doi.org/10.36721/PJPS.2026.39.3.REG.13264.1

Effect of linezolid combined with N-acetylcysteine on lung function, blood gas and inflammation in patients with severe pneumonia

Xiaoyan Bai[1], Yao Luo[1], Jiajia Huang[2] and Guangfeng Liu[2]*

[1]Chengdu Public Health Clinical Medical Center, Chengdu, China

[2]Department of Occupational Pulmonary Diseases, Shandong Academy of Occupational Health and Occupational Medicine, Shandong Province Hospital of Occupational Diseases, Jinan, China

Abstract: **Background**: Severe pneumonia is a serious lung disease. The continuous and regular administration of antibiotics is currently used for severe pneumonia. However, the single antibiotic may enhance the drug resistance and the overall efficacy is not ideal. **Objectives**: This study aimed to investigate the efficacy and safety of linezolid combined with N-acetylcysteine (NAC) on lung function, blood gas and inflammation in patients with severe pneumonia. **Methods**: Eighty-four severe pneumonia patients were divided into linezolid group and linezolid +NAC group, which received the treatment using linezolid and linezolid combined with NAC for ten days, respectively. The total treatment efficacy was assessed. Before and after treatment, the pulmonary function indexes, blood gas indexes inflammatory response indexes were determined. **Results**: Compared with linezolid group, in linezolid +NAC group the disappearance time of cough, sputum and lung rales were shortened, the total effective rate, peak expiratory flow, forced expiratory volume in one second/forced vital capacity, arterial oxygen partial pressure and blood oxygen saturation were increased, the arterial carbon dioxide partial pressure and serum tumor necrosis factor α, interleukin 6 and hypersensitive C-reactive protein levels were decreased (all $P < 0.05$). **Conclusion**: In treating severe pneumonia, linezolid combined with NAC can significantly improve the lung function of patients, improve the blood gas indicators and reduce the inflammatory response, thus alleviating the clinical symptoms.

Keywords: Acetylcysteine; Blood gas; Inflammation; Linezolid; Lung function; Severe pneumonia

Submitted on 19-08-2024 – Revised on 14-08-2025 – Accepted on 26-08-2025

INTRODUCTION

With the aggravation of environmental pollution, aging population and abuse of antibiotics, the incidence rate of severe pneumonia has increased significantly. Clinical study has shown that the occurrence of severe pneumonia is usually related to infections of pathogenic microorganisms such as viruses, fungi, bacteria, etc., which can cause the inflammation in alveoli, lung interstitium and terminal airways (Mizgerd, 2017). The severe pneumonia has the characteristic of sudden onset, serious condition and rapid development. If not treated timely, it can easily lead to the serious complications such as respiratory failure, multiple organ dysfunction syndrome and even death, posing a serious threat to the life quality and health of patients (De Pascale *et al.*, 2012). The continuous and regular administration of sufficient amounts of antibiotics to patients, combined with oxygen therapy, maintenance of water electrolyte balance and mechanical ventilation, is currently a routine clinical treatment for severe pneumonia. Linezolid is a class of oral oxazolidine antibiotic. It has good therapeutic effect on infections caused by gram-positive cocci such as methicillin-resistant *Staphylococcus aureus* and vancomycin-resistant *Enterococcus* (Narang and Gomber, 2004). In addition, it has no cross resistance with other antibacterial drugs that block the protein synthesis (Hashemian *et al.*, 2018). Linezolid is often used to treat severe pneumonia (Wu *et al.*, 2022). However, it is found that the efficacy of single linezolid is still not ideal in some patients and it needs to be combined with other drugs. N-acetylcysteine (NAC) is a new type of mucus solubilizer, which has strong effects on promoting mucus dissolution and inhibiting inflammatory reactions (Tardiolo *et al.*, 2018). The inhalation NAC nebulization therapy is a new technology for clearing the bronchitis and improving the lung function. It can quickly dissolve the mucus and thick viscous secretions, with less stimulation to patients and is safe and reliable (Li *et al.*, 2018; Mancini *et al.*, 2023). This study investigated the efficacy and safety of linezolid combined with NAC on lung function, blood gas and inflammation in patients with severe pneumonia.

