

Effects of curcumin on artery blood gas index of rats with pulmonary fibrosis caused by paraquat poisoning and the expression of Smad 4, Smurf 2, interleukin-4 and interferon- γ

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Abstract. Effects of curcumin on artery blood gas index of rats with pulmonary fibrosis caused by paraquat poisoning and the expression of Mothers against decapentaplegic homolog 4 (Smad4), Smad ubiquitination regulatory factor 2 (Smurf2), interleukin-4 (IL-4) and interferon- γ (IFN- γ) were explored. A total of 54 Wistar rats were randomly selected, of which 36 rats were selected for paraquat poisoning pulmonary fibrosis modeling, and 18 were used in the control group for normal feeding. Then, 18 rats were randomly selected from the modeled groups and injected with curcumin and classified as the curcumin group. The remaining 18 rats were not processed and 17 were successfully modeled as the paraquat group. The expression of SMAD4, Smurf2, IL-4 and INF- γ was detected by enzyme-linked immunosorbent assay. Abdominal aortic blood was taken for determination of pH, arterial partial pressure of oxygen (PaO₂) and arterial partial pressure of carbon dioxide (PaCO₂). The artery blood PaO₂ and serum INF- γ of the curcumin and paraquat groups were significantly higher on day 1 than those on day 5 (P<0.05). The artery blood PaO₂ and serum INF- γ in the curcumin group were higher than those in the paraquat group (P<0.05). The artery blood PaCO₂, serum Smad4, Smurf2 and IL-4 in the curcumin group were significantly lower on day 1 than those on day 5 (P<0.05). The artery blood PaCO₂, serum Smad4, Smurf2 and IL-4 in the paraquat group were significantly lower on day 1 than those on day 5 (P<0.05). The PaCO₂, serum Smad4, Smurf2 and IL-4 in the curcumin group were lower than those in the paraquat group (P<0.05). In conclusion, curcumin can effectively improve pulmonary fibrosis in rats after treatment

with paraquat poisoning. The results show that it is expected to be an effective drug for the treatment of paraquat, and provide effective reference and guidance for clinical treatment.

Introduction

Paraquat is a widely used non-selective herbicide, commonly used in agriculture (1). However, paraquat is also one of the herbicides mostly used for suicide. Paraquat has caused 20 deaths per million people worldwide, and the mortality rate is 60-70% (2,3). Paraquat poisoning toxicity involves multiple organs such as the digestive tract, skin and respiratory tract, which can lead to multiple organ dysfunction syndrome and renal failure (4). The main target organ of paraquat poisoning is the lung. In the later stage, the pulmonary alveolar and interstitial pulmonary fibrosis gradually occurred in patients. The reason of death is mostly due to respiratory failure caused by acute lung injury or acute respiratory distress syndrome in patients (5). Therefore, early diagnosis and early treatment are critical in patients with pulmonary fibrosis caused by paraquat poisoning. A large number of studies have found that curcumin is a phenolic pigment extracted from the underground rhizome of turmeric. It has antibacterial and anti-fibrotic pharmacological effects, and has become a major target of study in the medical field (6,7).

Currently, the condition and prognosis of patients with paraquat poisoning are mostly determined by blood and urinary paraquat content. However, there is no agreed evaluation standard in the medical community for the time being, so the search for reliable prognostic factors will be helpful for clinical guidance in treatment (8). The blood gas index can directly reflect the air function of the lungs in the body, and is used to measure the gas and acid-base balance in the blood of the body. It is currently used as an indicator to observe whether the patient has symptoms such as hypoxemia, respiratory failure and coma (9). The Mothers against decapentaplegic homolog 4 (Smad4) is a transforming growth factor- β 1 (TGF- β 1) that transmits signals to the nucleus through specific receptors on the cell membrane (10). However, Smad ubiquitination regulatory factor2 (Smurf2) mediates the Smad signaling pathway and plays a pivotal role in the regulation of TGF- β 1 signaling

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activity (11,12). Interferon- γ (IFN- γ) is a Th-1 type cytokine that inhibits the proliferation of fibroblasts and promotes the degradation of fibroblasts, and has anti-pulmonary fibrosis (13). Interleukin-4 (IL-4) is a Th-2 type cytokine that promotes the proliferation of fibroblasts and also fibrosis through anti-apoptotic effects (14).

