

## Review Article

# **Astragalus-based Chinese traditional medicine combined with chemotherapy for non-small-cell lung cancer treatment: meta-analysis of randomized trials**

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Received March 9, 2016; Accepted September 8, 2016; Epub November 15, 2016; Published November 30, 2016

**Abstract:** *Purpose:* Chemotherapy represents one of the major treatments for non-small-cell lung cancer (NSCLC), while its drug resistance and high toxicity raise big concerns. *Astragalus*-based Chinese traditional patent medicine combined with chemotherapy was frequently used for treatment of NSCLC in China. However, its effectiveness hasn't been systematically analyzed. The present study aimed to evaluate the benefits of *Astragalus*-based Chinese traditional patent medicine combined with chemotherapy for NSCLC. *Methods:* The randomized controlled trials involving NSCLC treatment with *Astragalus*-based Chinese traditional patent medicine combined with chemotherapy were screened. The Review Manager 5.3 software was employed for data analysis. Funnel plot were applied to evaluate publication bias. *Results:* 15 eligible studies met our criteria. 15 studies indicated increase tumor response. 8, 6, and 4 studies revealed reduced toxicity including leucopenia, thrombopenia, nausea and vomiting, respectively. *Conclusion:* *Astragalus*-based Chinese traditional patent medicine may benefit the treatment of NSCLC through increasing effectiveness and reducing the toxicity of chemotherapy. More full-scale randomized clinical trials and long-term effectiveness are recommended to further evaluate for treatment of NSCLC.

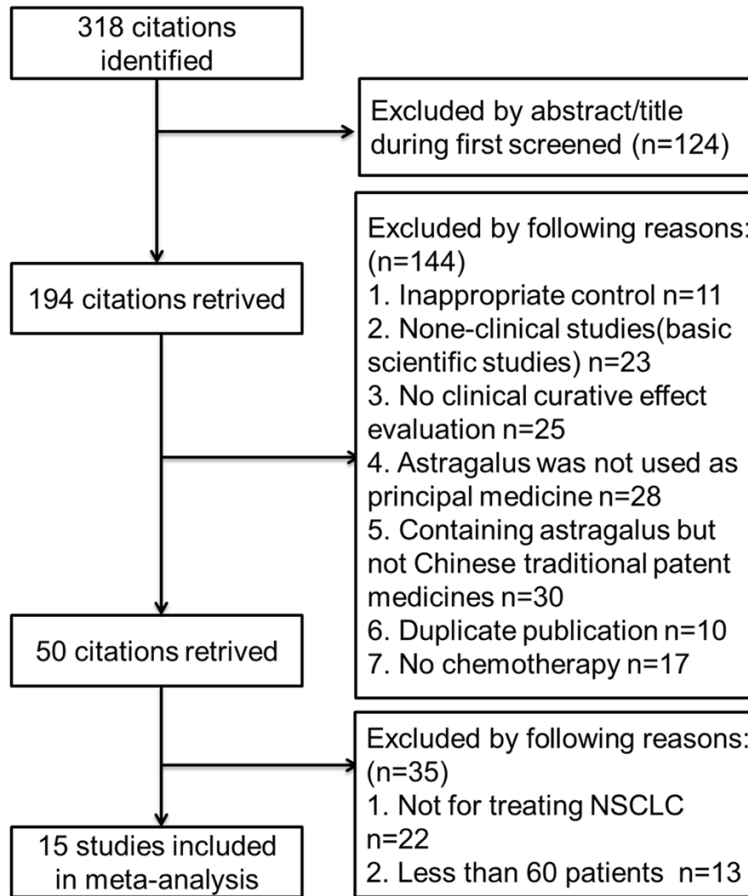
**Keywords:** *Astragalus*, chemotherapy, NSCLC, meta-analysis

## Introduction

Cancer has emerged as a major global public health problem with the incidence and mortality rates continue to rise. Moreover, non-small-cell lung cancer (NSCLC) is the lead cause of cancer mortality. Its treatment constitutes a constant challenge to surgeons [1]. Like many other cancers, chemotherapy represents one of the major treatments for NSCLC, which aims to kill cancer cells or to inhibit their proliferation. However, the same effect also acts on normal cells which would results in unpredicted toxicity. What's more, long-term use of chemotherapy drugs could induce drug resistance. Therefore, the major challenges for treatment of NSCLC chemotherapy are drug resistance and dose-dependent toxicity [2].

In recent years, the use of complementary and alternative medicine (CAM) gradually becomes

an effective means to attenuate drug resistance and toxicity of chemotherapy. Traditional Chinese medicine (TCM) has been used to treat cancer for thousands of years in China, Japan, and other Asian countries [3]. Numerous pre-clinical and clinical studies have demonstrated that TCM combined with chemotherapy could provide an effective treatment for NSCLC [4]. *Astragalus* is one of these TCM and *Astragalus*-based Chinese traditional patent medicine has been accepted as current form of CAM in NSCLC. *Astragalus* (*Radix Astragali* in Latin), a perennial herbaceous plant of the Leguminosae, is widely distributed in the temperate region. It has been used in China for more than 2000 years and documented in an ancient book called *Shennong Bencao Jing* in AD 200 [5]. The dried root of *Astragalus* possesses extensive pharmacological activities against cardiovascular disease, hepatitis, kidney disease [6]. More



**Figure 1.** Flow diagram showing the trial selection process for the systematic review.

ditional patent medicine combined with chemotherapy on NSCLC.

