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RESEARCH PAPER

Baicalin attenuates air embolism-induced acute lung injury in rat isolated lungs

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Background and purpose: Baicalin has been reported to have anti-inflammatory effects and protect against various tissue injuries. However, the effect of baicalin on air embolism-induced acute lung injury has not been tested yet.
Experimental approach: Acute lung injury was induced by infusion of air at a rate of 0.25 mL·min^{-1} for 1 min into the pulmonary artery of rat isolated lungs. At the end of the experiment, samples were collected for assessment of lung injury, biochemical analysis and histology. Different doses of baicalin (1, 2 and 4 mg·kg^{-1}) were given into the perfusate before air infusion.
Key results: Air embolism elicited a significant increase in microvascular permeability (K_f), lung weight gain, wet/dry weight ratio, pulmonary artery pressure and protein concentration in the bronchoalveolar lavage fluid. Levels of the cytokines, tumour necrosis factor α and cytokine-induced neutrophil chemoattractant-1 in perfusate, and malondialdehyde levels and myeloperoxidase activities in lung tissue were also significantly increased. In addition, histological examination showed increased neutrophil infiltration in lung tissues. Furthermore, nuclear factor-κB activity and degradation of IκB-α were significantly increased in lungs. Pretreatment of the lungs with baicalin (4 mg·kg^{-1}) showed a statistically significant difference in all of the assessed parameters, except for alteration in the pulmonary artery pressure.
Conclusions and implications: Our study suggests that baicalin attenuated air embolism-induced acute lung injury and may be considered a useful adjunct drug therapy in this clinical condition.
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Keywords: acute lung injury; air embolism; baicalin

Abbreviations: ALI, acute lung injury; CINC-1, cytokine-induced neutrophil chemoattractant-1; MDA, malondialdehyde; MPO, myeloperoxidase; NF-κB, nuclear factor-κB; PAP, pulmonary artery pressure; TNF-α, tumour necrosis factor α

Introduction

Large volumes of air within the pulmonary circulation can occur not only during diving and aviation but also during traumatic injuries and medical procedures (Muth and Shank, 2000; Souders, 2000). Under normal conditions, air is usually absorbed from pulmonary vasculature. However, when the amount of air exceeds the absorption capability of lung, adverse effects, even life-threatening complication may appear, which include acute lung injury and acute respiratory distress syndrome. Two possible consequences of air embolism have been suggested (Muth and Shank, 2000; Souders, 2000). First, mechanical obstruction of the blood flow to the pulmonary vessels may lead to tissue hypoxia. Second, air bubbles may interact with blood products or irritate pulmonary endothelium, which in turn induces a series of inflammatory response. Pulmonary vascular injury is manifested by pulmonary hypertension, ventilation–perfusion mismatch and acute pulmonary oedema. The current management of air embolism-induced acute lung injury has been supportive. Until now, no pharmacological intervention has been demonstrated to improve clinical outcome (Calfee and Matthay, 2007) and consequently, novel treatments for air embolism-induced acute lung injury are need to be developed.

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Baicalin is one of the major flavonoid components of *Scutellaria baicalensis* Georgi, which is a traditional Chinese herb, used in the treatment of various inflammatory diseases (Kubo *et al*., 1984). Lo *et al*. (2005) have demonstrated that baicalin attenuated lipopolysaccharide (LPS)-induced lung oedema in rats. In experimental heatstroke, baicalin protected against cerebrovascular dysfunction and brain inflammation (Chang *et al*., 2007a). In addition, baicalin was effective against liver injury-induced by concanavalin A and tert-butyl hydroperoxide (Hwang *et al*., 2005; Liu *et al*., 2007), as well as attenuated caerulein-induced acute pancreatitis and ischaemia–reperfusion-induced brain injury (Zhang *et al*., 2006; 2008). However, the effectiveness of baicalin in the prevention of air embolism-induced acute lung injury has not been studied. Our goal of this study was to investigate the effect of baicalin in a rat isolated lung model of air embolism-induced acute lung injury.

Methods

Preparation of isolated and perfused rat lungs

Animals in this study were cared for in accordance with the National Institutes of Health guidelines (National Academy Press, Washington, D.C., 1996), and approval of the project protocol was obtained from the National Science Council and Animal Review Committee at the National Defense Medical Center. We prepared the isolated, perfused lungs *in situ* as previously described (Wang *et al*., 1992; Chu *et al*., 2005a). Male Sprague-Dawley rats (weighing 250–350 g) were anaesthetized with pentobarbital sodium (i.p., 20–25 mg). A tracheotomy was performed to allow ventilation (rodent ventilator 7025; Ugo Basile, Comerio, VA, Italy) with 5% CO_2 in air at 65–70 breaths·min^{-1} with a tidal volume of 2 mL. After a median sternotomy was performed, heparin (1 U·g^{-1} of body weight) was injected into the right ventricle, and 10 mL of blood was collected from the right ventricle. This blood sample was mixed with 10 mL of normal saline containing 1.5% human serum albumin. This subsequently was used as a perfusing fluid for the isolated lungs.

