmatic drug effective rate. Herbal therapy could effectively result in increase of FEV1/FVC, reduce of inflammatory marker as well as reduce of ICU stay and ventilation time. In those patients with pneumonia, applying herbal therapy led to reduce symptoms score, reduce inflammatory biomarkers as well as improve level of quality of life. In the patients who experienced radiation-induced pneumonitis, herbal medicine could achieve increased Karnofsky Performance Status Scale (KPS) score and also reduced lung injury and dyspnea score. In a study that assessed the effects of

herbal medicine on acute respiratory distress syndrome (ARDS), PaO2/FiO2 index was successfully improved.

DISCUSSION

Many herbs and their,s compounds have been used for Asthma, Bronchitis and COPD [.60, 61].
Our review could show beneficial effects of different types of herbal drugs on a variety of inflammatory, sensitivity-based, obstructive, and even malignant pulmonary disorders in both children and adults. In this regard, reviewed clinical trials performed within recent six years showed high efficacy of herbal medicine in treatment of COPD, asthma, NSCLC, pneumonia, radiation-induced pneumonitis, and pulmonary contusion. In fact, the used herbal drugs could affect by different mechanisms including increase of pulmonary functional parameters including FEV1/FVC, PaO2/FiO2, and peak expiration flow rate as well as lowering inflammatory biomarkers such as cytokines of interleukin-6 (IL-6), interleukin-8, tumor necrosis factor-alpha, and transformation growth factor-beta1 leading improvement of clinical manifestations (indicated by lowering symptom score), increase of survival rate (in malignant states), reduce of ICU stay, reduce of ventilation time, improvement of quality of life, and lowering level of depression and anxiety. It seems that in some trials on disorders with immunosuppressive basis, the use of herbal drugs led to increase of serum immunoglobulin. In total, according to the pointed beneficial effects of herbal therapy, this option can be a good alternative for treatment with chemical drugs.

Besides the efficacy of herbal drugs on benign obstructive or inflammatory pulmonary disorders, the effects of herbs on cancer-related survival may be mediated by different mechanisms such as their anti-inflammatory effects (because inflammation is linked to increased risk of cancer), influence on carcinogen bioactive mediators such as cytochrome P450, alteration the proliferation of several cultured cancerous cells, as well as their antioxidant effects [62-67]. Of 177 drugs approved worldwide for treatment of cancer, more than 70% are based on natural products or mimetics, many of which are improved with combinatorial chemistry. Cancer therapeutics from plants include paclitaxel, isolated from the Pacific yew tree; camptothecin, derived from the Chinese “happy tree” Camptotheca acuminata and used to prepare irinotecan and topotecan; and combretastatin, derived from the South African bush willow [68]. More than 100 natural product–based drugs are in clinical studies [69], and of the total 252 drugs in the World Health Organization’s (WHO) essential medicine list, 11% are exclusively of plant origin [70]. However, herbal drugs against lung cancers are now under-assessed in world laboratories. Because of beneficial effects of herbal drugs, the side effects of these drugs should not be also ignored. Herbal extracts may be contaminated, adulterated, and may contain toxic compounds. The quality control of herbal medicines has a direct impact on their safety and efficacy. But, there is little data on the composition and quality of most herbal medicines not only due to lack of adequate policies or government requirements but also due to a lack of adequate or accepted research methodology for evaluating traditional medicines. In addition, there is very little research on whole herbal mixtures because the drug approval process does not accommodate undifferentiated mixtures of natural chemicals. These contents can be basis for further studies.