### Methods

#### Data sources and search strategies

Asystematic search was conducted in six databases: PubMed (1966 to December 2015), EMBase (1974 to December 2015), Cochrane Library (1988 to December 2015), Chinese National Knowledge Infrastructure (CNKI, 1994 to December 2015), Wan fang (1989 to December 2015), and VIP (1989 to December 2015). The following terms were retrieved in databases as keywords: “Chinese herbal medicine”, “Astragalus”, “non-small-cell lung cancer”, “chemotherapy”. The studies from bibliographies were also searched for additional references. No restrictions were placed on the publication language. Two reviewers (Ai Yue and Yong-Li Guo) independently identified studies.

than 100 bioactive compounds in Astragalus have been reported including polysaccharides, flavonoids, astragalosides and aminoacids [7], which may lead to increased sensitivity of chemotherapy and reduced side effects of chemotherapy when *Astragalus*-based Chinese traditional patent medicine combined with chemotherapy.

To date, studies on the effects of *Astragalus*-based Chinese traditional patent medicine combined with chemotherapy on NSCLC have been extensively explored. However, the result remains inconclusive and conflicting. To the best of our knowledge, the evidence for the effect of *Astragalus*-based Chinese traditional patent medicine combined with chemotherapy on NSCLC has not been systematically assessed. In the present study, a meta-analysis was performed to get a more concise estimation on effect of *Astragalus*-based Chinese tra-

#### Inclusion criteria

Studies included in the meta-analysis had to meet all of the following criteria. (1) Participants: NSCLC patients had to be diagnosed by pathological sections and were treated by chemotherapy. (2) Type of studies: only clinical randomized controlled trials (RCTs) were eligible. (3) Type of intervention: studies provided the treatment group with *Astragalus*-containing Chinese traditional patent medicine in combination with chemotherapy and the control group with chemotherapy alone were included for analysis. (4) Type of outcome measurements: tumor response was the main outcome measurements, other outcome measurements included remission in the toxicity of chemotherapy, such as the inhibition of nausea and vomiting, leucopenia and thrombopenia, were also investigated.

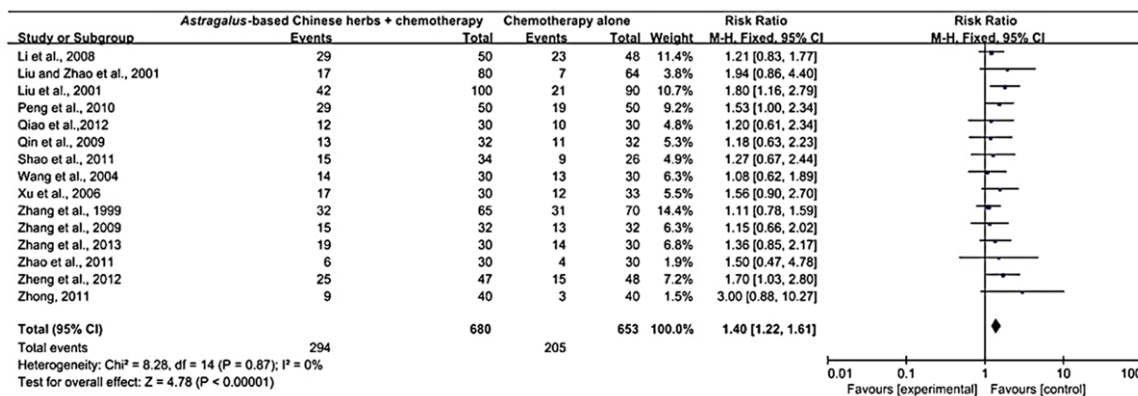
## Astragalus combined with chemotherapy for NSCLC