For constant-flow perfusion of the isolated lungs, a cannula was inserted into the pulmonary artery via a right ventricular puncture. A tight ligature was placed around the main trunk of the pulmonary artery. A wide-bore cannula was inserted into the left atrium via the left ventricle to divert pulmonary venous outflow into a reservoir. The wide-bore cannula then was fixed with a ligature at the apex of the heart. Another ligature was placed above the atrioventricular junction to prevent the flow of the perfusate into the ventricles. Both the pulmonary arterial pressure (PAP) and the pulmonary venous pressure (PVP) were recorded from side arms of the inflow and outflow cannulae. A roller pump was used to provide constant flow perfusion at a rate of approximately 8–10 mL·min^{-1} to stabilize the PAP at 15–20 cmH_2O. The PVP was set at 4–6 cmH_2O by adjusting the height of the venous reservoir. The isolated perfused lungs remained *in situ,* and the whole rat was placed on an electric balance. The digital signals of the electronic balance were converted to analog signals by a digital-to-analogue converter and were recorded on an oscillograph recorder.

Air infusion

Air was introduced with the rate of 0.25 mL·min^{-1} for 1 min into the lung via the pulmonary artery as previously described (Wang *et al*., 1992; Chu *et al*., 2005a).

Microvascular permeability

An index of microvascular permeability to water (K_f) was determined from the lung weight change induced by the elevation of venous pressure. During ventilation and lung perfusion, the PVP was rapidly elevated by 10 cmH_2O for at least 7 min. The slow, steady phase of weight gain as a function of time ($\Delta W/\Delta T$) was plotted on semi-logarithmic paper. The slow component then was extrapolated to zero time to obtain the initial rate of transcapillary filtration. From this plot, K_f was defined as the y-intercept (in g·min^{-1}) divided by the PVP (10 cmH_2O) and lung weight, and it was expressed in whole units of g·min^{-1}·cmH_2O^{-1} ×100 g.

Wet/dry weight ratio

After experiments, the part of right upper lung lobe was placed in an oven at 60°C for 48 h to allow determination of the wet/dry weight ratio.

Protein concentration in lung lavage fluid

Lung lavage fluid was obtained at the end of the experiment by irrigating the left lung with saline (2 × 2.5 mL). The fluid was centrifuged at 250× *g* for 10 min, and the concentration of protein in the supernatant was determined by using BCA protein assay reagents (Pierce, Rockford, IL, USA).

Measurement of tumour necrosis factor α and CINC-1 (cytokine-induced neutrophil chemoattractant) level in perfusate

Tumour necrosis factor α (TNF-α) and CINC-1 levels in the perfusate after experiment were measured by using an ELISA kit (R&D Systems Inc., Minneapolis, MN, USA).

Determination of malondialdehyde (MDA) level

The lung tissue was homogenized in 1.15% KCL solution. An aliquot (100 μL) of the homogenate was added to a reaction mixture containing 200 μL of 8.1% thiobarbituric acid and 700 μL of distilled water. Samples were then boiled for 30 min at 100°C and centrifuged at 3000× *g* for 10 min. The absorbance of the supernatant was measured spectrophotometrically at 532 nm (Chu *et al*., 2005b).

Determination of myeloperoxidase (MPO) activity

The part of the right lower lung lobe was freeze-thawed and sonicated three times. Homogenates were centrifuged at 15 000× *g* for 10 min at 4°C. A 100 μL aliquot of supernatant was mixed with 900 μL of 50 mmol·L^{-1} phosphate buffer (pH 6.0) containing 0.167 mg·mL^{-1} of o-dianisidine dihydrochloride and 0.0005% hydrogen peroxide. One unit of peroxidase activity is the amount of enzyme decomposing 1 μmol of hydrogen peroxide per minute at 25°C. Decomposition of

hydrogen peroxide was calculated from the oxidation of o-dianisidine by using an absorption coefficient of 11.3 $mmol \cdot L^{-1} \cdot cm^{-1}$ at 460 nm (Chu *et al*., 2005b).