Table 1: literacher review

Author	Year	N. of patients	Diagnosis	Herb	Effect
Guo	2014	140	COPD	BuFei granule: Radix Codonopsis Radix spp Pericarpium Citri Reticulatae	↓ Inflammatory markers, QOL ↑
Wang	2014	331	COPD	Herbal formulae	↑ FEV1/FVC, ↓ Inflammatory markers, 6MWD
Chen	2013	63	Contusion	Xuebijing: Cartami flos Angelica sinensis Saliva militoriza Radix spp	↑ FEV1/FVC, ↓ Inflammatory marker, ICU stay
Li	2013	75	Asthma	Herbal formulae: Sofora flavescnse Glycyrrhiza glabra Gonoderma lucidum	↓ Inflammatory marker, Survival rate
Li	2013	352	COPD	Bu-Fei Jiang-Pi: Astragalus propinquus Codonopsis pilosula Atractylodes macrocephala Poria cocos	↓ Symptom score, QOL ↑, ↓ depression-anxiety

				Ging seng	
Tang	2013	151	Asthma	Yang Warming Aconite root Ging seng rubra Zingiber officinalis Glycyrrhiza glabra	↓ Symptom score
Li	2013	98	NSCLC	Herbal formula Tussilago farfara Rhus versini Morus alba Platycodon grandiflorum Perilla frutescens Prunus armenica	↑ Survival rate
Liu	2013	60	NSCLC	Scutellariae Barbatae Oregano spp	↓ Inflammatory marker
Tian	2013	100	Asthma	Ginger	↓ Symptom score
Cai	2013	100	COPD	Lung supportive Pulmonaria officinalis Oregano spp	↓ Symptom score
Li	2012	240	Pneumonia	TCM	↓ Symptom score, ↑ QOL
You	2012	91	NSCLC	TCM	↓ Bone marrow suppression, ↑ survival
Feng	2012	90	NSCLC	TCM	↓ Tumor marker, ↑ QOL
Xu	2012	180	NSCLC	TCM	↑ Survival, ↑ QOL
Wang	2012	504	COPD	TCM	↓ Symptom score, ↑ QOL, ↑ 6MWD
Liu	2012	172	ARDS	xuebijing	↑ PaO2/FiO2
Li	2012	120	Asthma	TCM	↓ Symptom score, ↓ inflammatory markers
Yao	2012	118	NSCLC	Lavandula officinalis	↓ depression-anxiety
Tian	2012	60	Asthma	Glycyrrhiza glabra	↑ Expectorant Asthmatic drug effective rate
Park	2012	148	Asthma	Magnolia flos	↑ FEV1, ↑ peak expiration flow rate
Long	2011	133	NSCLC	Red Radix Ginseng Radix Aconitum Carmichaeli	↓ Symptom score, ↑ QOL
Li	2011	244	COPD	Zingiber officinalis Glycyrrhiza glabra	↓ Symptom score, ↑ QOL, ↑ 6MWD
Han	2011	84	Asthma	Astragalus propinquus	Recurrence rate, ↑ IgG
Jiang	2011	50	NSCLC	TCM	↑ QOL
Guo	2011	136	NSCLC	Astragalus	↑ Survival, ↑ QOL
Li	2011	244	COPD	Bu-Fei Yishen Condopsis pilosopa Radix Astrix Pricarpium citri	↓ Symptom score, ↑ QOL, ↑ 6MWD
Shan	2011	91	NSCLC	TCM	↓ Symptom score, ↑ QOL
Xue	2011	168	COPD	panax ginseng	↑ FEV1/FVC, ↑ QOL
Kligler	2011	154	Asthma	TCM	↑ QOL
Yan	2011	74	NSCLC	Kangliu Zengziao	↓ Symptom score, ↓ inflammatory markers, QOL
Qi	2011	80	Pneumonia	Astragalus spp Cassia Twig	↓ Inflammatory markers
Wei	2011	60	Asthma	Chaipo granule Ganoderma lucidum Radix Sophora flavescens Radix Glycyrrhiza uralensis	↓ Symptom score, ↓ inflammatory markers