Currently, there are only a few clinical studies on the arterial blood gas index and the expression of Smad4, Smurf2, IL-4 and IFN- γ in rats with pulmonary fibrosis induced by paraquat poisoning. Therefore, this study observed the rats with pulmonary fibrosis induced by paraquat poison, compared the changes of artery blood gas index and Smad4, Smurf2, IL-4 and IFN- γ expression in rats with pulmonary fibrosis induced by curcumin.

Materials and methods

Animal data. A total of 54 clean 6-week-old Wistar rats weighing 224.24 ± 4.36 g were purchased from the Experimental Center of Gansu University of traditional Chinese Medicine (production license no. SCXK 2012-0002; Gansu, China). The rats were raised at the temperature $24.00 \pm 2.00^\circ\text{C}$, humidity $50.00 \pm 5.00\%$, 12 h day and night alternative, in normal single cages and free feeding and drinking water environment. This experiment was approved by the Ethics Committee of Gansu Provincial Hospital (Lanzhou, China).

Modeling. After feeding the rats for one week, 36 rats were randomly selected to model the lung fibrosis of paraquat poisoning. Paraquat (20%) was diluted with distilled water 20 times to 0.2% paraquat (Beijing Bai Ao Si Biotechnology Co., Ltd., Beijing, China). The solution was configured with a concentration of 10 mg/ml, and the rats were given a single oral gavage at 20 mg/kg. There was no convulsion, death or vomiting during the intragastric administration. The pulmonary fibrosis was judged according to the rat lung diffusion function. The pulmonary fibrosis was determined according to the function of lung diffusion in rats. After 1 h of gavage, 18 rats were randomly selected to administer curcumin (Shanghai Baoman Bio-technology Co., Ltd., Shanghai, China) suspension of 200 mg/kg through intraperitoneal injection and classified as the curcumin group. The remaining 18 rats were given a saline injection of 10 ml/kg intraperitoneally and classified as the paraquat group. A further 18 rats were reared normally and were not processed, and classified as the control group.

Detection method. Rats in each group were randomly selected to obtain 0.5 ml of venous blood on days 1 and 5 after modeling. After leaving the blood for 30 min, the serum was separated by centrifugation at $3,000 \times g$ for 15 min at 4°C , stored at -20°C by using an enzyme-linked immunosorbent assay (ELISA) method. The following kits were used: rat SMAD4 ELISA kit (item no. H-EL-Smad4; Shanghai Zeye Biotechnology Co., Ltd., Shanghai, China), rat Smurf2 ELISA kit (article no. wu-EL082ra-s96; Shanghai Wuyi Biotechnology Co., Ltd., Shanghai, China), rat IL-4 ELISA kit (article no. RA20088; Wuhan Hualianke Biotechnology Co., Ltd., Wuhan, China), rat INF- γ ELISA kit (article no. 865.010.048; Beijing Borede Biotechnology Co., Ltd., Beijing, China). The expression levels of Smad4, Smurf2, IL-4 and INF- γ were measured in accordance with the

operating instructions. Then, 0.5 ml of abdominal aorta blood was drawn for the determination of pH, arterial partial pressure of oxygen (PaO_2) and arterial partial pressure of carbon dioxide (PaCO_2) using a Thunder ABL80 blood gas analyzer (Nanjing Li Ai Trading Co., Ltd., Nanjing, China). After the blood was drawn, the rats were sacrificed by cervical dislocation.

Statistical analysis. The data were analyzed and processed by SPSS19.6 statistical software (Beijing Sitron Weida Information Technology Co., Ltd., Beijing, China). The results of the experiments were expressed as the mean \pm standard deviation. Multivariate time comparison was performed by repeated measures of ANOVA and the LSD post hoc test. A comparison between the two pairs was performed using a paired t-test. $P < 0.05$ was considered to indicate a statistically significant difference.

Results

Modeling results. In the 54 modeled rats, 53 were successfully modeled, and the modeling success rate was 98.15%. There were 18 rats in the control group, 18 in the curcumin group, and 17 in the paraquat group.