Western blot analysis for IκB-α

Cytoplasmic and nuclear proteins were extracted from frozen lung tissue by Nuclear/Cytosol Extraction kit (BioVision, Inc., Mountain View, CA, USA) according to the manufacturer's instructions. Protein concentrations were determined by BCA protein assay kit (Pierce, Rockford, IL, USA). Samples were mixed with loading buffer and boiled for 5 min. And 30 μg of cytoplasmic protein was loaded into each lane and fractionated on 12% SDS-PAGE gels, and transferred to Hybond-PVDF membranes. Non-specific binding was blocked by incubation in phosphate-buffered saline (PBS) containing 0.1% Tween 20 (PBST) and 5% non-fat milk for 1 h at room temperature, then incubated with rat polyclonal anti-IκB-α antibodies (1:1000) (Cell Signaling Technology, Danvers, MA, USA) overnight at 4°C. The blots were then washed in PBST three times for 10 min. Blots were incubated with horseradish peroxidase-linked goat anti-rabbit antibody (1:20 000) for 1 h at room temperature, and then washed three times in PBST for 10 min. A chemiluminescent peroxidase substrate (Pierce, Rockford, IL, USA) was applied, and the images were visualized on X-ray films. The films were then digitized and quantified with an imaging system (Bio-Rad, Hercules, CA, USA). The blots were then stripped and incubated with an anti-β-actin antibody (1:10 000, Santa Cruz Biotechnology) to control protein loading.

Nuclear factor-κB (NF-κB) p65 activity assay

Nuclear factor-κB activity was tested as the nuclear translocation and DNA binding of the p65 subunit in lung tissues, by using a commercially available ELISA kit (TransAM NF-κB p65, Active Motif, Carlsbad, CA, USA) according to manufacture's instruction.

Lung histology

Part of the right lower lung lobe was stained with haematoxylin and eosin. The number of polymorphonuclear neutrophils in the lung interstitium was determined as the average number of polymorphonuclear neutrophils per high power field (×400). A minimum of 10 fields were randomly examined by an observer unaware of the protocol.

Experimental protocol

The isolated lung preparation was allowed to equilibrate for 20 min. We recorded the baseline PAP, PVP and weight change, and measured the initial K_f for 7 min. Then we allowed all parameters returning to the baseline values for 10 min. The rat lungs were randomly assigned to receive vehicle (PBS), baicalin only (4 $mg \cdot kg^{-1}$, Aldrich Sigma Chemical, St. Louis, MO, USA), air embolism or air embolism with different doses of baicalin (1, 2 and 4 $mg \cdot kg^{-1}$) ($n = 6$, in each group). Baicalin or PBS was added into the lung perfusate 10 min before air embolism. The lungs were perfused and ventilated for 60 min following air embolism and the measurement of K_f was repeated.

Drug and molecular target nomenclature

Drug and molecular target nomenclature conforms to the Guide to Receptors and Channels (Alexander *et al*., 2008).

Statistical analysis

The data are expressed as mean ± SEM. Statistical difference among group means was determined with one-way or two-way ANOVA with repeated measures, followed by a post hoc comparison by using Newman-Keuls test. Comparisons within each group for a given parameter were performed by using paired Student's *t*-tests. We considered $P < 0.05$ to be statistically significant.

Results

Change in PAP

In the control groups, the PAP showed almost no change throughout the 60 min experimental period (Figure 1). After infusion of air with the rate of 0.25 $mL \cdot min^{-1}$ for 1 min into the lung via the pulmonary artery, PAP increased steeply and reached its maximum when air infusion was stopped. The maximal increase of PAP in the group of air embolism was 42.5 ± 0.59 mmHg. PAP gradually declined therefore but remained significantly higher than the baseline 60 min after stopping the air infusion. Pretreatment with baicalin did not alter the effects of air embolism on PAP.

Lung weight gain

The lung weights of the control groups remained essentially constant during the 60 min experimental period (Figure 2A). Infusion of air caused a progressive increase in the lung