MATERIALS AND METHODS

Subjects

A retrospective analysis was performed on eighty-four severe pneumonia patients admitted to our hospital from May 2021 to May 2023. According to the treatment method, the patients were divided into linezolid group and linezolid + NAC group, with 42 cases in each group. In linezolid group there were 29 males and 13 females. The age ranged from 42 to 74 years old, with average of 55.32±4.69 years old. The disease course was 1-11 days, with average of 7.56±1.24 days. As for the basic diseases, there were 7 cases of diabetes, 8 cases of chronic

**Corresponding author:* e-mail: liugfsd1@126.com

obstructive pulmonary disease and 6 cases of hypertension. In linezolid+NAC group there were 27 males and 15 females. The age ranged from 41 to 76 years old, with average of 54.67±5.82 years old. The disease course was 1-10 days, with average of 7.01±1.32 days. As for the basic diseases, there were 8 cases of diabetes, 5 cases of chronic obstructive pulmonary disease and 7 cases of hypertension. There was no statistically significant difference in general data between two groups ($P > 0.05$).

Inclusion criteria and exclusion criteria

Inclusion criteria

(1) The patients were diagnosed as severe pneumonia through laboratory, physical sign and imaging examinations; (2) the patients had not received the anti-infection treatment before enrollment; (3) the patients were informed of this study and had signed the informed consent form.

Exclusion criteria

(1) The patients were with severe liver or kidney dysfunction; (2) the patients were with pulmonary fungal or viral infections; (3) the patients were allergies to drugs use in this study; (4) the patients were with hematological or immune system diseases.

Treatment strategy

All patients were given the standard supportive treatments such as fluid replacement, oxygen therapy, sputum aspiration, cough suppressing, bronchiectasis, antihistamine therapy, water electrolysis maintenance and nutritional support. The mechanical ventilation was performed for assisted respiration. In addition, in linezolid group, the patients were given linezolid injection (100 ml: 200 mg linezolid; Jiangsu Haosen Pharmaceutical Group Co., Ltd., Lianyungang, China) by intravenous drip, with dosage of 600 mg, once per 12 h. On the basis of treatment strategy in linezolid group, the linezolid+NAC group was given NAC (0.3 g NAC was dissolved in 3 ml normal saline; Ruiyang Pharmaceutical Co., Ltd., Zibo, China) by nebulized inhalation, 10 min per time, twice per day. The treatment was performed for ten successive days. During the treatment, the disappearance time of clinical symptoms such as cough, sputum and lung rales of patients was recorded and the drug-related adverse reactions were observed.

Assessment of total treatment efficacy

After treatment, the total treatment efficacy was assessed as follows: remarkably effective: compared with before treatment, the clinical symptoms of patients completely disappeared and the pulmonary inflammation completely disappeared; effective: compared with before treatment, the clinical symptoms of patients were significantly improved and the pulmonary inflammation showed significant improvement; ineffective: compared with before treatment, the clinical symptoms of patients were not improved and the pulmonary inflammation was not improved or even aggravated. The total effective rate was calculated as follows: total effective rate (%) = [(number of remarkably effective cases + number of effective cases) / total case number] × 100%.

Measurement of pulmonary function

Before and after treatment, the pulmonary function of patients was measured. The forced expiratory volume in one second (FEV1), forced vital capacity (FVC) and peak expiratory flow (PEF) were recorded and the FEV1/FVC was calculated.

Blood gas analysis

Before and after treatment, the arterial blood was collected for blood gas analysis. The arterial oxygen partial pressure (PaO_2), arterial carbon dioxide partial pressure ($PaCO_2$) and blood oxygen saturation (SaO_2) were measured.

