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Herbal Formula of *Polygonatum sibiricum* Polysaccharide, Pachymaran and Astragalus Polysaccharide Exert Immunomodulatory Effects in Mouse models of Immunosuppression and Lung Cancer

La Fórmula Herbaria de Polisacárido de *Polygonatum sibiricum*, Paquimarán y Polisacárido de Astrágalo Ejerce Efectos Inmunomoduladores en Modelos Murinos de Inmunosupresión y Cáncer de Pulmón

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ZHOU, X; WANG, Z.; TANG, M.; GONG, D.; LUO, Y.; LIU, F. & ZHANG, L. Herbal formula of *Polygonatum sibiricum* polysaccharide, pachymaran and astragalus polysaccharide exert immunomodulatory effects in mouse models of immunosuppression and lung cancer. *Int. J. Morphol., 43(1)*:326-334, 2025.

SUMMARY: This study is to investigate the immunomodulatory and anti-cancer effects of the herbal formula of *Polygonatum sibiricum* polysaccharide (PSP), pachymaran (P) and Astragalus polysaccharide (APS) in mouse models of immunosuppression and lung cancer. The immunosuppressive model was established in Kunming mice, which were divided into normal control group, immunosuppressive model group and PSP+P+APS group. The lung cancer model was established inC57 mice with Lewis cells. These mice were divided into normal control, lung cancer model, PSP+P+APS, and ADM group. Peripheral white blood cells (WBC) were detected with an automatic blood cell analyzer. Percentage of peripheral blood $CD4^+$ and $CD8^+$Tlymphocytes were detected by flow cytometry. Spleen and thymus indices and tumor inhibition rate were calculated. Serum levels of TNF, IFN-γ, IL-4, IL-6, IL-10, andIL-17A were detected with the BD cytometric bead array. Compared with the respective model group, administration of the herbal formula PSP+P+APS group significantly increased the number of WBC, thymus index, spleen index, $CD4^+/CD8^+$ratio, TNF, IFN-γ, and IL-17Afor both the immune suppressive model and lung cancer model mice ($P<0.05$). On the contrary, the levels of IL-6 and IL-10 were significantly decreased in the PSP+P+APS group ($P<0.05$). In addition, the herbal formula significantly reduced the tumor weight of the lung cancer model mice. The PSP+P+APS herbal formula plays an important role in the immunomodulation and tumor inhibition in the mice with immunosuppression and lung cancer.

KEY WORDS: *Polygonatum sibiricum* polysaccharide; Pachymaran; Astragalus polysaccharide; Herbal formula; Lung cancer.

INTRODUCTION

Lung cancer is a common malignant tumor of respiratory system in clinic, and can severely threaten the human life and health (Ren & Chen, 2016; Zhang *et al*., 2016). In recent 50 years, the morbidity and mortality rates of lung cancer rank the first place among all malignant tumors (Liu *et al*., 2023b; Zhang *et al*., 2023). Non-small cell lung cancer is a common type in the clinic, including squamous-cell carcinoma, adenocarcinoma and large cell carcinoma, whose cell division is slower than others, with later invasion and metastasis (Chen *et al*., 2016b; Xiong *et al*., 2016). Due to its slower cell division, as well as delayed invasion and metastasis (Chen *et al*., 2016a,b; Xiong *et al*., 2016), most cases of non-small cell lung cancer are diagnosed at moderate or advanced stages, with low 5-year survival rate (Tong *et al*., 2016; Zhu *et al*., 2016). Previous studies have shown that the patients' immune system plays a key role in regulating the development of lung cancer (Mazzoccoli *et al*., 2012; Chen *et al*., 2017; Karaboue *et al*., 2022). However, a large amount of researches verify that radiotherapy, operation, and chemotherapy can produce a

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certain suppressive effect on the immunological function (Lei *et al*., 2016); therefore, how to effectively treat lung cancer and reduce the effect on immunological function as much as possible has been the hot issue of clinical research. Until now, several anti-cancer vaccination approaches and antigen-independent immunomodulatory drugs have been developed and trialed (Bilek *et al*., 2016).