Comparison of pH values of arterial whole blood in three groups of rats. The pH values of artery blood on days 1 and 5 in the curcumin group were 7.37 ± 0.08 and 7.39 ± 0.06 , respectively. The pH values of artery blood on days 1 and 5 in the paraquat group were 7.40 ± 0.04 and 7.41 ± 0.02 , respectively. The pH values of artery blood on days 1 and 5 in the control group were 7.37 ± 0.06 and 7.38 ± 0.03 , respectively. There was no significant difference in the pH value of artery blood between days 1 and 5 in the curcumin group, the paraquat group or the control group ($P > 0.05$; Fig. 1). On days 1 and 5, the artery blood pH of the three groups was measured. There was no significant difference and it was not statistically significant ($P > 0.05$).

Comparison of PaO_2 in artery blood of rats between the three groups. The PaO_2 of arterial blood on days 1 and 5 in the curcumin group was 83.75 ± 13.65 and 67.39 ± 15.57 mmHg, respectively. The PaO_2 of artery blood on days 1 and 5 in the paraquat group was 76.37 ± 13.19 and 50.40 ± 16.53 mmHg, the artery blood PaO_2 of the control group on days 1 and 5 was 89.65 ± 16.43 and 87.38 ± 12.34 mmHg, respectively (Fig. 2).

The artery blood PaO_2 of rats in the curcumin group was significantly higher on day 1 than day 5, which was statistically significant ($t = 3.352$, $P = 0.002$). The artery blood PaO_2 of rats in the paraquat group was significantly higher on day 1 than that on day 5, which was statistically significant ($t = 5.063$, $P < 0.001$). There was no significant difference in PaO_2 of artery blood on days 1 and 5 in the control group, which was not statistically significant ($P > 0.05$). On days 1 and 5, the artery blood PaO_2 of rats in the three groups was statistically significant ($F = 3.666$, $P = 0.033$; $F = 27.080$, $P < 0.001$) (data not shown). The artery blood PaO_2 in the control group was higher than that in the curcumin and paraquat groups, and were statistically significant ($P < 0.05$). The PaO_2 of the artery blood in the curcumin group was higher than that in the paraquat group ($P < 0.05$; Fig. 2).

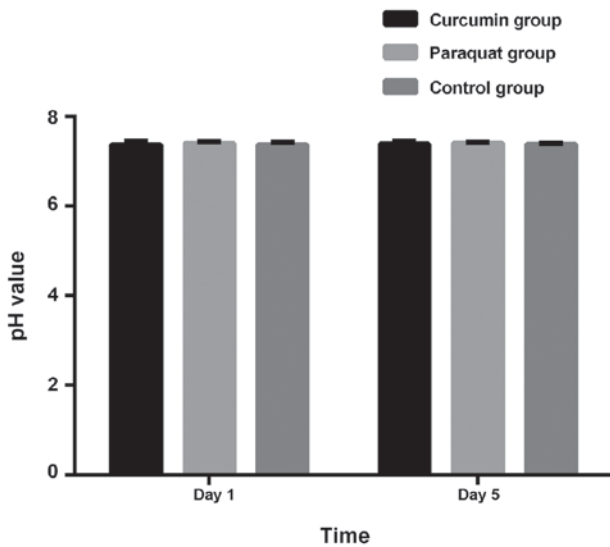


Figure 1. Comparison of artery blood pH values of rats between the three groups. The pH values of artery blood on days 1 and 5 in curcumin group were 7.37±0.08 and 7.39±0.06, respectively. The pH values of artery blood on days 1 and 5 in paraquat group were 7.40±0.04 and 7.41±0.02, respectively. The pH values of artery blood on days 1 and 5 in the control group were 7.37±0.06 and 7.38±0.03, respectively. There was no significant difference in the pH value of artery blood between days 1 and 5 in the curcumin group, the paraquat group and the control group (P>0.05). On days 1 and 5, the artery blood pH values of the three groups was measured, and there was no significant difference and was not statistically significant (P>0.05).