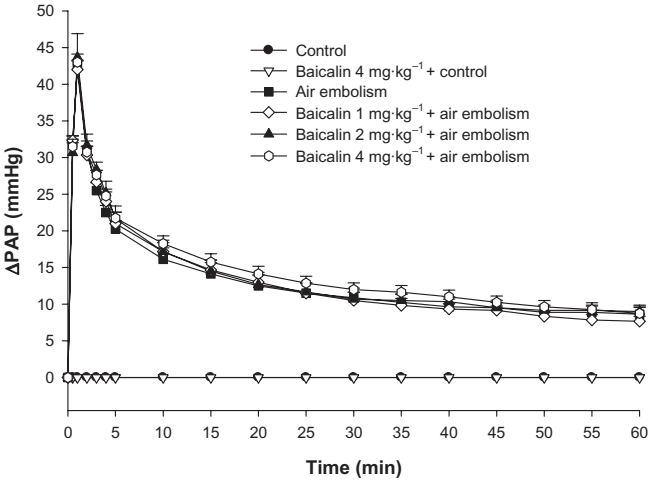

Figure 1 Effects of baicalin on the increase in pulmonary artery pressure in isolated lungs induced by air embolism. Infusion of air at a rate of 0.25 $mL \cdot min^{-1}$ for 1 min caused an increase of pulmonary arterial pressure (ΔPAP). Baicalin, added to the lung perfusate, at any dose, did not prevent pulmonary hypertension after air infusion.

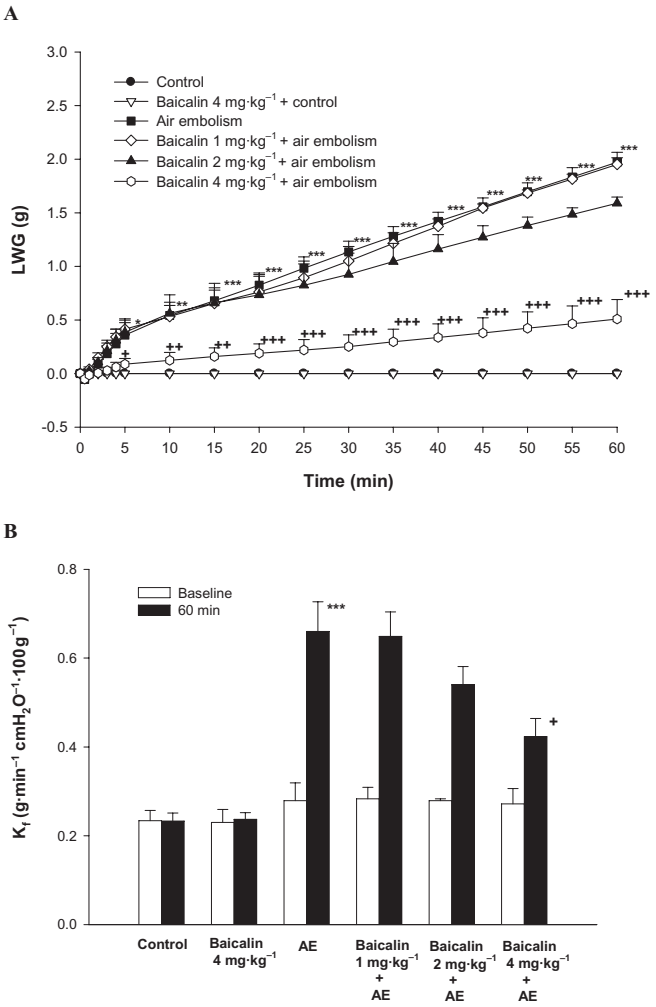

Figure 2 Alterations in lung weight gain (LWG) and filtration coefficient of the pulmonary vasculature (K_f) during the experiment. (A) Air infusion caused a significant increase in LWG. Baicalin (4 mg·kg^{-1}) attenuated the increase in LWG. (B) Air infusion after 60 min significantly increased K_f compared with baseline, although K_f did not change after 60 min of perfusion for the baicalin-only group. Pretreatment with baicalin (4 mg·kg^{-1}) significantly attenuated the increase in K_f compared with the air embolism group. ***$P < 0.001$ versus control group; $^{+}P < 0.05$ versus air embolism-only group.

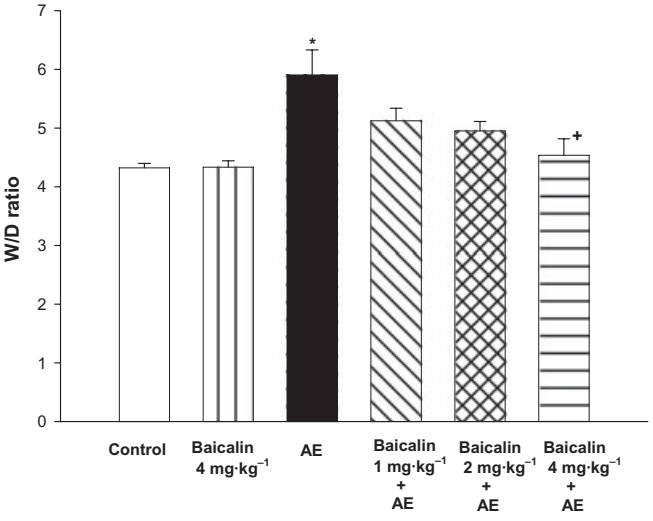

Figure 3 Alterations in wet/dry weight (W/D) ratio during experiments. Baicalin at 4 mg·kg^{-1} but not 1 or 2 mg·kg^{-1} significantly reduced the increase in wet/dry weight ratio compared with air embolism (AE) group. *$P < 0.05$ versus control group; $^{+}P < 0.05$ versus air embolism-only group.