Traditional Chinese medicine (TCM) can prevent the problems of immune suppression, since fewer side-effects have been reported with the use of herbal medicine in the treatment of cancer (Vaou *et al*., 2021). It is well-known that multi-herb therapy is one of the most important characteristics of TCM (Wei *et al*., 2022). In this article, the combination of the polysaccharides of *Polygonatum sibiricum*, Astragalusmongholicus and Poriacocos were researched, all of which have anti-cancer effects. *Polygonatum sibiricum*is cultivated as a traditional medicinal herb and foodstuff in China. It has been reported that *Polygonatum sibiricum* polysaccharide (PSP) has different biological properties, such as antioxidant, anti-inflammatory, anti-diabetic, antitumor, and immunomodulatory activities (Tomshich *et al*., 1997). Astragalus polysaccharide (APS) is extracted from Astragalusmoholicus and is reported to have a variety of immunomodulatory activities (Han *et al*., 2021; Salehi *et al*., 2021; Aleebrahim-Dehkordi *et al*., 2022). Poriacocos is used in TCM to treat edema and clear febrile illnesses. In particular, pachymaran (P) has long been proven to exhibit strong antitumor and immunomodulatory activities (Eswar *et al*., 2023). However, the combined effect of APS +P+ PSP in lung cancer is not clear.

Herein, this study investigated the effects of the herbal formula of APS+P+PSP in mouse models of immunosuppression and lung cancer. The PSP +P+APS herbal formula could up-regulate the immunity of both mice models, and even showed a strong inhibitive effect on the growth of lung cancer. This provides experimental evidence for the use of PSP +P+APS herbal formula in the treatment of lung cancer.

MATERIAL AND METHOD

Animals. Kunming (KM) mice (n=60; female, aged 4-5 weeks, with the body weight of 20±2 g) and C57 mice (n=80; female, aged 4-5 weeks, with the body weight of 20±2 g) were obtained from the Animal Laboratory of Chongqing Medical University. The animals were housed under standard conditions of temperature 20 ± 2 oC and relative humidity 36 , and had free access to diet and water. This study was conducted in strict accordance with the recommendations of the National Institutes of Health's Guide for the Care and Use of Laboratory Animals. The research protocol with animal experimentation was approved by the Army Medical University (Protocol Number: AMUWEC20234843). All methods were performed in accordance with ARRIVE guidelines (*https://arriveguidelines.org/*). Every effort was made to minimize suffering.

Determination of the optimal formula of PSP+P+APS. PSP (65 % purity) and P (75 % purity) were purchased from Xi'an Yuensun Biological Technology Co, Ltd. (Xi'an, China). APS (80 % purity) was purchased from Kamaishu Biological Technology Co., Ltd. (Shanghai, China).

A preliminary orthogonal experiment (three factors and three levels) of three drug concentrations was performed to test the synergistic and antagonistic factors, and the optional composition from the preliminary experiments was chosen for the study accordingly. In advance of the experiments, PSP+P+APS were mixed with saline (15 %, v/v in 0.9 % NaCl) and boiled for 1 h and then stored at 4 ^{o}C.

Cell culture. Lewis lung carcinoma cell line was kindly donated by Prof. FangYang (Central Laboratory, Xinqiao Hospital, the Third Military Medical University Affiliated Hospital). The cells were cultured in Dulbecco's modification of Eagle's medium (DMEM) supplemented with 10 % fetal bovine serum at 37 ^{o}C in a humidified atmosphere of 5 % CO_2.

Immunosuppressive model establishment and animal grouping. KM mice were randomly divided into normal control (NC) group, immunosuppressive model (IM) group and PSP+P+APS group, with 20 mice in each group.IM model was established by intraperitoneal injection of 4 mg/kg doxorubicin hydrochloride (ADM; the Second Affiliated Hospital of Chongqing Medical University, Chongqing, China) once daily for 3 consecutive days for the IM and PSP+P+APS groups. Mice of the NC group received equal volume of normal saline. One day after model establishment, the mice of the PSP+P+APS group started to bead ministered with 0.2 mL of the herbal formula of PSP+P+APS by gavage. Four cycles of administration of the formula were performed, with four consecutive daily administration and one day rest in each cycle. Meanwhile, the mice of the NC group and IM group were administered with normal saline of the same volume.

Establishment of lung cancer model and animal grouping. C57 mice were randomly divided into NC group, lung cancer model (LCM) group, PSP+P+APS group, and ADM group, with 20 mice in each group. LCM was established for the LCM group, PSP+P+APS group, and ADM group. Briefly, 0.1 ml of Lewis cells ($1\times l0^7$ cells/ml) was injected into the right axillary subcutaneous tissue of the mice under aseptic condition. Tumors were formed after

6 days of injection. Mice in the NC group were injected with equal volume of normal saline. One day after the model establishment, mice of the PSP+P+APS group received PSP+P+APS treatment as above described. Mice of the ADM group were given 4 mg/kg ADM by intraperitoneal injection on daily for 4 consecutive days. Mice from the NC group and LCM group received equal volume of normal saline.