Comparison of PaCO₂ values in artery blood of rats in the three groups. The PaCO₂ of artery blood on days 1 and 5 in the curcumin group was 40.41±5.16 and 53.73±5.72 mmHg, respectively. The PaCO₂ of artery blood on days 1 and 5 in the paraquat group was 43.56±6.39 and 69.67±6.53 mmHg, respectively. PaCO₂ of artery blood on days 1 and 5 in the control group were 35.48±5.92 and 36.54±5.61 mmHg, respectively (Fig. 3). The artery blood PaCO₂ of rats in the curcumin group was significantly lower on day 1 than that on day 5, which was statistically significant (t=4.230, P<0.001). The artery blood PaCO₂ of rats in the paraquat group was significantly lower on day 1 than that on day 5, which was statistically significant (t=4.014, P<0.001). There was no significant difference in PaCO₂ between the control group on days 1 and 5, which was not statistically significant (P>0.05). On days 1 and 5, the artery blood PaCO₂ of rats in the three groups was statistically significant (F=8.366, P<0.001; F=26.030, P<0.001) (data not shown). The arterial blood PaCO₂ of the control group was lower than that in the curcumin and paraquat groups, which was statistically significant (P<0.05). The PaCO₂ of artery blood in the curcumin group was lower than that in the paraquat group (P<0.05; Fig. 3).

Comparison of serum Smad4 values in rats between the three groups. The serum Smad4 of the curcumin group was lower on day 1 than that on day 5, which was statistically significant (t=2.260, P=0.030). The serum Smad4 of the paraquat group was significantly lower on day 1 than that on day 5, which was statistically significant (t=5.223, P<0.001); There was no significant difference in serum Smad4 between days 1 and 5 in the control (P>0.05). On days 1 and 5, the serum Smad4 of rats in the three group was statistically significant (F=28.420,

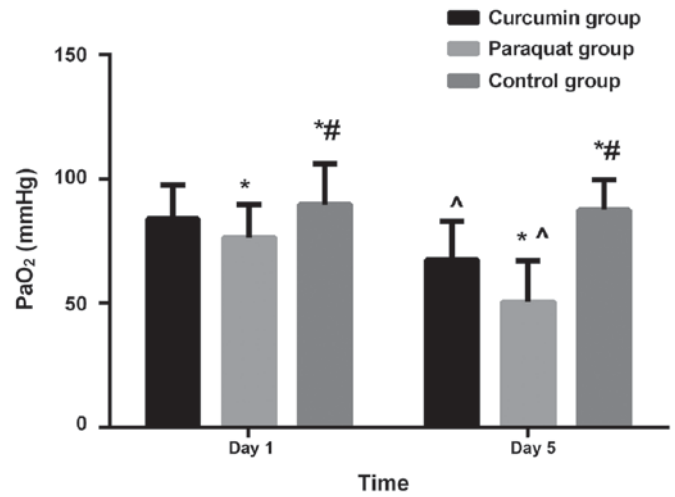


Figure 2. Comparison of PaO₂ in artery blood of rats between the three groups. The PaO₂ of artery blood on days 1 and 5 in the curcumin group was 83.75±13.65 and 67.39±15.57 mmHg, respectively. The PaO₂ of artery blood on days 1 and 5 in the paraquat group was 76.37±13.19 and 50.40±16.53 mmHg, respectively, the artery blood PaO₂ of the control group on days 1 and 5 were 89.65±16.43 and 87.38±12.34 mmHg, respectively. PaO₂ in artery blood of rats in the curcumin group on day 1 was significantly higher than that on day 5, which was statistically significant (P<0.05). PaO₂ in artery blood of rats in the paraquat group was significantly higher on day 1 than that on day 5, which was statistically significant (P<0.001). There was no significant difference in PaO₂ of artery blood on days 1 and 5 in the control group, which was not statistically significant (P>0.05). On days 1 and 5, PaO₂ in the artery blood of rats between the three groups was statistically significant (P<0.001). The artery blood PaO₂ of the control group was higher than that in the curcumin group and paraquat group, which were statistically significant (P<0.05). The PaO₂ of artery blood in the curcumin group was higher than that in the paraquat group, which was statistically significant (P<0.05). *P<0.05, when compared with the curcumin group; #P<0.05, when compared with the paraquat group and ^P<0.05, when compared to day 1.

P<0.001; F=92.180, P<0.001). The serum Smad4 of rats in the control group was significantly lower than that in the curcumin and paraquat group (P<0.05). The serum Smad4 in the curcumin group was lower than that in the paraquat group (P<0.05; Table I).