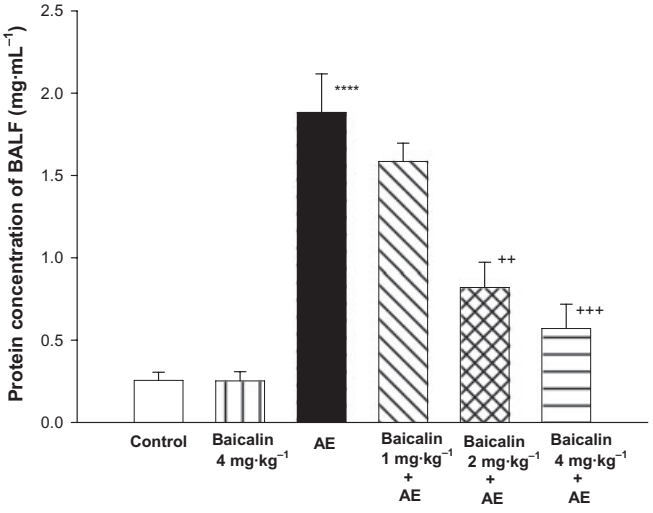

Figure 4 Effect of baicalin on the protein concentration of bronchoalveolar lavage fluid (BALF) in the control and various treatment groups. Baicalin (2 and 4 mg·kg^{-1}) but not at 1 mg·kg^{-1} significantly reduced the increase in protein concentration in BALF compared with air embolism (AE) group. ****$P < 0.001$ versus control group; $^{++}P < 0.05$; $^{+++}P < 0.001$ versus air embolism-only group.

weight. The gain in lung weight in the air embolism group was significantly higher than those in the control group ($P < 0.001$). This gain in lung weight was decreased only at the highest dose of baicalin (4 mg·kg^{-1}; $P < 0.001$).

Pulmonary filtration coefficient

Figure 2B shows the microvascular permeability changes due to air infusion expressed as K_f in the isolated rat lungs at different doses of baicalin. Air infusion significantly increased K_f ($P < 0.001$) after 60 min of air infusion, although K_f did not change after 60 min of perfusion for the control and baicalin-only groups. Pretreatment with baicalin (4 mg·kg^{-1}) significantly reduced the increase in K_f ($P < 0.05$).

Wet/dry weight ratio

After air infusion, the wet/dry weight ratios significantly increased in the air embolism group compared with the control group (Figure 3; $P < 0.05$). Pretreatment with baicalin (4 mg·kg^{-1}) significantly reduced the wet/dry weight ratios compared with the air embolism group ($P < 0.05$).

Lung lavage protein concentration

The lung lavage protein concentration was significantly higher in the air embolism group than that in the control group (Figure 4; $P < 0.001$). For this assay, a significant effect was provided by baicalin (2 or 4 mg·kg^{-1}) but not at the lowest dose (1 mg·kg^{-1}), compared with the air embolism group ($P < 0.01$ and $P < 0.001$, respectively).