Xu	2011	121	NSCLC	TCM	↑Survival
Mukaida	2011	24	COPD	Desmodium triflorum	↓Symptom score
Jeong	2010	82	NSCLC	HangAm-Dan	↑Survival
Ye	2010	82	Pneumonia	Gingfeihuayu	↓Inflammatory marker
Xiao	2010	100	Pneumonitis	Liangxue	↑KPS score, ↓lung injury
Dou	2010	46	Pneumonitis	Dixiong	↑KPS score, ↓dyspnea score
Li	2010	90	COPD	Tanreqing	↓Symptom score, ↓Inflammatory markers, QOL
Liu	2010	90	Pneumonia	TCM	↓Symptom score, ↓Inflammatory markers
Rouhi	2009	76	Cough	Althea officinalis	↓Symptom score
Rouhi	2009	60	Asthma	Zingiber officinalis Althea officinalis	↓Inflammatory markers, ↑ QOL, Symptom score
Fazio	2009	9655 (5181 children)	COPD	Prospan® Ivy (Hedera helix)	↑ FEV1, ↑ peak expiration flow rate. Inflammatory markers

CONFLICT OF INTEREST
There is no conflict of interest.

ACKNOWLEDGEMENTS
None

FINANCIAL DISCLOSURE
None

REFERENCES

[1] World Health Organization (WHO). National Policy on Traditional Medicine and Regulation of Herbal Medicines. Report of WHO global survey. Geneva. Engebretson, J. Culture and complementary therapies. 2005; Ther Nurs Midwifery 8:177–184.

[2] Conboy L, Kaptchuk D, Eisenberg M, Gottlieb B, Acevedo-Garcia D.[2007] The relationship between social factors and attitudes toward conventional and CAM practitioners. Complement Ther Clin Pract 13:146–57.

[3] Rishton, G. M. Natural products as a robust source of new drugs and drug leads: Past successes and Present day issues. Am J Cardiol 2008;101:43D–9D.

[4] Rouhi-Boroujeni H, Heidarian E, Rouhi-Boroujeni H, Deris F, Rafieian-Kopaei M. Medicinal plants with multiple effects on cardiovascular diseases: A systematic review. Curr Pharm Des. 2016. [Epub ahead of print].

[5] Xutian S, Zhang J, Louise W.[2009] New exploration and understanding of traditional Chinese medicine.;Am J Chin Med 37:411–26.

[6] Rouhi-Boroujeni H, Rouhi-Boroujeni H.A, Heidarian E, Mohammadizadeh F, Rafieian-Kopaei M. Herbs with antilipid effects and their interactions with statins as a chemical anti- hyperlipidemia group drugs: A systematic review.ARYA Atheroscler 2015, 11; 4: 252-8.

[7] Rouhi-Boroujeni H , Rouhi-Boroujeni HA , Gharipour M , Mohammadizadeh F , Rafieian-kopaei M. A systematic review on safety and drug interaction of herbal therapy in hyperlipidemia: a guide for internist Acta Biomed 2015; Vol. 86, N. 2: 130-136

[8] Barnes PM, B Bloom, R Nahin.[2008] Complementary and alternative medicine use among adults and children: United States, 2007. CDC National Health Statistics Report # 12.

[9] Eisenberg DM., Davis SL. Appel S, Wilkey S, Rompay M Van, Kessler RC[1998]. Trends in alternative medicine use in the United States, 1990–1997: Results of a follow-up national survey. JAMA 280:1569–75.

[10] Harrison RA, D Holt, DJ Pattison, PJ Elton. [2004]. Who and how many people are taking herbal supplements? A survey of 21,923 adults. Int J Vitam Nutr Res 74:183–186.

[11] Ernst EK, Schmidt, B Wider.[2005] CAM research in Britain: The last 10 years. Complement Ther Clin Pract;11:17–20.

[12] Food and Drug Administration (FDA). [2010]. Overview of dietary supplements. website: www.fda.gov/food/ dietary supplements/consumer information (accessed November 5, 2010).

[13] Guo S, Sun Z, Liu E, Feng J, Fu M, Li Y, Wu Q. Effect of bufei granule on stable chronic obstructive pulmonary disease: a randomized, double blinded, placebo-controlled, and multicenter clinical study. J Tradit Chin Med. 2014;34(4):437-44.