**Table 1.** Characteristics of the eligible studies

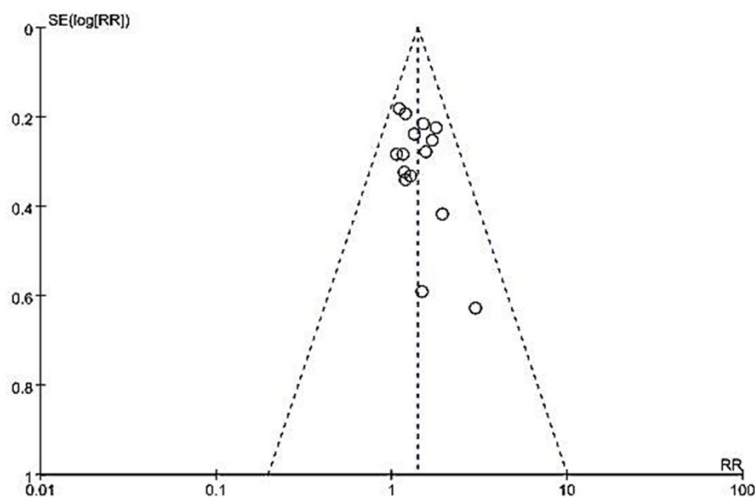
Study	No. of patients	Stage	Protocol	Herbel ingredients	Duration (weeks)
Zhang et al., 2009 [11]	64	III-IV	AP+GP	Astragalus, Radix codonopsis, Atractylodes macrocephala koidz, Poria cocos, Citrus, Magnolia obavata, Fritillaria cirrhosa, Semen Lepidii, Cortex mori radices, Aster.	9
Peng et al., 2010 [12]	100	III-IV	AP+NP	Astragalus, radix curcuma, Rithoma Curcuma, Prunella vulgaris, Raw oyster shell, Hedyotis diffusa, Nidus vespaee, Heterophylly falsestarwort root.	8-9
Qiao, 2012 [13]	60	II-IV	AP+TP	Astragalus, Radix codonopsis.	6
Wang et al., 2004 [14]	60	III-IV	AP+VP	Astragalus injection	8-9
Zhang et al., 1999 [15]	135	III-IV	AP+MVP	Astragalus injection	3
Zhong, 2011 [16]	80	NR	AP+NP	Astragalus injection	6-8
Liu et al., 2001 [17]	190	II-IV	AP+CAP/MVP	Astragalus, Radix glehniae, Asparagus fern, Ligustrum lucidum ait, Selaginella doederleinii Hieron, Paris polyphylla.	8-9
Zheng et al., 2012 [18]	95	IV	AP+NP	Astragalus polysaccharide injection	12
Zhao et al., 2011 [19]	60	IIIb-IV	AP+TP	Astragalus, Fructus lycii, Heterophylly falsestarwort root, Arisacma consanguineum, Alum processed pinellia, almond, Hedyotis diffusa.	6
Xu et al., 2006 [24]	63	II-IV	AP+NP	Astragalus, Adenophora stricta, Radix ophiopogonis, Polygonatum odoratum, Heterophylly falsestarwort root, Cordyceps sinensis, Hedyotis diffusa, Radix Stephaniae Tetrandrae, Mulberry leaf, Panax notoginseng, Radix fici hirtae.	8
Liu and Zhao et al., 2001 [20]	144	II-IV	AP+MAP	Astragalus, Radix glehniae, Asparagus fern, Ligustrum lucidum ait, Selaginella doederleinii, Rhizoma paridis.	8-9
Shao et al., 2011 [21]	60	IIIb-IV	AP+NP	Astragalus, Atractylodes macrocephala koidz, Poria cocos, Scrophulariae, Radix ophiopogonis, Bile arisaema, Selaginella doederleinii, Salvia chinensis, Hedyotis diffusa, Raw oyster shell, Trichosanthes ovigera, Gecko.	6
Qin et al., 2009 [18]	64	IIIb-IV	AP+GP	Astragalus polysaccharide injection	6
Zhang et al., 2013 [22]	60	III-IV	AP+TP	Astragalus polysaccharide injection	6
Li et al., 2008 [23]	98	III-IV	AP+NP/TP	Astragalus polysaccharide injection	6-8

Abbreviations: AP: *Astragalus* prescription; GP: gemcitabine, cisplatin; NP: vinorelbine, cisplatin; TP: taxol, cisplatin; VP: vindesine, cisplatin; CAP: cyclophosphamide, doxorubicin, cisplatin; MVP, mitomycin, vindesine, cisplatin; MAP, mitomycin, doxorubicin, cisplatin.

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**Figure 2.** Tumor response with *Astragalus*-containing Chinese herbal combined with chemotherapy versus chemotherapy alone.



**Figure 3.** Funnel plot of studies testing for tumor response.

### Data extraction and quality assessment

Two reviewers (Ai Yue and Yong-Li Guo) independently extracted data on patient characteristics, treatment details, clinical outcomes, and study quality [8]. Any disagreements were resolved by consensus or by a third reviewer (Guo-Xia Wang). Methodological quality of included studies was assessed independently by two review authors (Ai Yue and Yong-Li Guo) with the criteria in the Cochrane Handbook for Systematic Reviews of Interventions 5.1.0 [9]. Sequence generation, allocation concealment, blinding method, selective outcome reporting, incomplete data assessment, and other sources of bias were assessed with three potential responses: yes, no and unclear. The differences were resolved by consensus or referral to a third reviewer (Tao-Li Sun).