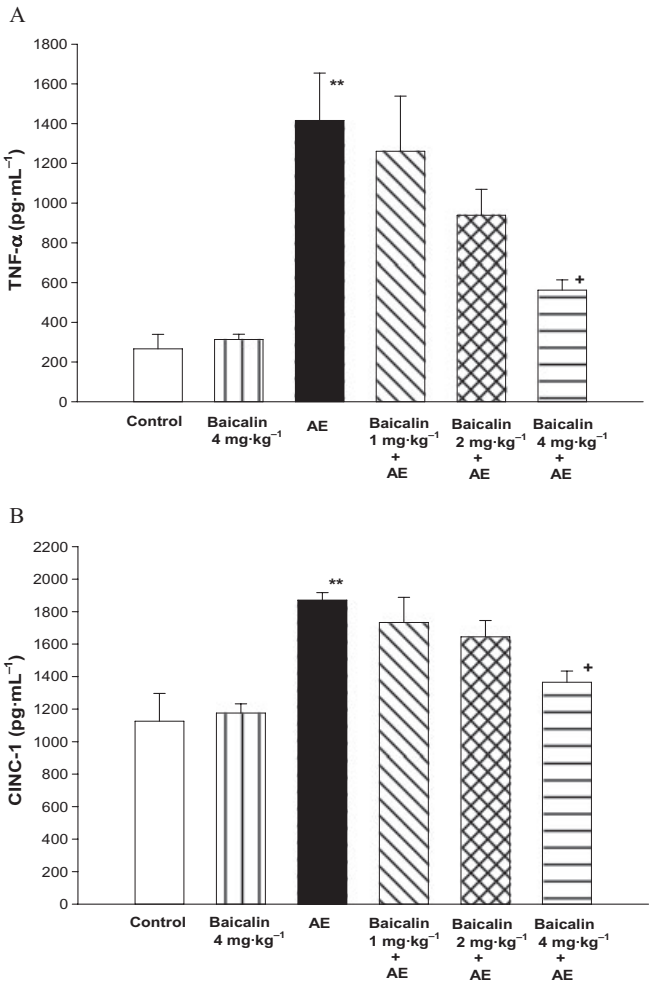

Figure 5 Effect of baicalin on the tumour necrosis factor α (TNF-α) and cytokine-induced neutrophil chemoattractant-1 (CINC-1) concentrations in lung perfusate. Air embolism (AE) significantly increased the concentrations of TNF-α and CINC-1 in perfusate compared with control group. Baicalin (4 mg·kg^{-1}) significantly reduced these increases. $^{**}P < 0.01$ versus control group; $^{+}P < 0.05$ versus air embolism-only group.

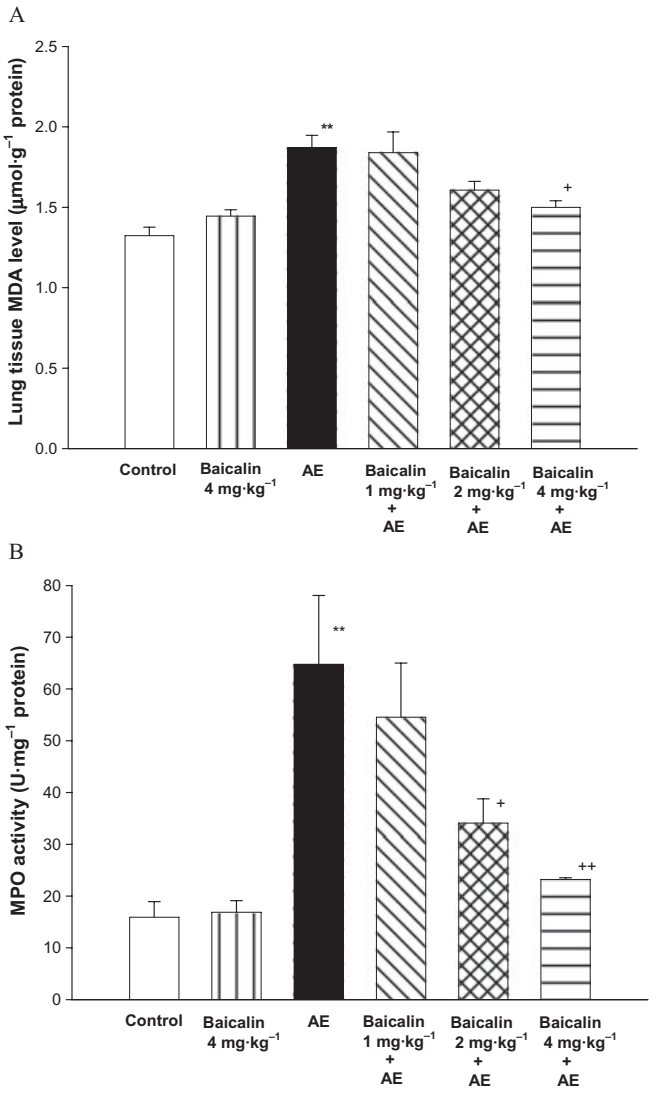

Figure 6 Effect of baicalin on malondialdehyde (MDA) concentration (A) and myeloperoxidase (MPO) activity (B) in lung tissue. Air embolism (AE) significantly increased the MDA concentration and MPO activity in lung tissue compared with control group. Baicalin (4 mg·kg^{-1}) significantly reduced these increases. $^{**}P < 0.01$ versus control group; $^{+}P < 0.05$; $^{++}P < 0.001$ versus air embolism-only group.

TNF-α and CINC-1 levels in perfusate

Air embolism significantly increased the TNF-α and CINC-1 levels in perfusate compared with the control group ($P < 0.01$). Baicalin (4 mg·kg^{-1}) significantly decreased the increase in TNF-α and CINC-1 levels in perfusate ($P < 0.05$) (Figure 5).