Determination of inflammatory response indexes

Before and after treatment, the venous blood was taken. After centrifuging at 3500 r/min for 10 min, the serum was obtained. The inflammatory response indexes including tumor necrosis factor α (TNF-α), interleukin 6 (IL-6) and hypersensitive C-reactive protein (hs-CRP) were determined by enzyme-linked immunosorbent assays.

Statistical analysis

SPSS 22.0 statistical software was used for statistical analysis. The counting data (number or rate) were compared using χ^2 test. The measurement data (mean±standard deviation) were compared using t test. The difference was statistically significant with $P < 0.05$.

RESULTS

Disappearance time of clinical symptoms

As shown in table 1, the disappearance time of cough, sputum and lung rales in linezolid + NAC group was obviously shorter than that in linezolid group, respectively ($P < 0.05$).

Total treatment efficacy

After treatment, the total effective rate in linezolid + NAC group was 90.48%, which was significantly higher than 71.43% in linezolid group ($P < 0.05$) (Table 2).

Pulmonary function parameters

Before treatment, there was no significant difference of PEF or FEV1/FVC between two groups ($P > 0.05$). After treatment, in each group the PEF and FEV1/FVC were significantly higher than before treatment ($P < 0.05$) and each index in linezolid + NAC group was significantly higher than linezolid group ($P < 0.05$) (Table 3).

Blood gas indexes

Before treatment, the PaO_2, $PaCO_2$ and SaO_2 had no significant difference between two groups, respectively ($P > 0.05$). After treatment, in each group the PaO_2 and SaO_2 were significantly higher than before treatment ($P < 0.05$) and the $PaCO_2$ was significantly lower than before treatment ($P < 0.05$). Compared with linezolid group, in linezolid+NAC group the PaO_2 and SaO_2 were further increased ($P < 0.05$) and the $PaCO_2$ was further decreased ($P > 0.05$) (Table 4).

Inflammatory response indexes

Before treatment, there was no significant difference of serum TNF-α, IL-6 or hs-CRP level between two groups ($P > 0.05$). After treatment, in two groups each index was significantly higher than before treatment ($P < 0.05$) and each index in linezolid + NAC group was significantly lower than linezolid group ($P < 0.05$) (Table 5).

Adverse reactions

During the treatment, the incidence of adverse reactions in linezolid and linezolid + NAC groups was 9.52% and 16.67%, respectively, with no significant difference between two groups ($P > 0.05$) (Table 6).

DISCUSSION

Severe pneumonia often presents with symptoms such as fever, dyspnea and expectoration. If this disease is not treated in a timely manner, the systemic inflammatory reactions may occur, which are difficult to control and easily accompanied by various comorbidities, leading to multiple organ failure in the body and directly threatening the life safety (Ching and Pedersen, 2025). In the clinical practice the reasonable medication is the key to treating severe pneumonia.

Linezolid belongs to the oxazolone class of antibiotic and has a unique antibacterial mechanism. It is another new antibacterial drug after sulfonamide and quinolone and is widely used in severe inflammatory diseases caused by Gram-positive bacterial infections (Batts, 2000). NAC is a potent drug for dissolving thick secretions, with highly effective anti-inflammatory and antioxidant effects (Ghafarizadeh *et al.*, 2021; Cepaityte *et al.*, 2023). NAC can significantly improve the condition of pneumonia patients (Paraskevas *et al.*, 2023). It can be used as a lavage solution when performing pulmonary lavage for patients with severe pneumonia (Song *et al.*, 2024). This study explored the efficacy and safety of linezolid combined with NAC for patients with severe pneumonia. After ten days of treatment, compared with linezolid group, the total effective rate in linezolid+NAC group was significantly increased. This indicates that, compared with single use of linezolid, the linezolid combined with NAC is more effective for treatment of severe pneumonia. In addition, during the treatment, the incidence of adverse reactions had no significant difference between two groups, indicating that this combined strategy cannot decrease the safety of treatment.