Sampling. During the experimental period, the animals were daily examined and recorded for clinical symptoms (weight, eating status, hair, and mental state). One day after the last drug administration, the blood samples were collected from the eye obit, and the mice were weighed and then sacrificed. Serum was isolated by centrifugation. The tumor of C57 mice were removed and weighed. The spleen and thymus of the KM mice and C57 mice were removed and weighed.

Calculation of the thymus index, spleen index and tumor inhibition rate. The thymus and spleen indices, as well as the tumor inhibition rate, were calculated according to the following formula:

Spleen index=spleen (g)/ body mass (g)
Thymus index=thymus (g)/ body mass (g)

Tumor inhibition rate = tumor weight of (LCM group-treatment group)/ tumor weight of LCM group ×100 %.

Blood cell analysis. The white blood cells (WBCs) in peripheral blood were detected with the BC-6800 automatic blood cell analyzer (BC-6800/SH-27000360, Mindray, Shenzhen, China) according to the manufacturer's instructions.

Flow cytometry. Totally 50 μL anti-coagulated blood sample were used for detecting the percentage of CD4+ and CD8+ cells. The antibodies of 0.7 mL anti-mouse CD3 PerCP-eFluor™710 (No46-0032; Affymetrixe Bioscience, San Diego, CA, US), 0.7 mL PE-labeled anti-mouseCD8a (No11-0081; Affymetrixe Bioscience, San Diego, CA, US) and 0.3ML FITC-labeled anti-mouse CD4 (No11-0041; Affymetrixe Bioscience, San Diego, CA, US) antibodies were added and incubated in dark for 15 min at room temperature. After that, the percentages of peripheral blood $CD4^+$ and $CD8^+$ lymphocytes were measured with a NAVIOS10COLLORS flow cytometer (Beckman Coulter Commercial Enterprise Co., Ltd., USA), and the $CD4^+$/ $CD8^+$ratio was calculated accordingly.

Cytometric bead array (CBA) analysis. The BD™ CBA mouse Th1/Th2/Th17 cytokine kits (No. 560485; Becton, Dickinson and Company, Franklin Lakes, NJ, USA) were used according to the manufacturer's instruction. Briefly, 50mL serum sample and 50 μL mixed capture beads were mixed and incubated in dark for 2 h at room temperature. Then, the serum cytokines of Th1 (TNF, and IFN-γ), Th2 (IL-4, IL-6, and IL-10), and Th17 (IL-17A) were measured by a BD FACS Canto TMII flow cytometer (Becton, Dickinson and Company, Franklin Lakes, NJ, USA).

Statistical analysis. Statistical analysis was performed using the SPSS software (version 13.0; SPSS, Chicago, IL, USA). Data were expressed as mean ± standard deviation (SD). One-way analysis of variance (ANOVA) and t-test were used for group comparison. $P<0.05$ was considered statistically significant.

RESULTS

The herbal formula of PSP+P+APS improves the symptoms of model mice. To determine whether the formula could improve the immunity of the two models of mice, the general clinical symptoms were observed. For the IM, the mice in the NC group were very active and swift during the entire experimental period. Their hair was healthy and shiny. After IM establishment with the ADM injection, the mice showed lack of appetite, lethargy, having rough clothing hair and low spirits. After the gastric administration of the herbal formula of PSP+P+APS for 25 days, the above symptoms were obviously alleviated for the mice in the PSP+P+APS group, compared with the IM group.

In addition, for the LCM, the NC mice showed normal activity. After the LCM establishment, the mice showed depression, lack of appetite, rough clothing hair, and even secondary respiratory diseases. After the gastric administration of the herbal formula of PSP+P+APS for four cycles, the conditions of the mice in the PSP+P+APS group were obviously improved, compared with the LCM group. In addition, the mice in the ADM group showed good color, appetite and activity.

These results suggest that, the herbal formula of PSP+P+APS treatment can obviously improve the symptoms of the IM and LCM mice.

The herbal formula of PSP+P+APS improves the WBC number of the model mice. In order to determine the effect of the herbal formula on WBCs, the WBC number was detected with the blood cell analyzer. Compared with the respective NC group, the WBC numbers of the IM group were reduced, while those of the LCM group were increased (Fig. 1). After the gastric administration of the herbal formula of PSP+P+APS for 25days, the WBC numbers were significantly increased than the IM group and the LCM group, respectively (P<0. 05). On the contrary, the WBC number was significantly decreased in the ADM group of

the LCM (P<0. 05). These results suggest that the herbal formula of PSP+P+APS may improve the WBC reduction in the immunosuppressive and LCM mice.