[14] Wang G, Liu B, Cao Y, Du Y, Zhang H, Luo Q, Li B, Wu J, Lv Y, Sun J, Jin H, Wei K,Zhao Z, Kong L, Zhou X, Miao Q, Wang G, Zhou Q, Dong J. Effects of two Chinese herbal formulae for the treatment of moderate to severe stable chronic obstructive pulmonary disease: a multicenter, double-blind, randomized controlled trial. PLoS One. 2014: 13;9(8):e103168

[15] Chen Y, Tong H, Zhang W, Zhang X, Pan Z, Qiu J, Pan R, Su L.[2013] Curative effect of Xuebijing injection on severe pulmonary contusion. J Tradit Chin Med;33(6):743-751.

[16] Li S, Wang Y, Shi Y, Yu J, Sun W, Hu H, Zhang Y. [2013]Regulatory effects of stage-treatment with established Chinese herbal formulas on inflammatory mediators in pediatric asthma. J Tradit Chin Med33(6):727-732.

[17] Li JS, Li SY, Xie Y, et al.[2013] The effective evaluation on symptoms and quality of life of chronic obstructive pulmonary disease patients treated by comprehensive therapy based on traditional Chinese medicine patterns. Complement Ther Med. 21(6):595-602.

[18] Tang B, Shi K, Li X, Wang H, Fang H, Xiong B, Wu Y.[2013] Effect of "yang-warming and kidney essence-replenishing" herbalpaste on cold-related asthma exacerbation. J Tradit Chin Med. 33(4):468-472.

[19] Lin G, Li Y, Chen S, Jiang H. [2013]Integrated Chinese-western therapy versus western therapy alone on survival rate in patients with non-small-cell lung cancer at middle-late stage. J Tradit Chin Med. 33(4):433-438.