PEF and FEV1/FVC are important indicators reflecting the lung function in clinical practice (Buran Cirak *et al.*, 2022). The research has shown that in severe pneumonia patients a large amount of inflammatory secretions are produced in the airways, causing abnormal aggregation of neutrophils and macrophages in the respiratory mucosa. This can damage the airway mucosa and seriously affect the lung function, which exacerbates the disease progression and causes a series of clinical symptoms (Wang *et al.*, 2021). The hypoxia and hypercapnia are typical manifestations of severe pneumonia, typically characterized by decreased PaO^2 and SaO^2 and increased $PaCO_2$ (Alwadhi *et al.*, 2017; Gates *et al.*, 2013). It is found that, NAC can obviously improve the lung function of patients with pulmonary tuberculosis (Wallis *et al.*, 2024) and patients with chronic obstructive pulmonary disease (Zhou *et al.*, 2024). In our study, during the treatment the disappearance time of cough, sputum and lung rales in linezolid + NAC group was obviously shorter than that in linezolid group, respectively. After treatment, the PEF and FEV1/FVC in linezolid + NAC group were significantly higher than those in linezolid group, respectively. In addition, Compared with linezolid group, in linezolid + NAC group the PaO_2 and SaO_2 were increased, respectively and the $PaCO_2$ was decreased. This suggests that, compared with single use of linezolid, the linezolid combined with NAC can further enhance the lung function of patients with severe pneumonia, improve the blood gas indicators and alleviate the clinical symptoms.

Inflammatory response is an important pathogenesis of severe pneumonia. When the body's immune defense system and respiratory tract are damaged locally, a large number of pathogens invade the respiratory tract, resulting in the pneumonia. When the respiratory tract is invaded by pathogenic microorganisms, the immune cells such as neutrophils and macrophages are activated, triggering the immune response. The inflammatory mediators are generated in large quantities, releasing a series of inflammatory chemokines and cytokines (Torres *et al.*, 2015). TNF-α and IL-6 are the typical pro-inflammatory factor. They can stimulate the aggregation, chemotaxis and migration of various inflammatory cells to the site of injury and increase the activity of cytokines, thereby exacerbating pulmonary vascular endothelial injury (Qin and Qiu, 2019). Hs-CRP is synthesized and secreted by liver cells in the body. The severe pneumonia patients are in a state of severe inflammatory response and lung tissue damage and hs-CRP is produced in large quantities and enters the blood circulation (Smilowitz *et al.*, 2021). It is found that, NAC has obvious anti-inflammatory property. As shown in study from Zhao *et*

Table 1: Disappearance time of clinical symptoms (days).

Group	n	Cough	Sputum	Lung rales
Linezolid	42	17.34±3.05	14.04±2.03	13.20±2.62
Linezolid + NAC	42	14.18±2.71	9.26±1.56	8.12±1.42
t		5.019	12.100	11.047
P		< 0.001	< 0.001	< 0.001

NAC, N-acetylcysteine.

Table 2: Total treatment efficacy.

Group	n	Remarkably effective (n)	Effective (n)	Ineffective (n)	Total effective rate (%)
Linezolid	42	9	21	12	71.43
Linezolid +NAC	42	13	25	4	90.48
χ^2					4.941
P					0.026

NAC, N-acetylcysteine.

Table 3: Pulmonary function parameters.

Index	Group	n	Before treatment	After treatment	t	P
PEF (L/s)	Linezolid	42	2.11±0.34	2.78±0.56	6.628	< 0.001
	Linezolid+NAC	42	2.01±0.42	3.35±0.55	12.549	< 0.001
	t		1.199	4.706		
	P		0.234	< 0.001		
FEV1/FVC (%)	Linezolid	42	62.05±11.34	67.27±8.72	2.365	0.020
	Linezolid+NAC	42	63.18±12.43	71.32±7.71	3.607	0.001
	t		0.435	2.255		
	P		0.665	0.027		

NAC, N-acetylcysteine; PEF, peak expiratory flow; FEV1, forced expiratory volume in one second; FVC, forced vital capacity.