MDA levels and MPO activity in lung tissue

As shown in Figure 6, air embolism induced significant increases in MDA levels and MPO activity in lung tissues compared with those in the control group ($P < 0.01$).

Pretreatment with baicalin (4 mg·kg^{-1}) significantly decreased MDA level compared with air embolism group ($P < 0.05$). However, the increase in MPO activity in lung tissues after air embolism was reduced by pretreatment with baicalin [2 mg·kg^{-1} ($P < 0.05$) or 4 mg·kg^{-1} ($P < 0.01$)].

NF-κB activation

As demonstrated in Figure 7, IκB-α levels in the cytoplasm decreased by 62%, 60 min after air embolism ($P < 0.01$). Pretreatment with baicalin (1 or 2 mg·kg^{-1}) did not change the cytoplasmic levels of IκB-α in the air embolism group. Pretreatment with the highest dose of baicalin (4 mg·kg^{-1}) significantly increased the cytoplasmic levels of IκB-α by 56% compared with the air embolism group ($P < 0.01$). NF-κB activity in the lungs increased by 60% 60 min after air embolism (Figure 8). Pretreatment with baicalin (1 or 2 mg·kg^{-1}) had no effect on this increase, but at 4 mg·kg^{-1} baicalin did significantly reduce the NF-κB activity by 24% compared with the air embolism group ($P < 0.05$). This result indicates that baicalin treatment inhibits the degradation of IκB-α and prevents the translocation of NF-κB into the nucleus.

Histopathological findings

As indicated in Figure 9, the control group showed normal architecture and no cellular influx. Lung pathology in the air

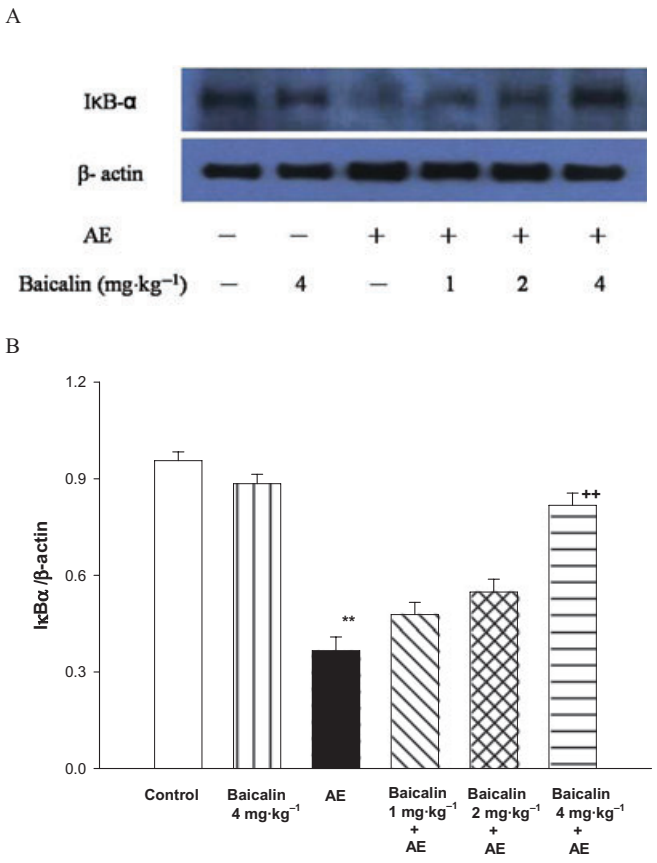

Figure 7 Effect of baicalin on the IκB-α level of rat lung. (A) Western blot analysis for IκB-α in cytoplasmic protein of lung tissue. (B) The relative levels of proteins detected by densitometry of the bands. Air embolism (AE) significantly decreased the IκB-α level in lung tissue compared with control group. Baicalin (4 mg·kg^{-1}) significantly restored these reductions. $^{**}P < 0.01$ versus control group; $^{++}P < 0.001$ versus air embolism-only group.