[20] Liu J1, Liu Y. [2013] Influence of erbanxiao solution on inhibiting angiogenesis in stasis toxin stagnation of non-small cell lung cancer. J Tradit Chin Med. 33(3):303-306.
[21] Tian HY1, Hu J, Wang L.[2013] Controlled observation of non-blister acupoint sticking and electroacupuncture for bronchial asthma. Zhongguo Zhen Jiu.;33(6):485-9.
[22] Cai Y, Shi R, Song H, Shang M, Shen T, Shariff M, Kami K, Gu P, Nguyen T, Rao J.[2013] Effects of Lung Support Formula on respiratory symptoms among older adults: results of a three-month follow-up study in Shanghai, China. Nutr J. 6;12:57.
[23] Xie Y, Li JS, Yu XQ, et al.. [2013]Effectiveness of Bufei Yishen Granule combined with acupoint sticking therapy on quality of life in patients with stable chronic obstructive pulmonary disease. Chin J Integr Med. 19(4):260-268.
[24] Li J1, Yu X, Li S, Wang H, Bai Y, Wang M, Sun Z, Zhang W, Zhou Z, Jia X, Zhou Q. Randomized controlled multicenter clinical trial for integrated treatment of community-acquired pneumonia based on traditional Chinese medicine syndrome differentiation. J Tradit Chin Med. 2012;32(4):554-60.
[25] Wu F, Yao MH, Zhu Y. [2012]Clinical study on prevention of recurrence of asthma in children by Xiaochuangao acupoint paste: treating winter diseases in summer. Zhongguo Zhong Yao Za Zhi. 37(17):2646-268.
[26] Li SY, Li JS, Wang MH, Xie Y, Yu XQ, Sun ZK, Ma LJ, Zhang W, Zhang HL, Cao F, Pan YC. Effects of comprehensive therapy based on traditional Chinesemedicine patterns in stable chronic obstructive pulmonary disease: a four-center, open-label, randomized, controlled study. BMC Complement Altern Med. 2012 Oct 29;12:197. doi: 10.1186/1472-6882-12-197.
[27] You J, Shan MJ, Zhao H. Clinical study of integrative treatment for ninety-one elderly patients with advanced non-small cell lung cancer. Zhongguo Zhong Xi Yi Jie He Za Zhi. 2012 Jun;32(6):774-8.
[28] Feng Y, Xiao YY, Li SD, et al.[2012] The treatment of non-small cell lung cancer by interstitial I-125 seeds implantation combined with chemotherapy and Chinese medicine. Chin J Integr Med;18(9):663-669.
[29] Xu L, Li H, Xu Z, Wang Z, Liu L, Tian J, Sun J, Zhou L, Yao Y, Jiao L, Su W, Guo H, Chen P, Liu J. [2012]Multi-center randomized double-blind controlled clinical study of chemotherapy combined with or without traditional Chinese medicineon quality of life of postoperative non-small cell lung cancer patients. BMC Complement Altern Med. 1;12:112.
[30] Wang M, Li J, Li S, Wang H, Yu X, Zhang H. Effect of traditional Chinese medicine on outcomes in patients with mild/moderate chronic obstructive pulmonary disease: study protocol for a randomized placebo-controlled trial. Trials. 2012 Jul 16;13:109.
[31] LIU SQ, ZHENG RQ, LI MQ, YAN J, CHEN HY, MU XW, CHANG RH, YE ZL, LI XS, GAO YH, QIU XH, HUANG YZ, GUO FM, YANG Y, QIU HB. Effect of Xuebijing injection treatment on acute respiratory distress syndrome: a multicenter prospective randomized control clinical trial. Zhonghua Yi Xue Za Zhi. 2012 Apr 17;92(15):1017-1022.
[32] Deng SQ, Ouyang XN, Yu ZY, Dai XH, Chen X, Fang FZ, Wang WW, Liu ZZ.[2012] Influence of Chinese herbal medicine Feitai Capsule on completion or delay of chemotherapy in patients with stage IIIB/IV non-small-celllung cancer: a randomized controlled trial. Zhong Xi Yi Jie He Xue Bao. 10(6):635-40.
[33] Li YM, Liu Q, Li XY. New percutaneous absorption herbal patch for asthma of paracmasis and its effect on the relative transcription factors of patients. Zhongguo Zhen Jiu. 2012 May;32(5):459-63.
[34] Yao Y, Li H, Liu L, Zhao L, Xu L, Sun J. Study on the effect of Feiji Decoction for soothing the liver combined with psychotherapy on the quality of life for primary lung cancer patients. Zhongguo Fei Ai Za Zhi. 2012 Apr;15(4):213-7.
[35] Tian XF, Xu ZL.[2012] Treatment of infantile asthma in remission stage with Chinesemedicine and new moxibustion-massage apparatus. Zhongguo Zhen Jiu. 32(2):163-165.