Table 4: Blood gas indexes.

Index	Group	n	Before treatment	After treatment	t	P
PaO_2 (mmHg)	Linezolid	42	51.56±9.16	71.61±13.12	8.116	< 0.001
	Linezolid+NAC	42	50.02±8.31	78.52±15.82	10.353	< 0.001
	t		0.817	2.184		
	P		0.416	0.032		
$PaCO_2$ (mmHg)	Linezolid	42	62.32±11.28	47.34±7.05	7.298	< 0.001
	Linezolid+NAC	42	60.17±13.91	40.16±8.17	8.043	< 0.001
	t		0.778	4.312		
	P		0.439	< 0.001		
SaO_2 (%)	Linezolid	42	70.63±14.43	87.21±15.62	5.056	< 0.001
	Linezolid+NAC	42	72.16±15.63	94.38±14.29	6.800	< 0.001
	t		0.466	2.196		
	P		0.642	0.031		

NAC, N-acetylcysteine; PaO_2, arterial oxygen partial pressure; $PaCO_2$, arterial carbon dioxide partial pressure; SaO_2, blood oxygen

al., (2022), NAC can reduce the serum TNF-α and IL-6 levels during the acute lung injury. Askari *et al.*, (2020) have found that, the oral NAC supplementation can reduce the serum level of CRP and IL-6.

In our study, after treatment, the serum TNF-α, IL-6 and hs-CRP levels in linezolid+NAC group were significantly lower than those in linezolid group, respectively. This indicates that, compared with single use of linezolid,

Table 5: Inflammatory response indexes.

Index	Group	n	Before treatment	After treatment	t	P
TNF-α (pg/ml)	Linezolid	42	23.27±4.06	18.71±3.81	5.308	< 0.001
	Linezolid+NAC	42	22.16±3.21	14.62±2.89	11.313	< 0.001
	t		1.390	5.543		
	P		0.168	< 0.001		
IL-6 (ng/ml)	Linezolid	42	72.42±15.24	61.29±12.15	3.701	< 0.001
	Linezolid+NAC	42	69.81±16.08	43.15±9.27	9.305	< 0.001
	t		0.766	7.692		
	P		0.446	< 0.001		
hs-CRP (μg/ml)	Linezolid	42	34.60±8.04	21.28±5.32	8.954	< 0.001
	Linezolid+NAC	42	33.04±6.17	14.72±3.41	16.853	< 0.001
	t		0.998	6.734		
	P		0.321	< 0.001		

NAC, N-acetylcysteine; TNF-α, tumor necrosis factor α; IL-6, interleukin 6; hs-CRP, hypersensitive C-reactive protein.

Table 6: Adverse reactions.

Group	n	Diarrhea (n)	Nausea/vomiting (n)	Abnormal liver function (n)	Incidence (%)
Linezolid	42	1	1	2	9.52
Linezolid+NAC	42	2	2	3	16.67
χ^2					0.942
P					0.332

NAC, N-acetylcysteine.

linezolid combined with NAC can further reduce the inflammatory response, thus alleviating the clinical symptoms of severe pneumonia patients.

CONCLUSION

In conclusion, in treating the severe pneumonia, linezolid combined with NAC can obviously enhance the lung function of patients, improve the blood gas indicators and reduce the inflammatory response, thus alleviating the clinical symptoms. This treatment strategy has obvious clinical promotion value. However, due to the small sample size, the findings of this study still needs to be further verified and deep research is needed to obtain more accurate results.

Acknowledgement
Not available.