Comparison of serum Smurf2 values of rats in the three groups. The serum Smurf2 of the curcumin group was lower on day 1 than that on day 5, which was statistically significant (t=5.188, P<0.001). The serum Smurf2 of the paraquat group was significantly lower on day 1 than that on day 5, which was statistically significant (t=4.786, P<0.001); There was no significant difference in serum Smurf2 between the control group on days 1 and 5 (P>0.05). On days 1 and 5, the serum Smurf2 of rats between the three groups was statistically significant (F=66.480, P<0.001; F=135.000, P<0.001). Serum Smurf2 in the control group was significantly lower than that in the curcumin and paraquat groups (P<0.05). Serum Smurf2 in the curcumin group was lower than that in the paraquat group (P<0.05; Table II).

Comparison of serum IL-4 in rats in the three groups. Serum IL-4 in the curcumin group was lower on day 1 than that on day 5, which was statistically significant (t=4.749, P<0.001). The serum IL-4 level in the paraquat group was significantly lower on day 1 than that on day 5, which was statistically

Table I. Comparison of serum Smad4 values in rats between the three groups (pg/ml).

Groups	Day 1	Day 5	t	P-value
Curcumin group (n=18)	58.45±12.36	67.35±11.24	2.260	0.030
Paraquat group (n=17)	75.27±13.73 ^a	100.92±14.88 ^a	5.223	<0.001
Control group (n=18)	44.73±9.62 ^{a,b}	45.19±10.15 ^{a,b}	0.140	0.890
F	28.420	92.180		
P-value	<0.001	<0.001		

^aStatistical difference (P<0.05), when compared with the curcumin group; ^bStatistical difference (P<0.05), when compared with the paraquat group.

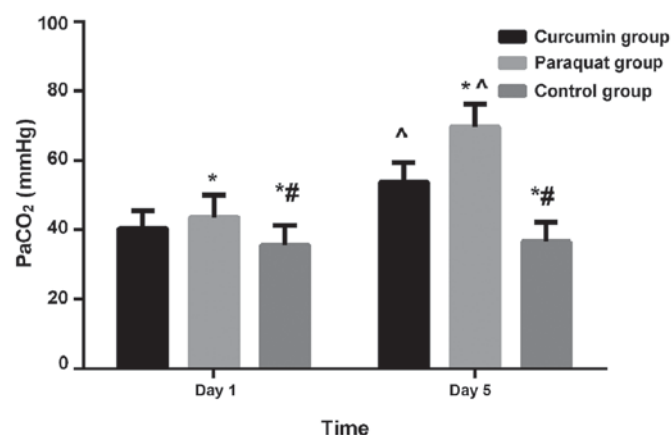


Figure 3. Comparison of artery blood PaCO₂ values of rats between the three groups. The PaCO₂ of artery whole blood on days 1 and 5 in the curcumin group were 40.41±5.16 mmHg and 53.73±5.72 mmHg, respectively. The PaCO₂ of artery blood on days 1 and 5 in the paraquat group was 43.56±6.39 mmHg and 69.67±6.53 mmHg, respectively. The PaCO₂ of artery blood days 1 and 5 in the control group was 35.48±5.92 mmHg and 36.54±5.61 mmHg, respectively. PaCO₂ in artery blood of rats in the curcumin group was significantly lower on day 1 than that on day 5, which was statistically significant (P<0.001). PaCO₂ in artery blood of rats in the paraquat group was significantly lower on day 1 than that on day 5, which was statistically significant (P<0.001); There was no significant difference in PaCO₂ on days 1 and 5 in the control group, which was not statistically significant (P>0.05). On days 1 and 5, the artery blood PaCO₂ of rats between the three groups was statistically significant (P<0.001); The artery blood PaCO₂ of the control group was lower than that in the curcumin group and paraquat group, which were statistically significant (P<0.05). The PaCO₂ of artery blood in the curcumin group was lower than that in the paraquat group, which was statistically significant (P<0.05). *P<0.05, when compared with the curcumin group; #P<0.05, when compared with the paraquat group and ^P<0.05, compared to day 1.

significant (t=6.248, P<0.001). There was no significant difference in serum IL-4 between days 1 and 5 in the control group, which was not statistically significant (P>0.05). On days 1 and 5, serum IL-4 of rats in the three groups was statistically significant (F=202.200, P<0.001; F=330.400, P<0.001). Serum IL-4 in the control group was significantly lower than that in the curcumin group and the paraquat group (P<0.05). Serum IL-4 was lower in the curcumin group than that in the paraquat group, which was statistically significant (P<0.05; Table III).