### Outcome measures

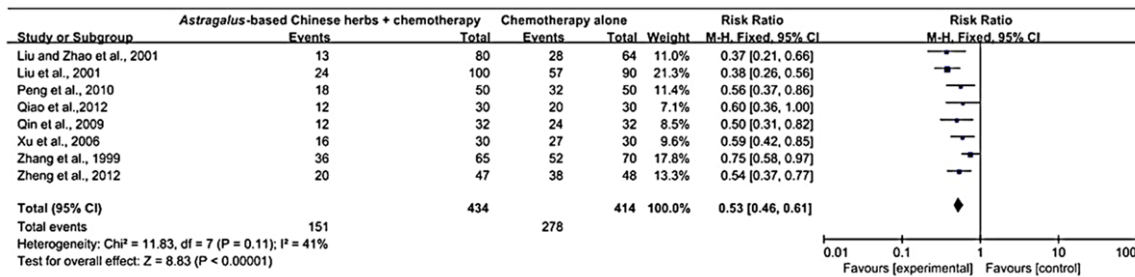
Tumor response was calculated as the number of patients with complete response (CR) plus partial response (PR) based on the WHO scale [10] divided by the total number of patients in each treatment group. Chemotherapy toxicity was investigated including nausea and vomiting, leucopenia and thrombopenia. Leucopenia and thrombopenia was calculated as the number of patients with reduction of leucocyte and platelet respectively divided by the total number of patients in each treatment group.

Nausea and vomiting was calculated as the number of patients with symptom of nausea and vomiting divided by the total number of patients in each treatment group.

### Data analysis

Data analysis was conducted by Review Manager 5.3 software (<http://www.cochrane.org/>). The results were reported as relative risk (RR) with 95% confidence interval (CI). A random model was applied when the heterogeneity existed in pooled studies ( $I^2 > 50\%$ ), otherwise, the fix model was applied. A probability value  $< 0.05$  ( $P < 0.05$ ) was considered significant. Funnel plot the potential publication bias was investigated and expressed as Funnel plot if the number of trials available was more than ten for a meta-analysis [9].

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**Figure 4.** Leucopenia with *Astragalus*-containing Chinese herbal combined with chemotherapy versus chemotherapy alone.

## Results

### Description of studies

318 articles were screened out as shown in **Figure 1** after primary search from the 6 databases, of which 194 were identified as requiring relevant abstracts or title retrieval. Close screening of the 194 abstracts excluded 144 due to inappropriate controls (n = 11), non-clinical studies (n = 23), no clinical curative effect evaluation (n = 25), *Astragalus* was not used as principal medicine (n = 28), containing *Astragalus* but not Chinese traditional patent medicines (n = 30), duplicate publication (n = 10), and no chemotherapy (n = 17). 50 full-text articles were further screened for eligibility. 35 articles were excluded because of not for treating NSCLC (n = 22), and less than 60 patients (n = 13). Therefore, the total of 15 articles were found to be eligible and accepted for the current meta-analysis.

### Characteristics of the eligible studies

The included trials enrolled 1333 patients with NSCLC, of which 680 received Chinese traditional patent medicine treatment. As shown in **Table 1**, all of 15 eligible studies [11-23] were conducted in China and were published between 1999 and 2013 in Chinese journals. The stages of NSCLC patients recruited in these studies were as follows: 6 [11, 12, 14, 15, 22, 23], 4 [13, 17, 24], 3 [18, 19, 21], 1 [25] studies were at III to IV, II to IV, III b to IV, IV, respectively. 1 [16] study did not mention the stage condition. These studies involved 7 kinds of chemotherapeutic drug combinations as follows: GP (gemcitabine, cisplatin), NP (vinorelbine, cisplatin), TP (taxol, cisplatin), VP (vindesine, cisplatin), CAP (cyclophosphamide, doxo-

rubicin, cisplatin), MVP (mitomycin, vindesine, cisplatin), and MAP (mitomycin, doxorubicin, cisplatin). The durations of the treatments varied from 3 to 12 weeks in the included studies, and most of durations were 6 weeks and 8-9 weeks.

## Outcome measures

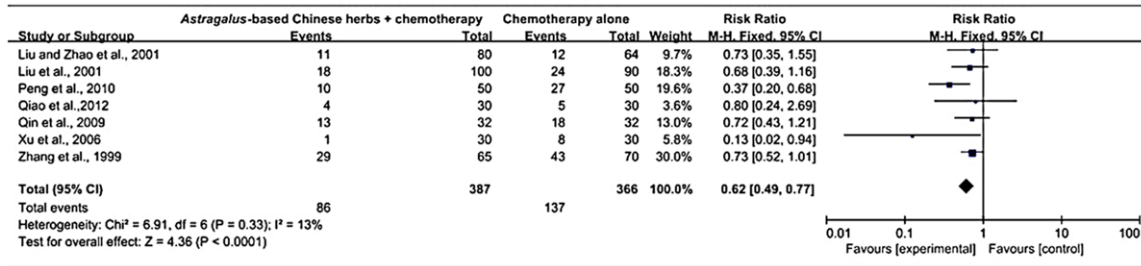
### Tumor response

15 Studies [11-23] including 1333 patients that reported the tumor response were identified in **Figure 2**. The analytical results with fixed effects model (homogeneity, chi-square = 8.28,  $I^2 = 0\%$ ,  $P = 0.87$ ) demonstrated that the combination treatment of *Astragalus*-containing Chinese traditional patent medicine with chemotherapy was associated with a significant increase in the number of patients reported complete and partial response when compared with the chemotherapy alone group (RR 1.40; 95% CI, 1.22 to 1.61). The symmetry of the funnel plot indicated no significant publication bias (**Figure 3**).