Authors' contributions
Xiaoyan Bai designed the study, Yao Luo collected and analyzed the data, Jiajia Huang wrote the manuscript and Guangfeng Liu revised the manuscript.

Funding
None.

Data availability statements
The datasets generated during and/or analysed during the current study are available from the corresponding author on reasonable request.

Ethical approval
This study was reviewed and approved by the ethics committee of Chengdu Public Health Clinical Medical Center (20230721001). Written informed consent was obtained from all participants.

Conflict of interest
The authors declare no conflict of interest.

REFERENCES

Alwadhi V, Dewan P, Malhotra RK, Shah D and Gupta P (2017). Tachypnea and other danger signs vs pulse oximetry for prediction of hypoxia in severe pneumonia/very severe disease. *Indian Pediatr.*, **54**(9): 729-734.

Askari M, Faryabi R, Mozaffari H and Darooghegi Mofrad M (2020). The effects of N-Acetylcysteine on serum level of inflammatory biomarkers in adults. Findings from a systematic review and meta-analysis of randomized clinical trials. *Cytokine*, **135**: 155239.

Batts DH (2000). Linezolid-a new option for treating gram-positive infections. *Oncology (Williston Park)*, **14**(8 Suppl 6): 23-29.

Buran Cirak Y, Yilmaz Yelvar GD and Durustkan Elbasi N (2022). Effectiveness of 12-week inspiratory muscle training with manual therapy in patients with COPD: A randomized controlled study. *Clin. Respir. J.*, **16**(4): 317-328.

Cepaityte D, Leivaditis K, Varouktsi G, Roumeliotis A,

Roumeliotis S and Liakopoulos V (2023). N-Acetylcysteine: More than preventing contrast-induced nephropathy in uremic patients-focus on the antioxidant and anti-inflammatory properties. *Int. Urol. Nephrol.*, **55**(6): 1481-1492.

Ching PR and Pedersen LL (2025). Severe pneumonia. *Med. Clin. North. Am.*, **109**(3): 705-720.

De Pascale G, Bello G, Tumbarello M and Antonelli M (2012). Severe pneumonia in intensive care: Cause, diagnosis, treatment and management: A review of the literature. *Curr. Opin. Pulm. Med.*, **18**(3): 213-221.

Gates KL, Howell HA, Nair A, Vohwinkel CU, Welch LC, Beitel GJ, Hauser AR, Sznajder JI and Sporn PH (2013). Hypercapnia impairs lung neutrophil function and increases mortality in murine *Pseudomonas pneumonia*. *Am. J. Respir. Cell Mol. Biol.*, **49**(5): 821-828.

Ghafarizadeh A, Malmir M, Naderi Noreini S and Faraji T (2021). Antioxidant effects of N-acetylcysteine on the male reproductive system: A systematic review. *Andrologia*, **53**(1): e13898.

Hashemian SMR, Farhadi T and Ganjparvar M (2018). Linezolid: A review of its properties, function and use in critical care. *Drug Des. Devel. Ther.*, **12**: 1759-1767.

Li X, Wei X, Chen C, Zhang Z, Liu D, Hei Z and Yao W (2018). N-Acetylcysteine inhalation improves pulmonary function in patients received liver transplantation. *Biosci. Rep.*, **38**(5): BSR20180858.

Mancini L, Paolantoni M, Schoubben A and Ricci M (2023). Development of spray-dried N-acetylcysteine dry powder for inhalation. *Int. J. Pharm.*, **631**: 122550.

Mizgerd JP (2017). Pathogenesis of severe pneumonia: Advances and knowledge gaps. *Curr. Opin. Pulm. Med.*, **23**(3): 193-197.

Narang M and Gomber S (2004). Linezolid. *Indian Pediatr.*, **41**(11): 1129-1132.