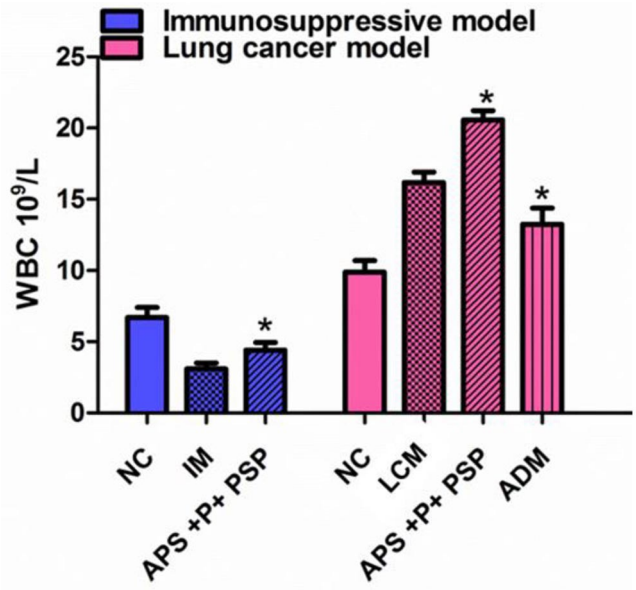

Fig. 1. The effect of the PSP+P+APS herbal formula on the WBC numbers. Mice of the model groups and PSP+P+APS group were orally administered with normal saline and the PSP+P+APS herbal formula, respectively. Mice from the ADM group were given 4 mg/kg ADM. Peripheral WBC was determined by an automatic blood cell analyzer. Compared with the respective model group, **P*<0.05.

The herbal formula of PSP+P+APS improves the spleen and thymus indices of the model mice. In order to observe the effect of PSP+P+APS on immune system, Viscera index was measured. Compared with the respective model group, the mice of the PSP+P+APS group showed significantly increased spleen and thymus indices (*P*<0.05) (Fig. 2A,B). On the contrary, the spleen and thymus indices were decreased in the ADM group of the LCM. The results showed that the herbal formula of PSP+P+APS improved the spleen and thymus indices in both IM and LCM, suggesting a positive effect on the immune system.

The herbal formula of PSP+P+APS reduces tumor weight in LCM mice. In order to determine if the herbal formula of PSP+P+APS has anti-cancer effect, the tumor inhibitory rate was measured. For the mice model of lung cancer, the tumor volumes of the ADM and PSP+P+APS groups were much smaller than that of the NC group (data not shown). The tumor weight of the ADM and PSP+P+APS groups was also significantly lower than that of the LCM group (Table I). In addition, it was interesting to find that

Table I. The effects of PSP+P+APS herbal formula on tumor weight and inhibition rate.

	Tumor weight (g)	Tumor inhibition rate
Lung cancer model group	7.47±0.95	-
Treatment group	5.54±0.76*	25.8 %
ADM group	5.28±0.68*	29.3 %

Note: Compared with the lung cancer model group, **P*< 0.05.