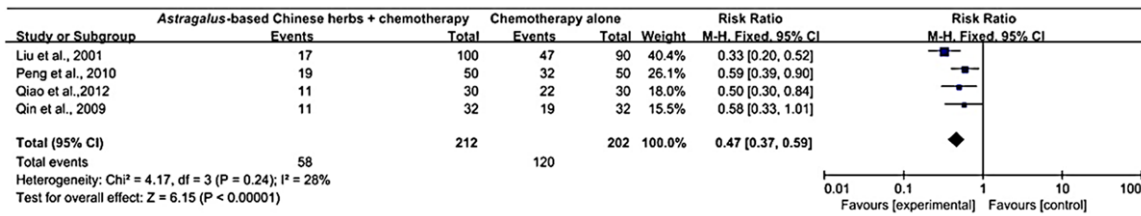
### Reduction in chemotherapy-induced leucopenia

Leucopenia is one of the main side effects that chemotherapy resulted in. As can be seen in **Figure 4**, 8 studies [11-13, 17, 18, 20, 24, 25] including 848 patients which were detected the amount of leucocyte in blood. The 8 trials showed homogeneity (chi-square = 11.83,  $I^2 = 41\%$ ,  $P = 0.11$ ), and fixed-effects model was used. The combination treatment with *Astragalus*-containing Chinese traditional patent medicine plus chemotherapy significantly reduced the number of patients with the leucopenia when compared with the chemotherapy

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**Figure 5.** Thrombopenia with *Astragalus*-containing Chinese herbal combined with chemotherapy.



**Figure 6.** Nausea and vomiting with *Astragalus*-containing Chinese herbal combined with chemotherapy versus chemotherapy alone.

alone group (RR 0.53; 95% CI, 0.46 to 0.61). The number of studies reporting performance status was less than ten, so a funnel plot was not applicable.

### Reduction in chemotherapy-induced thrombopenia

Chemotherapy frequently induces platelet descend, also called thrombopenia. We identified 7 [11-13, 17, 18, 20, 24, 25] studies including 753 patients which were detected the amount of platelet in blood (**Figure 5**). The 7 trials showed homogeneity (chi-square = 6.91,  $I^2 = 13%$ ,  $P = 0.33$ ). The statistical analysis with fixed-effects model revealed that *Astragalus*-containing Chinese traditional patent medicine plus chemotherapy had a significant decrease in the number of patients with thrombopenia when compared with the chemotherapy alone group (RR 0.62; 95% CI, 0.49 to 0.77). The number of studies reporting performance status was less than ten, so a funnel plot was not applicable.

### Reduction in chemotherapy-induced nausea and vomiting

Chemotherapy also induces nausea and vomiting. As shown in **Figure 6**, 4 studies including 414 patients which were observed the symp-

tom of nausea and vomiting. As the 4 [12, 13, 17, 18] trials showed homogeneity (chi-square = 4.17,  $I^2 = 28%$ ,  $P = 0.24$ ), the fixed-effects model was used for statistical analysis. The results revealed that the patients with the combination treatment of *Astragalus*-containing Chinese traditional patent medicine plus chemotherapy showed significantly less patients with nausea and vomiting compared with the chemotherapy alone group (RR 0.47; 95% CI, 0.37 to 0.59). The number of studies reporting performance status was less than ten, so a funnel plot was not applicable.

## Discussion

Although numerous studies have reported the anticancer activity of *Astragalus*, however, the exact anticancer active substances in *Astragalus* are rarely reported. *Astragalus* abounds with polysaccharides, flavonoids, saponins, polysaccharides, amino acids, and other compounds [7]. The polysaccharides, saponins, and flavonoids may be the major anti-tumor constituents of *Astragalus* [6]. *Astragalus* polysaccharides exerted a synergistic anti-tumor effect with adriamycin on H22 tumor-bearing mice. It could alleviate the decrease in the sizes of the spleen and thymus induced by Adriamycin [26]. Astragaloside IV and II, two kinds of active saponins, have been shown the potential anti-