Comparison of serum INF- γ in rats between the three groups. Serum INF- γ in the curcumin group was significantly higher

on day 1 than that on day 5, which was statistically significant (t=5.959, P<0.001). The serum INF- γ in the paraquat group was significantly higher on day 1 than that on day 5, which was statistically significant (t=4.118, P<0.001); there was no significant difference in serum INF- γ between days 1 and 5 in the control group, which was not statistically significant (P>0.05). On days 1 and 5, serum INF- γ of rats in the three groups was statistically significant (F=9.138, P<0.001; F=26.030, P<0.001). The serum INF- γ of the control group was significantly higher than that in the curcumin group and the paraquat group (P<0.05). The serum INF- γ of the curcumin group was higher than that in the paraquat group, which was statistically significant (P<0.05; Table IV).

Discussion

Pulmonary fibrosis caused by paraquat is a chronic progressive inflammatory disease that can cause diffuse alveolitis and alveolar structural disorders. However, due to the lack of effective treatment methods, the mortality rate remains high and seriously endangers the life and health of patients (15). In recent years, it has been reported that curcumin can inhibit the transformation of epithelial to mesenchymal, and has anti-angiogenic, pro-apoptotic and immunomodulatory effects, which can inhibit the occurrence and development of tumors and make curcumin a focus of research (16,17). Curcumin has the characteristics of large safe concentration of drug, small adverse reaction and low price, and has been widely used in the treatment of many diseases, such as colorectal cancer, lung cancer and inflammatory diseases (18-20). Therefore, this study investigated the effects of curcumin on a rat model of pulmonary fibrosis induced by paraquat.

In this study, we found that the PaO₂ in the artery blood of the curcumin group was higher than that in the paraquat group, the PaCO₂ was lower than that in the paraquat group. The PaO₂ and PaCO₂ levels can be used to determine whether a patient has symptoms such as CO₂ retention and hypoxia, and can reflect the degree or type of respiratory disease of the patient (21). Due to the massive replacement of alveolar fibrosis in the absence of gas exchange function in pulmonary fibrosis, normal lung tissue structure degeneration and partial lung function loss, CO₂ retention may occur in the blood, which may lead to poor breathing, hypoxia, and can even lead to death of the patient (22). According to studies reported by Lelli *et al* (23), curcumin has a variety of pro-growth effects,

Table II. Comparison of serum Smurf2 values in rats between the three groups (pg/ml).

Groups	Day 1	Day 5	t	P-value
Curcumin group (n=18)	53.41±8.72	68.83±9.11	5.188	<0.001
Paraquat group (n=17)	64.55±9.28 ^a	81.56±11.34 ^a	4.786	<0.001
Control group (n=18)	31.62±7.84 ^{a,b}	30.77±8.05 ^{a,b}	0.321	0.750
F	66.480	135.000		
P-value	<0.001	<0.001		

Statistical difference (P<0.05), when compared with the ^acurcumin and ^bparaquat groups.

Table III. Comparison of serum IL-4 values of rats between the three groups (ng/l).

Groups	Day 1	Day 5	t	P-value
Curcumin group (n=18)	262.73±9.81	278.54±10.16	4.749	<0.001
Paraquat group (n=17)	284.49±10.72 ^a	308.48±11.65 ^a	6.248	<0.001
Control group (n=18)	221.52±7.58 ^{a,b}	222.69±8.13 ^{a,b}	0.447	0.658
F	202.200	330.400		
P-value	<0.001	<0.001		

Statistical difference (P<0.05), when compared with the ^acurcumin and ^bparaquat groups.

Table IV. Comparison of serum INF-γ values of rats between the three groups (ng/l).