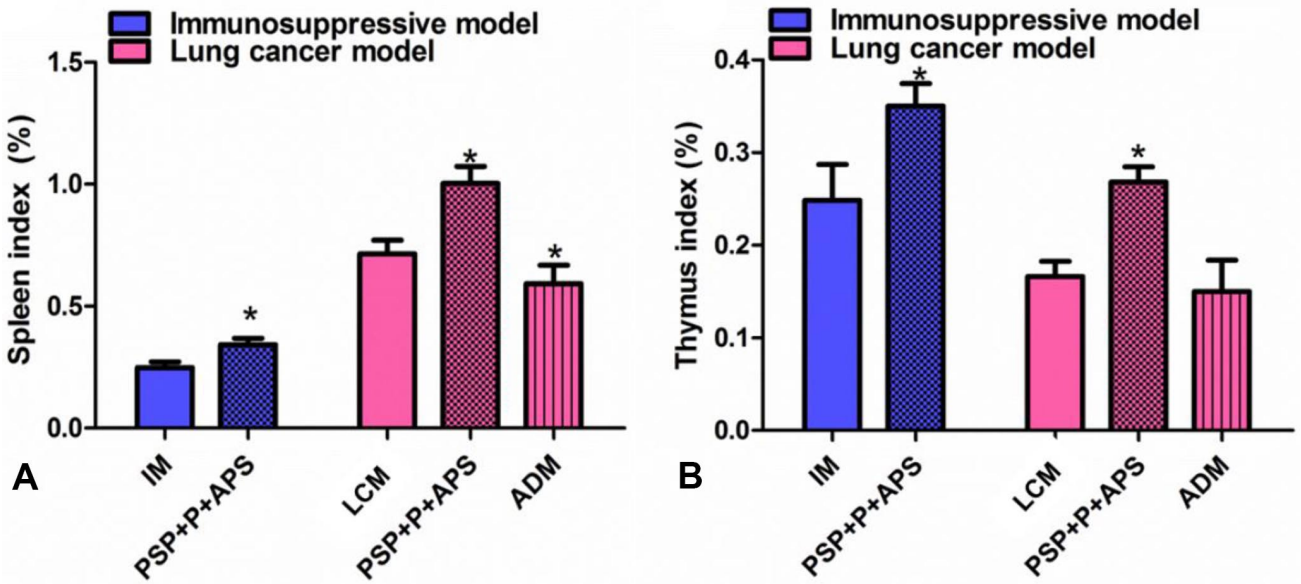

Fig. 2. The effect of the PSP+P+APS herbal formula on immune organ indices. Mice of the model groups and PSP+P+APS group were orally administered with normal saline and the PSP+P+APS herbal formula, respectively. Mice from the ADM group were given 4 mg/kg ADM. The spleen and thymus were isolated to calculate the immune organ index. (A) The spleen index of each group. (B) The thymus index of each group. Compared with the respective model group, *P<0.05.

the tumor inhibitory rate of the PSP+P+APS group was just slightly lower than that of the ADM group (25.8 % *vs.* 29.3 %). These results indicate that the herbal formula of PSP+P+APS may have a preventive effect on lung cancer.

The herbal formula of PSP+P+APS increases theCD4$^+$/CD8$^+$ ratio of the model mice. To test if the herbal formula has a regulatory effect on CD4$^+$ cells, flow cytometry was performed. After treatment with the herbal formula of PSP+P+APS for 25 days, the CD4$^+$/CD8$^+$ ratio in the PSP+P+APS group was significantly higher than that in the IM group and the LCM group, respectively (P<0. 05) (Fig. 3 and Table II). In addition, CD4$^+$ in the PSP+P+APS group was higher than those in the IM and LCM groups, respectively, but without significant difference ($P > 0.05$) (Table II). These results suggest that the treatment with the herbal formula of PSP+P+APS may enhance the immunological function by regulating the CD4$^+$ and CD8+ cells.

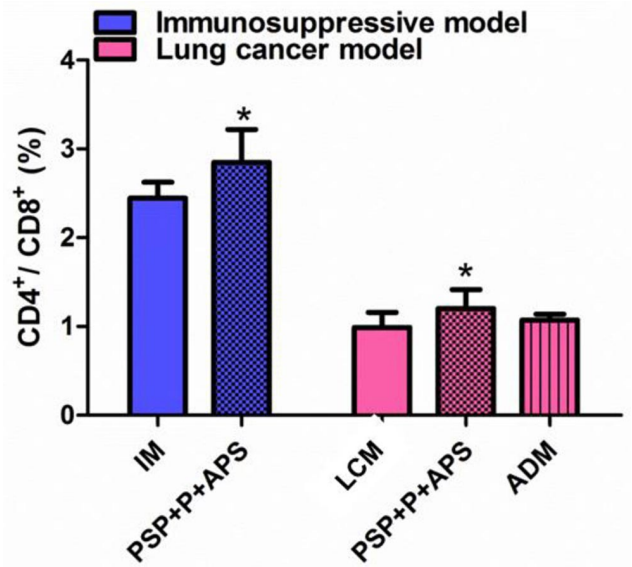

Fig. 3. The effect of the PSP+P+APS herbal formula on the CD4+/CD8+ ratio. Mice of the model groups and PSP+P+APS group were orally administered with normal saline and the PSP+P+APS herbal formula, respectively. Mice from the ADM group were given 4 mg/kg ADM. The percentage of the peripheral blood CD4$^+$ and CD8$^+$ lymphocytes were tested by flow cytometry, and the CD4$^+$/CD8$^+$ ratios were calculated. Compared with the respective model group, *P<0.05.

Effects of herbal formula of PSP+P+APS on the Th1, Th17, and Th2 cytokines of model mice. To determine cytokine levels in each model, CBA was carried out. Compared with the respective model group, the PSP+P+APS group had significantly higher levels of TNF (Fig. 4A) and IFN-γ (Fig. 4B)for both of the IM and LCM (P<0.05). However, the levels of IL-6 (Fig. 4C) and IL-10 (Fig. 4D) in the PSP+P+APS groups were significantly decreased than those in the IM group and the LCM group, respectively (P<0. 05). The changes in the levels of IL-4 (Fig. 4E) were not statistically significant (P>0. 05) in the IM mice. Meanwhile, the IL-4 levels in the PSP+P+APS group and ADM group were significantly lower than that in the LCM group (P< 0.05). In addition, the PSP+P+APS group exhibited significantly higher levels of IL-17A (Fig. 4F) than the respective IM group and LCM group (P<0. 05). These results demonstrate that the herbal formula of PSP+P+APS may have immunomodulatory effects by raising TNF, IFN-γ, andIL-17A, while decreasing IL-6 and IL-10 in both IM mice and the LCM mice.