[36] Park CS, Kim TB, Lee JY, et al. [2012] Effects of add-on therapy with NDC-052, an extract from Magnoliae Flos, in adult asthmatic patients receiving inhaled corticosteroids. Korean J Intern Med. 27(1):84-90.
[37] Jiang F, Yan Y, Yang L, Song Q, Li Y. [2011]Impact of Chinese herb on quality of life of stable chronic obstructivepulmonary disease: a randomized controlled study. Zhongguo Zhong Yao Za Zhi. 36(22):3203-3206.
[38] Yao Y.[2012] Effects of Feiji decoction for soothing the liver combined with psychotherapy on quality of life in primary lung cancer patients. Zhongguo Fei Ai Za Zhi. 15(1):27-33.
[39] Long SQ, Liao GY, He WF, et al. [2011]Influence of Shenfu Injection on the quality of life of lung cancer patients receiving chemotherapy. Nan Fang Yi Ke Da Xue Xue Bao. 31(12):2090-2092.
[40] Li JS, Li SY, Yu XQ, Xie Y. Bufei Yishen Granule combined with acupoint-sticking therapy in patients with stable chronic obstructive pulmonary disease: study protocol of a multicenter, randomized, double-blind, active-controlled trial. 011 Dec;9(12):1312-8.
[41] Han JY, Cui JP. Effect of biantong huangqi ointment combined with western medicineon the recurrence of children's bronchial asthma. Zhongguo Zhong Xi Yi Jie He Za Zhi. 2011;Oct;31(10):1346-1348.
[42] Guo L, Bai SP, Zhao L, Wang XH.[2012] Astragalus polysaccharide injection integrated with vinorelbine and cisplatin for patients with advanced non-small cell lung cancer: effects on quality of life and survival. Med Oncol. 29(3):1656-1662.
[43] Li JS, Li SY, Yu XQ, et al.2012] Shen granule combined with acupoint sticking therapy in patients with stable chronic obstructive pulmonary disease: a randomized, double-blind, double-dummy, active-controlled, 4-center study. J Ethnopharmacol. 1;141(2):584-591.
[44] Shan MJ, Han BH, You J. Assessment of therapeutic efficacy on treating advanced non-small cell lung cancer in the aged by Chinese medicine adopting the international questionnaire of quality of life. Zhongguo Zhong Xi Yi Jie He Za Zhi. 2011 Jul;31(7):873-9.
[45] Xue CC, Shergis JL, Zhang AL, Worsnop C, Fong H, Story D, Da Costa C, Thien FC. Panax ginseng C.A Meyer root extract for moderate chronic obstructive pulmonary disease (COPD): study protocol for a randomised controlled trial. Trials. 2011 Jun 30;12:164.
[46] Kligler B, Homel P, Blank AE, Kenney J, Levenson H, Merrell W. [2011]Randomized trial of the effect of an integrative medicine approach to the management of asthma in adults on disease-related quality of life and pulmonary function. Altern Ther Health Med. J17(1):10-15.
[47] Yan GY, Xu ZY, Deng HB, Wan ZY, Zhang L, Zhu JY. [2011]Effects of chemotherapy combined with Chinese herbal medicine Kangliu Zengxiao decoction on tumor markers of patients with advanced non-small-cell lung cancer: a randomized, controlled trial. Zhong Xi Yi Jie He Xue Bao. 9(5):525-530.
[48] Qi F1, Liang ZX, She DY, Yan GT, Chen LA. [2011]A clinical study on the effects and mechanism of xuebijing injection in severe pneumonia patients. J Tradit Chin Med. 31(1):46-49.
[49] Wei CH, Wen MC, Yu N. Clinical effect of chaipo granule combined with routine treatment on refractory asthma. Zhongguo Zhong Xi Yi Jie He Za Zhi. 2011 Jan;31(1):33-6.
[50] Xu ZY, Jin CJ, Zhou CC, Wang ZQ, Zhou WD, Deng HB, Zhang M, Su W, Cai XY. Treatment of advanced non-small-cell lung cancer with Chinese herbal medicine by stages combined with chemotherapy. J Cancer Res Clin Oncol. 2011 Jul;137(7):1117-22.
[51] Mukaida K, Hattori N, Kondo K, Morita N, Murakami I, Haruta Y, Yokoyama A, Kohno N. A pilot study of the multiherb Kampo medicine bakumondoto for cough in patients with chronic obstructive pulmonary disease. Phytomedicine. 2011 Jun 15;18(8-9):625-9.
[52] Jeong TY, Park BK, Lee YW, Cho CK, Yoo HS. Prospective analysis on survival outcomes of nonsmall cell lungcancer stages over IIIb treated with HangAm-Dan. Zhongguo Fei Ai Za Zhi. 2010 Nov;13(11):1009-15.
[53] Ye S, Gong G, Zheng H, Hu G, Xia T. [2010] Cytokine changes in community-acquired pneumonia in elderly and intervention of traditional Chinese medicine. Zhongguo Zhong Yao Za Zhi. 35(11):1486-1489.