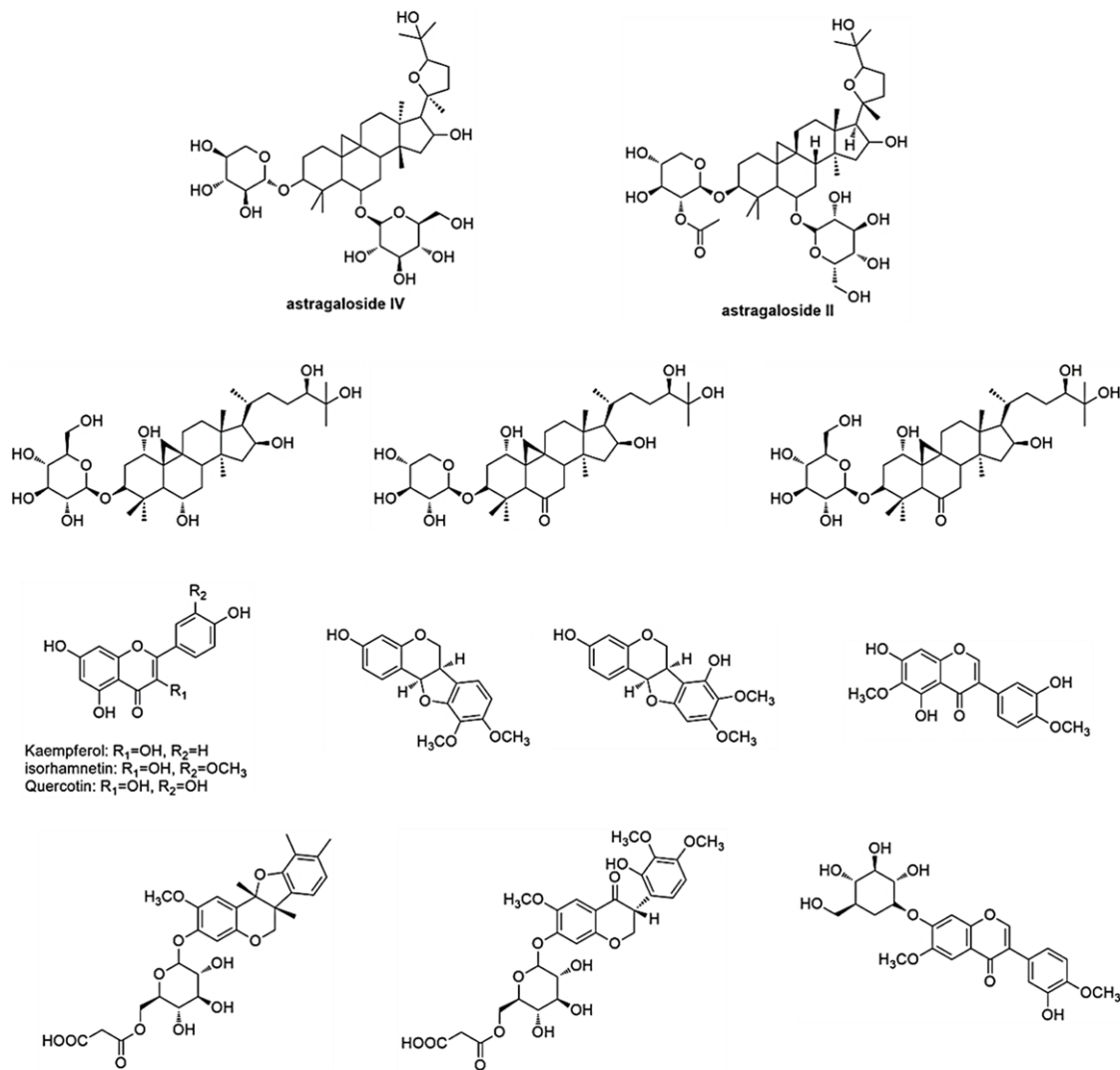


Figure 7. Major active compounds in *Astragalus*.

tumor activity against liver cancer [27, 28]. Total flavonoids of *Astragalus* and calycosin could also inhibit the proliferation of K562 cells [29]. As shown in **Figure 7**, some compounds from *Astragalus* have been demonstrated the antioxidant and immunomodulatory activity [7], their anticancer activities deserve further study.

The antioxidant activities of *Astragalus* has been widely reported in vitro due to its considerable scavenging activities against hydroxyl-radical, 1, 1-diphenyl-2 picrylhydrazyl radical, super oxideanion, and hydrogenperoxide [30-32]. What's more, *Astragalus* could increase the number of lymphocytes to active both cel-

lular and humoral immune response [33]. Numerous studies both in vivo and vitro have certified the immunomodulatory effects of *Astragalus* [34, 35]. It is well known that the immunosuppression and free radicals are two main factors to inducing the formation and development of cancer [36]. Therefore, antioxidant and immunomodulatory effects of *Astragalus* may be the mechanism on synergistic effect of *Astragalus*-based Chinese traditional patent medicine combined with chemotherapy against cancer.

In the present study, 15 studies with 318 individuals suffering from NSCLC were screened out. The results suggested that *Astragalus*-

based Chinese traditional patent medicine combined with chemotherapy in the treatment of NSCLC may increase tumor response and reduce the side effect including leucopenia, thrombopenia, nausea and vomiting when compared with the chemotherapy alone. Those effects of *Astragalus*-based Chinese traditional patent medicine might directly associate with the benefits to NSCLC. However, in order to clarify the herbal prescriptions function when combined with chemotherapy, the specific mechanisms and bioactive components of herbal prescriptions may be the focus of future studies. All of studies were only based on the information of short-term effectiveness. There was few data on the long-term effectiveness of treatment provided for analysis. Meanwhile, in view of the generally weak methodological quality of the currently included studies, we are unable to make solid conclusions, and confirmation must await investigation in future trials.

It has to be acknowledged that there are several limitations in the study. Most of trials didn't report an exact randomization method. It wasn't clear that whether placebo controlled and blinded assessors were set, whereas drop-outs and withdrawals were not mentioned in any study. Moreover, of all used anti-cancer drugs were chemotherapeutic drugs, but the drug combinations and types were different. Hence, performance bias would be inevitable. Moreover, publication bias indicated by funnel plots was another limitation of present study. Just because of discussion as above-mentioned, it is essential to improve methodological quality of randomized controlled trials for future study and more methodologically rigorous studies are justified to confirm or refute the present study.