DISCUSSION

Previous studies have shown that inflammatory molecules and cells may function to initiate and maintain tumor immunity (Jian *et al*., 2023; Qi *et al*., 2023). Many kinds of polysaccharides from the TCM have immunomodulatory effects (Jian *et al*., 2021; Chen *et al*., 2022; Zhou *et al*., 2022). For the TCM, a combination of different compositions could result in specific therapeutic effects different from single components, even with enhanced effects from all aspects (Wei *et al*., 2022; Wang *et al*., 2023a). In a previous research (Wang *et al*., 2017), we have already respectively investigated the immune-regulating effects of PSP, P and ASP. This study investigated the tumor-associated immunological mechanisms of the herbal formula of PSP+P+ASP in order to evaluate its potential application in the treatment of lung cancer.

The inflammatory cytokines in serum and peripheral blood in a cancer disease appear to be a promising field to search for cancer prognostic markers (Benej *et al*., 2017). WBC count may also be influenced by the size of tumor and

Table II. The effects of PSP+P+APS herbal formula on the peripheral blood CD4+ and CD8+ lymphocytes, and CD4+/CD8+ rate.

	Immunosuppressive model			Lung cancer model		
	CD4$^+$ lymphocytes (10^9/L)	CD8$^+$ lymphocytes (10^9/L)	CD4$^+$/CD8$^+$ ratio (%)	CD4$^+$ lymphocytes (10^9/L)	CD8$^+$ lymphocytes (10^9/L)	CD4$^+$/CD8$^+$ ratio (%)
Model group	44.93±3.08	18.37±1.41	2.45±0.07	14.64±1.15	15. 21±1.83	0.99±0.06
Treatment group	45.19±1.85	15.94±0.46*	2.85±0.13*	18.18±1.51	15.38±1.48	1.20±0.08*
ADM group	-	-	-	16.65±0.88	15.57±1.20	1.07±0.03

Note: Compared with the respective model group, *P< 0.05.