Groups	Day 1	Day 5	t	P-value
Curcumin group (n=18)	528.91±18.42	491.66±19.08	5.959	<0.001
Paraquat group (n=17)	473.15±19.86 ^a	445.95±18.63 ^a	4.118	<0.001
Control group (n=18)	580.62±20.75 ^{a,b}	577.36±18.28 ^{a,b}	0.500	0.620
F	9.138	26.030		
P-value	<0.001	<0.001		

Statistical difference (P<0.05), when compared with the ^acurcumin and ^bparaquat groups.

which may play a role in the treatment of lung diseases such as lung cancer, as well as the regulation of transcription factors, cytokines, adhesion molecules and enzymes that play a key role in inflammation and cancer. Therefore, rats with pulmonary fibrosis caused by paraquat poisoning had lower PaO₂ and higher PaCO₂ than normal rats. When paraquat-poisoned rats were treated with curcumin, their blood gas indexes were normal compared with those in the paraquat group. Recent studies have found that curcumin has an obvious anti-pulmonary fibrosis effect, and its conclusions can be used to support our research (24). In recent years, it has been reported that TGF-β plays a key role in the development and progression of pulmonary fibrosis, and TGF-β1 causes pulmonary fibrosis by promoting the proliferation, invasion and activation of lung fibroblasts (25). Smurfs plays a pivotal role in the regulation of TGF-β1 signaling by selectively mediating the degradation of key components in the Smad signaling pathway, and its dysfunction leads to abnormal TGF-β1/Smads signaling and to a series of pathophysiological

changes. It has been reported that Smad4 and Smurf2 can promote the development of pulmonary fibroblasts in pulmonary fibrosis (26,27). Furthermore, they have a key role in pulmonary fibrosis, which is in agreement with our research results. The report of Yallapu *et al* (28), indicates that curcumin inhibits the synthesis of extracellular matrix and inhibits collagen synthesis through Smad-mediated signaling pathway, thereby reducing cardiac repair and improving cardiac function after ischemia-reperfusion. It was found that curcumin can reduce myocardial ischemia and fibrosis as well as significantly downregulated the expression of TGF-β1 and Smad in ischemia-reperfusion myocardium (28). Furthermore, curcumin, not only reduced myocardial ischemia and fibrosis, but significantly downregulated the expression of TGF-β1 and Smad in ischemia-reperfusion myocardium (28). Those findings may support our research results. When the stress response is repaired after the lung is damaged, IFN-γ can inhibit the activation and proliferation of fibroblasts and promote the synthesis of collagen (29). The

expression of TGF- β 1 and Smad in ischemia-reperfusion myocardium were also significantly downregulated, which may support our findings. When lung damage occurs and stress response is repaired, IFN- γ can inhibit the activation and proliferation of fibroblasts and promote collagen synthesis (29). IL-4 can induce fibroblast proliferation and promote exogenous collagen to cause fibrosis, which accumulates in the lungs and causes lung damage through oxidation and inflammation processes (30). When the body is normal, IFN- γ and IL-4 are in a state of equilibrium, which plays a key regulatory role in the body's immune response. However, fibrosis occurs when IL-4 is transferred. According to the *in vitro* studies of LITERAT (31), curcumin can inhibit the production of alveolar inflammatory cytokines IL- β 1 and IL-8. In addition, the nasal administration of curcumin can inhibit airway inflammation and pulmonary fibrosis (32), which further validates our experiment.

Further aspects remain to be explored, including the mechanism influence of curcumin on paraquat poisoning. Of note, differences between animal models and human body should be considered. Consequently, experiments regarding the effect of curcumin on paraquat poisoning in human are to be conducted in future studies.

In summary, curcumin can effectively improve pulmonary fibrosis in rats after treatment of paraquat poisoning. In addition, it is expected to be an effective drug for treating paraquat and providing effective reference and guidance for clinical treatment.

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Availability of data and materials

The datasets used and/or analyzed during the present study are available from the corresponding author on reasonable request.

Authors' contributions

HC wrote the manuscript. HC and XF were responsible for construction of the lung fibrosis model. HC and RY performed ELISA. RY and YT helped with determination of pH, PaO₂ and PaCO₂. All authors read and approved the final manuscript.

Ethics approval and consent to participate

The study was approved by the Ethics Committee of Gansu Provincial Hospital (Lanzhou, China).

Patient consent for publication

Not applicable.

Competing interests

The authors declare that they have no competing interests.

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