In conclusion, we found evidence that *Astragalus*-based Chinese traditional patent medicine combined with chemotherapy in the treatment of NSCLC may increase effectiveness (by improving the tumor response) and reduce the toxicity of chemotherapy (by attenuating leucopenia, thrombopenia, nausea and vomiting). However, more full-scale randomized clinical trials and long-term effectiveness are required before more firm conclusions about this therapy can be drawn for treatment of NSCLC.

### Acknowledgements

The present work was supported by a grant from Hunan Province Traditional Chinese medicine scientific research project (No. 201242, and NO. 201413).

### Disclosure of conflict of interest

None.

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### References

- [1] Siegel R, Ma J, Zou Z, Jemal A. Cancer statistics, 2014. *CA Cancer J Clin* 2014; 64: 9-29.
- [2] Miao J, Zhang W, Hu X, Chen S, Hu B, Li H. Clinical evaluation of postoperative chemotherapy based on genetic testing in patients with stage IIIA non-small cell lung cancer. *Thoracic Cancer* 2016; 7: 44-9.
- [3] Li SG, Chen HY, Ou-Yang CS, Wang XX, Yang ZJ, Tong Y, Cho WC. The efficacy of Chinese herbal medicine as an adjunctive therapy for advanced non-small cell lung cancer: a systematic review and meta-analysis. *PLoS One* 2013; 8: e57604.
- [4] Park C, Hong SH, Kim GY, Choi YH. So-Cheong-Ryong-Tang induces apoptosis through activation of the intrinsic and extrinsic apoptosis pathways, and inhibition of the PI3K/Akt signaling pathway in non-small-cell lung cancer A549 cells. *BMC Complement Altern Med* 2015; 15: 113.
- [5] Jin M, Zhao K, Huang Q, Shang P. Structural features and biological activities of the polysaccharides from *Astragalus membranaceus*. *Int J Biol Macromol* 2014; 64: 257-66.
- [6] Li X, Qu L, Dong Y, Han L, Liu E, Fang S, Zhang Y, Wang T. A review of recent research progress on the astragalus genus. *Molecules* 2014; 19: 18850-80.
- [7] Fu J, Wang Z, Huang L, Zheng S, Wang D, Chen S, Zhang H, Yang S. Review of the botanical characteristics, phytochemistry, and pharmacology of *Astragalus membranaceus* (Huangqi). *Phytother Res* 2014; 28: 1275-83.
- [8] Wu L, Chen Y, Xu Y, Guo X, Li X, Zhang AL, May BH, Xue CC, Wen Z, Lin L. Oral huangqi formulae for stable chronic obstructive pulmonary disease: a systematic review and meta-analysis. *Evid Based Complement Alternat Med* 2013; 2013: 705315.