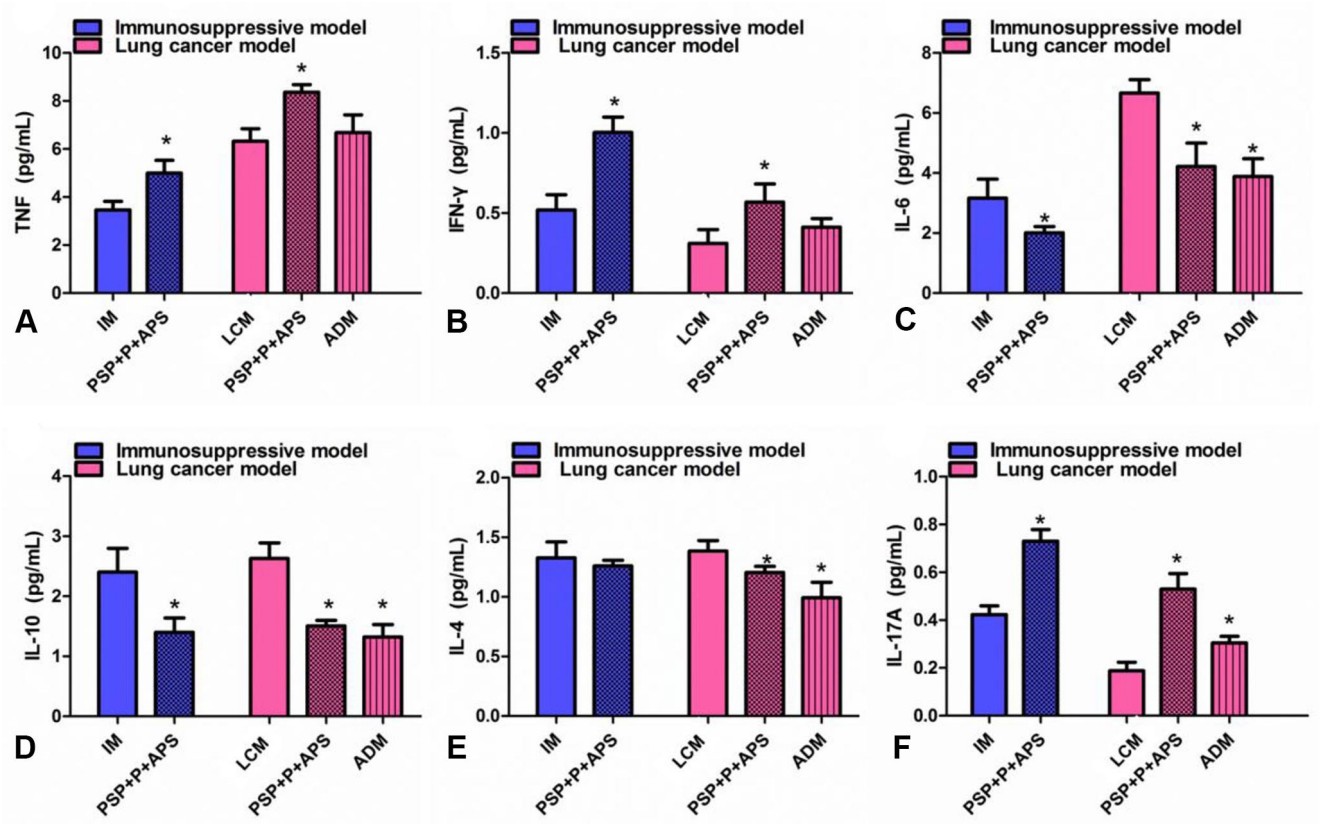

Fig. 4. The effect of the PSP+P+APS herbal formula on serum cytokine levels. Mice of the model groups and PSP+P+APS group were orally administered with normal saline and the PSP+P+APS herbal formula, respectively. Mice from the ADM group were given 4 mg/kg ADM. The serum levels of (A) TNF, (B) IFN-γ, (C) IL-6, (D) IL-10, (E) IL-4 and (F) IL-17A were detected by BD cytometric bead array (CBA) mouse Th1/Th2/Th17 cytokine kit. Compared with the respective model group, **P*<0.05.

the "total tumor mass" (Hwang *et al*., 2021). In addition, most chemotherapeutic agents inhibit innate and adaptive immunity, especially the WBC number (Wang *et al*., 2023b). In order to determine whether the PSP+P+APS herbal formula can enhance the immunity, the WBC number was examined. Compared with the NC group, the WBC number of the IM was reduced, while that was increased in the model of lung cancer, without significant difference. After the administration of the herbal formula for 25 days, the WBC number was markedly increased than each model group. The mechanism might be related to the increased contents of immune factors, including WBC, CD4 and CD8 T cells, IL-2, IL-4 and TNF-γ. These results suggest that the PSP+P+APS herbal formula could help to improve the chemotherapy-induced WBC reduction and immunity decline. Spleen and thymus are two main immune organs in animals, and their index could reflect the immune status (Moudgil & Venkatesha, 2022). This study showed that the spleen and thymus indices significantly increased after the treatment with the herbal formula PSP+P+ASP, compared with the model groups, indicating an enhancement of both humoral and cellular immunity of the model mice.

At present, the anti-tumor treatments mainly focus on two aspects, i.e., improving the anti-tumor immunity of patients and inducing tumor suppression (Schreiber *et al*., 2021). In this study, after the treatment with the herbal formula PSP+P+APS, the tumor weight was lower than that of the LCM group, suggesting that the herbal formula have certain tumor suppressing effects. However, the specific mechanism is unclear. In addition, the PSP+P+APS group showed a comparable inhibition rate to the ADM group for the LCM. These results suggest that the effect of the herbal formula in tumor suppression is similar to that of ADM.

Adaptive immunity is mediated by antibodies, $CD4^+$ and $CD8^+$ T cells, and it usually exploits an indirect pathway to achieve the initial recognition of cancer (Liu *et al*., 2023a). $CD4^+$ cells can identify the MHC class II antigens, and participate in delayed hypersensitivity and the activation of macrophages, NK and CTL cells. $CD8^+$ cells can identify the MHC class I antigens, which specifically and directly kill the target cells, thus exerting the immunosuppressive and cytotoxic effects (Monette

& Mouland, 2019). It showed that, after 25 days of treatment with the herbal formula, the CD4+/CD8+ ratio was much higher than that of the respective model group. Additionally, the number of CD4+cells was higher than that in the immunosuppression model group. These results suggest that the herbal formula may enhance the immunological function, and even exert significant anti-tumor activity by increasing the CD4+/CD8+ ratio.