[54] Xiao C, Ding HJ, Feng LC, Qu BL, Dou YQ. Efficacy of Liangxue Jiedu Huoxue Decoction in prevention of radiation pneumonitis: a randomized controlled trial. Zhong Xi Yi Jie He Xue Bao. 2010 Jul;8(7):624-628.

[55] Dou YQ, Yang MH, Wei ZM, Xiao C, Yang XH. The study of early application with Dixiong Decoction (地芎汤) for non-small cell lung cancer to decrease the incidence and severity of radiation pneumonitis: A prospective, randomized clinical trial. Chin J Integr Med. 2010 Oct;16(5):411-6.

[56] Li W, Mao B, Wang G, Wang L, Chang J, Zhang Y, Wan MH, Guo J, Zheng YQ. Effect of Tanreqing Injection on treatment of acute exacerbation of chronic obstructive pulmonary disease with Chinese medicine syndrome of retention of phlegm and heat in Fei. Chin J Integr Med. 2010;16(2):131-7.

[57] Liu DJ, Zheng B, Cai BH, Zhou WM, Yu BX.[2010] Traditional Chinese and Western medicine treatment of mycoplasmal pneumonia in children and the serum cytokine changes. Nan Fang Yi Ke Da Xue Xue Bao.;30(3):626-7

[58] Rouhi -Broujeni H , Ganji F , Roohi Broujeni P.[2009 The effect of combination of Zingeber and Althea officinalis extracts in acute bronchitis-induced cough. J Shahrekord Univ Med Sci.; 10(4): 17-21.

[59] Fazio S1, Pouso J, Dolinsky D, Fernandez A, Hernandez M, Clavier G, Hecker M.[2009]Tolerance, safety and efficacy of Hedera helix extract in inflammatory bronchial diseases under clinical practice conditions: a prospective, open, multicentre post marketing study in 9657 patients. Phytomedicine .16; 1 : 17-24.

[60] Rouhi-Boroujeni H, Ganji F , Nasri H. [2007]Effects of Ginger on the improvement of asthma [the evaluation of Its treatmental effects] Pakistan Journal of Nutrition. 5 (4):373-37

[61] Rouhi-BOROUJENI H, Ganji F. Effect of Althaea officinalis on cough associated with ACE inhibitorsPak. J Nutr.2007; 6 (3): 256-258.

[62] Antosiewicz J, Ziolkowski W, Kar S, Powolny AA, Singh SV. Role of reactive oxygen intermediates in cellular responses to dietary cancer chemopreventive agents. Planta Med 2008; 74:1570–9.

[63] Aruna K, Sivaramakrishnan VM.[1990] Plant products as protective agents against cancer. Indian J Exp Biol. 28:1008–1011.

[64] Banerjee S, Sharma R, Kale RK, Rao AR. [1994] Influence of certain essential oils on carcinogen metabolizing enzymes and acid-soluble sulfhydryls in mouse liver. Nutr Cancer. 21:263–269.

[65] Cao G, Prior RL.[1998] Comparison of different analytical methods for assessing total antioxidant capacity of human serum. Clin Chem 44:1309–1315.

[66] Kaefer CM, Milner JA.[2008] The role of herbs and spices in cancer prevention. J Nutr Biochem.19:347–61.

[67] Krishnaswamy K.[2008] Traditional Indian spices and their health significance. Asia Pac J Clin Nutr; 17(Suppl. 1):265–8.

[68] Brower V.[2008] Back to nature: Extinction of medicinal plants threatens drug discovery. J Natl Cancer Inst. 100:838–839.

[69] Li J. Vederas C. [2009] Drug discovery and natural products: End of an era or an endless frontier? Science; 325:161–5.

[70] Sahoo N. Choudhury K, Manchikanti. P.[2009] Manufacturing of biodrugs: Need for harmonization in regulatory standards. BioDrugs; 23(4):217–229.