## Astragalus combined with chemotherapy for NSCLC

- [9] Higgins JPT and Green S. "Cochrane Handbook for Systematic Reviews of Interventions Version 5.1.0". The Cochrane Collaboration, <http://www.cochrane.org/training/cochrane-handbook>. 2011.
- [10] The World Health Organization, 1979. WHO Handbook for Reporting Results of Cancer Treatment, World Health Organization, Geneva, Switzerland (in Chinese).
- [11] Zhang XL HT, Huang L GP. Regimen Combined with YiQiHuaTan Soup in the Treatment for 64 Cases with Advanced Non-small Cell Lung Cancer. *Journal of Chinese Oncology* 2009; 15: 568-9.
- [12] Peng WW and Jia YJ. Clinical observation of advanced NP regimen combined with Jiedu Quyu in the treatment of non-small cell lung cancer. *Liaoning Journal of Traditional Chinese Medicine* 2010; 37: 1303-1304.
- [13] Qiao SL. Effect of Shenqi Fuzheng Injection combined with chemotherapy in treatment of advanced non-small cell lung cancer clinical observation. *China Prac Med* 2012; 7: 25-26.
- [14] Wang HC, Li RM and Guo YW. Clinical efficacy of Astragalus combined with VP regimen in the treatment of advanced non-small cell lung cancer. *Henan Journal of Oncology* 2004; 17: 131.
- [15] DR ZZaL. Clinical observation of Astragalus in the treatment of non small cell lung cancer with chemotherapy. *Shanghai Medical & Pharmaceutical Journal* 1999; 20.
- [16] Zhong FH. Short term efficacy of Astragalus injection combined with chemotherapy in the treatment of advanced non small cell lung cancer. *Journal of Shaanxi College of Traditional Chinese Medicine* 2011; 34: 51-52.
- [17] Liu JX, Pan MQ and Li YH. Clinical study of Jin Fu Kang oral liquid for treating non-small cell lung cancer. *Cancer* 2001; 21: 463-465.
- [18] Qin ZQ, Lu LQ, Yuan GR, Wu GQ, Xu Q and Gao L. Clinical Observation of Huang qi duo tang Injection Combined with GP Regimen to Treat Patients with Advanced Non-small Cell Lung Cancer. *Chinese Archives of Traditional Chinese Medicine* 2009; 27: 664-665.
- [19] Zhao YH and Liang J. Clinical Observation of the curative effect of Qi Qi Qu Tan He Ji combined with western medicine treatment of advanced non-small cell lung cancer. *Shaanxi Journal of Traditional Chinese Medicine* 2011; 32: 1571-1572.
- [20] Xu M and Zhou B. Clinical study on toxicity of Shashen Maidong Decoction on chemotherapy of non-small cell lung cancer. *New Journal of Traditional Chinese Medicine* 2006; 38: 29-30.
- [21] Liu JX, Zhao LH, et al. Clinical Observation of "Lung-Nourishing Anti-tumor Beverage" in Treating Nonsmall-Cell Lung Cancer in 271 Cases. *Shanghai Journal of Traditional Chinese Medicine* 2001; 2: 4-6.
- [22] Shao CD. Yifei Yin Xiaoji decoction combined with chemotherapy in treatment of advanced non-small cell lung cancer and its influence on quality of life. *Shaanxi Journal of Traditional Chinese Medicine* 2011; 32: 941-942.
- [23] Qin ZQ, Lu LQ, Yuan GR, Wu GQ, Xu Q and Gao L. Clinical Observation of Huang qi duo tang Injection Combined with GP Regimen to Treat Patients with Advanced Non-small Cell Lung Cancer. *Chinese Archives of Traditional Chinese Medicine* 2009; 27: 664-665.
- [24] Zhang XJ, Wang XX, Gen JX, Zhang H. Clinical observation on the treatment of advanced non-small cell lung cancer with Astragalus polysaccharide combined with TP. *Chinese Journal of Traditional Medical Science and Technology* 2013; 20: 667-668.
- [25] Li XJ, Jia YJ, Sun YY, Chen L, Zhang Y and Chen LW. Clinical efficacy of injection of Astragalus Polysaccharides combined with chemotherapy in the treatment of advanced non-small cell lung cancer. *Chinese Journal of Clinical Oncology* 2008; 35: 919-921.
- [26] Tian QE, Yan M, Cai HL, Tan QY and Zhang WY. Astragalus polysaccharides can regulate cytokine and P-glycoprotein expression in H22 tumor-bearing mice. *World J Gastroentero* 2012; 18: 7079-86.
- [27] Qi H, Wei L, Han Y, Zhang Q, Lau AS and Rong J. Proteomic characterization of the cellular response to chemopreventive triterpenoid astragaloside IV in human hepatocellular carcinoma cell line HepG2. *Int J Oncol* 2010; 36: 725-35.
- [28] Huang C, Xu D, Xia Q, Wang P, Rong C, Su Y. Reversal of P-glycoprotein-mediated multidrug resistance of human hepatic cancer cells by Astragaloside II. *J Pharm Pharmacol* 2012; 64: 1741-50.
- [29] Zhang D, Zhuang Y, Pan J, Wang H, Li H, Yu Y, Wang D. Investigation of effects and mechanisms of total flavonoids of Astragalus and calycosin on human erythroleukemia cells. *Oxid Med Cell Longev* 2012; 2012: 209843.
- [30] Li R CW, Wang WP, Tian WY and Zhang XG. Antioxidant activity of Astragalus polysaccharides and antitumor activity of the polysaccharides and siRNA. *Carbohydrate Polymers* 2010; 82: 240-4.
- [31] Li XT ZY, Kuang HX, Jin FX, Liu DW, Gao MB, Liu Z and Xin XJ. Mitochondrial Protection and Anti-aging Activity of Astragalus Polysaccharides and Their Potential Mechanism. *Int J Mol Sci* 2012; 13: 1747-61.
- [32] Niu YG, Wang HY, Xie ZhH, Whent Monica, Gao XD, Zhang X, Zou S and Yao WB. Structural

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- analysis and bioactivity of a polysaccharide from the roots of *Astragalus* (Fisch) Bge. var. *mongolicus* (Bge.) Hsiao. *Food Chem* 2011; 128: 620-6.
- [33] Yuan SL, Piao XS, Li DF, Kim SW, Lee HS and Quo PF. Effects of dietary *Astragalus* polysaccharide on growth performance and immune function in weaned pigs. *Anim Sci* 2006; 82: 501-7.
- [34] Li SP, Zhao XJ, Wang JY. Synergy of *Astragalus* polysaccharides and probiotics (*Lactobacillus* and *Bacillus cereus*) on immunity and intestinal microbiota in chicks. *Poultry Science* 2009; 88: 519-25.
- [35] Qiu HH, Cheng GL, Xu JQ, Zhang NW, Liu FH, Zhu XY, Zhao J and Zhang YJ. Effects of *Astragalus* Polysaccharides on Associated Immune Cells and Cytokines in Immunosuppressive Dogs. *Procedia in Vaccinology* 2010; 2: 26-33.
- [36] Wijesekara I, Pangestuti R and Kim SK. Biological activities and potential health benefits of sulfated polysaccharides derived from marine algae. *Carbohydrate Polymers* 2011; 84: 14-21.