Paraskevas T, Kantanis A, Karalis I, Michailides C, Karamouzos V, Koniari I, Pierrakos C and Velissaris D (2023). N-acetylcysteine efficacy in patients hospitalized with COVID-19 pneumonia: A systematic review and meta-analysis. *Rom. J. Intern. Med.*, **61**(1): 41-52.

Qin M and Qiu Z (2019). Changes in TNF-α, IL-6, IL-10 and VEGF in rats with ARDS and the effects of dexamethasone. *Exp. Ther. Med.*, **17**(1): 383-387.

Smilowitz NR, Kunichoff D, Garshick M, Shah B, Pillinger M, Hochman JS and Berger JS (2021). C-reactive protein and clinical outcomes in patients with COVID-19. *Eur. Heart J.*, **42**(23): 2270-2279.

Song Z, Xu X, Zhang Y and Zhao Y (2024). Observation of therapeutic effect of inhaled N-acetylcysteine pulmonary lavage in patients with severe pneumonia. *Minerva Gastroenterol. (Torino)*, **70**(1): 119-121.

Tardiolo G, Bramanti P and Mazzon E (2018). Overview on the effects of N-acetylcysteine in neurodegenerative diseases. *Molecules*, **23**(12): 3305.

Torres A, Sibila O, Ferrer M, Polverino E, Menendez R, Mensa J, Gabarrus A, Sellares J, Restrepo MI, Anzueto A, Niederman MS and Agusti C (2015). Effect of corticosteroids on treatment failure among hospitalized patients with severe community-acquired pneumonia and high inflammatory response: A randomized clinical trial. *JAMA*, **313**(7): 677-686.

Wallis RS, Sabi I, Lalashowi J, Bakuli A, Mapamba D, Olomi W, Siyame E, Ngaraguza B, Chimbe O, Charalambous S, Rachow A, Ivanova O, Zurba L, Myombe B, Kunambi R, Hoelscher M, Ntinginya N and Churchyard G (2024). Adjunctive N-acetylcysteine and lung function in pulmonary tuberculosis. *NEJM Evid.*, **3**(9): EVIDoa2300332.

Wang F, Nan K, Hao L, Li H, Wang C, Zhang L, Jiang L and Tian Y (2021). Effects of a combination of erythromycin sequential therapy and azithromycin on lung function and inflammatory factors in children with severe *Mycoplasma pneumonia*. *Pak. J. Pharm. Sci.*, **34**(6 Special): 2447-2454.

Wu W, Li L, Duan S and Wang Y (2022). Clinical effectiveness and reliability of linezolid in the treatment of pulmonary tuberculosis complicated with severe pneumonia: A meta-analysis. *Am. J. Transl. Res.*, **14**(11): 7622-7631.

Zhao H, Fu L, Xiang HX, Xiang Y, Li MD, Lv BB, Tan ZX, Gao L, Zhang C and Xu DX (2022). N-acetylcysteine alleviates pulmonary inflammatory response during benzo[a]pyrene-evoked acute lung injury. *Environ. Sci. Pollut. Res. Int.*, **29**(3): 3474-3486.

Zhou Y, Wu F, Shi Z, Cao J, Tian J, Yao W, Wei L, Li F, Cai S, Shen Y, Wang Z, Zhang H, Chen Y, Fu Y, He Z, Chang C, Jiang Y, Chen S, Yang C, Yu S, Tian H, Cheng Q, Zhao Z, Ying Y, Zhou Y, Liu S, Deng Z, Huang P, Zhang Y, Luo X, Zhao H, Gui J, Lai W, Hu G, Liu C, Su L, Liu Z, Huang J, Zhao D, Zhong N, Ran P and China N-acetylcysteine in Mild-to-moderate COPD Study Group (2024). Effect of high-dose N-acetylcysteine on exacerbations and lung function in patients with mild-to-moderate COPD: A double-blind, parallel group, multicentre randomised clinical trial. *Nat. Commun.*, **15**(1): 8468.