In the tumor microenvironment,Th1, Th2, and Th17 cytokines play important roles in modulating the innate and adaptive immune mechanisms (Cui *et al*., 2023). T1cells, producing pro-inflammatory cytokines (TNF and IFN-γ), support cell-mediated immunity and as a consequence promote inflammation, cytotoxicity, and delayed-type hypersensitivity, whereas T2 cells, secreting anti-inflammatory cytokines (IL-4, IL-6 and IL-10), support humoral immunity and down regulate the inflammatory actions of T1 cells (Kim *et al*., 2022; Zhao *et al*., 2023). In the present study, the PSP+P+APS group exhibited higher levels of TNF and IFN-γ cytokines than the IM group and the LCM group, respectively. On the other hand, the IL-6 and IL-10 levels were markedly decreased. Hence, it is hypothesized that the Th1cytokines exhibit protective functions, whereas Th2 cytokines support tumor growth in lung cancer. Previous studies have reported that Th1 responses are suppressed and Th2 responses are elevated systemically in ovarian cancer patients, suggesting that Th2 cytokines may mediate immunosuppression (Morgado & Carson, 2017). Th17 cells, primarily producing IL-17A, have gained extensive attention as a novel subset of T cells in the field of tumor biology (Liu *et al*., 2022). However, its specific function remains unclear. This study showed that the high expression of Th17A in the tumor microenvironment were associated with relatively good conditions of the LCM mice. Some studies have indicated that Th17 cells have an inhibitory effect on tumor growth (Filip-Psurska *et al*., 2022). This study suggests that the PSP +P+APS herbal formula may exert the immunomodulatory and even anti-tumor effects by increasing TNF, IFN-γ and IL-17A, and decreasing IL-6 and IL-10.

CONCLUSION

In summary, this study demonstrates that the PSP+P+APS herbal formula can up-regulate the immunity of the IM mice and LCM mice, and even show a strong inhibitive effect on the growth of lung cancer. These findings may provide experimental evidence for the use of PSP +P+APS herbal formula in the treatment of lung cancer.

ZHOU, X; WANG, Z.; TANG, M.; GONG, D.; LUO, Y.; LIU, F. & ZHANG, L. La fórmula herbaria de polisacárido de *Polygonatum sibiricum*, paquimarán y polisacárido de astrágalo ejerce efectos inmunomoduladores en modelos murinos de inmunosupresión y cáncer de pulmón. *Int. J. Morphol., 43(1)*:326-334, 2025.

RESUMEN: Este estudio tuvo como objetivo investigar los efectos inmunomoduladores y anticancerígenos de la fórmula a base de hierbas de polisacárido de *Polygonatum sibiricum* (PSP), paquimarán (P) y polisacárido de astrágalo (APS) en modelos murinos de inmunosupresión y cáncer de pulmón. El modelo inmunosupresor se estableció en ratones Kunming, los cuales se dividieron en un grupo control normal, un grupo modelo inmunosupresor y un grupo PSP+P+APS. El modelo de cáncer de pulmón se estableció en ratones C57 con células de Lewis. Estos ratones se dividieron en grupo control normal, modelo de cáncer de pulmón, PSP+P+APS y ADM. Los glóbulos blancos periféricos (WBC) se detectaron con un analizador automático de células sanguíneas. El porcentaje de linfocitos T $CD4^+$ y $CD8^+$ de sangre periférica se detectó mediante citometría de flujo. Se calcularon los índices del bazo y timo y la tasa de inhibición tumoral. Los niveles séricos de TNF, IFN-γ, IL-4, IL-6, IL-10 e IL-17A se detectaron con la matriz de perlas citométricas BD. En comparación con el grupo modelo respectivo, la administración de la fórmula a base de hierbas del grupo PSP+P+APS aumentó significativamente el número de leucocitos, el índice del timo, el índice del bazo, la proporción $CD4^+/CD8^+$, TNF,IFN-γ e IL-17A para el sistema inmunológico en ratones modelo supresor como también en modelo de cáncer de pulmón (P <0,05). Por el contrario, los niveles de IL-6 e IL-10 disminuyeron significativamente en el grupo PSP+P+APS (P<0,05). Además, la fórmula a base de hierbas redujo significativamente el peso del tumor en los ratones modelo con cáncer de pulmón. La fórmula herbal PSP+P+APS juega un papel importante en la inmunomodulación e inhibición tumoral en ratones con inmunosupresión y cáncer de pulmón.

PALABRAS CLAVE: Polisacárido de *Polygonatum sibiricum*; Paquimarán; Polisacárido de astrágalo; Fórmula a base de hierbas; Cáncer de pulmón.

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