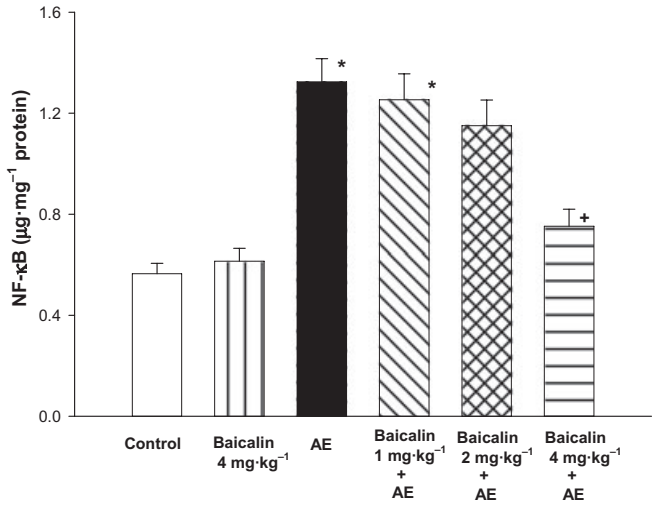

Figure 8 Nuclear factor-κB (NF-κB) p65 activity assay. The activity of NF-κB was significantly increased in air embolism (AE) compared with control group. Baicalin (4 mg·kg^{-1}) significantly suppressed the increase compared with air embolism group. $^{*}P < 0.05$ versus control group; $^{+}P < 0.05$ versus air embolism-only group.

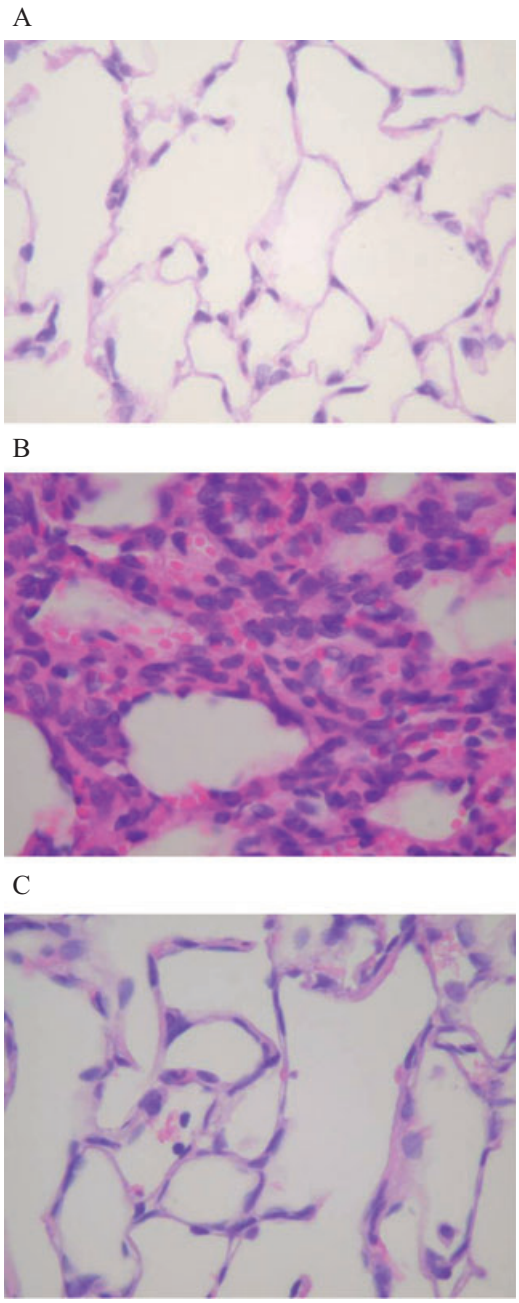

Figure 9 Histological appearance of lung tissue as determined by photomicrography. (A) Control group (magnification ×400). (B) Tissue from lungs treated with air embolism (magnification ×400). (C) Tissue from lungs treated with baicalin (4 mg·kg^{-1}) 10 min prior to air embolism (magnification ×400). Baicalin significantly improved the lung pathology compared with air embolism group.

embolism group was marked by inflammatory cell infiltration with neutrophils in the interstitium and alveoli of the lungs. Septal thickening and vascular congestion were also observed (Figure 9). Pretreatment with baicalin (4 mg·kg^{-1}) improved the lung pathology. The numbers of neutrophils per high-power field (400-fold magnification) were significantly higher ($P < 0.01$) in the air embolism group (259.8 ± 22.1) than in the control group (90.8 ± 7.0). Pretreatment with baicalin (4 mg·kg^{-1}) significantly attenuated neutrophil numbers

(155.4 ± 6.5) compared with the air embolism group ($P < 0.05$).

Discussion

In our study, air embolism induced increases in PAP, lung weight gain, K_f, wet/dry weight ratio, protein concentration in the bronchoalveolar lavage fluid, TNF-α and CINC-1 levels in perfusate, MDA levels and MPO activities in lung tissue. Air embolism also induced neutrophil influx and septal thickening in the perfused lungs. In addition, degradation of IκB-α and NF-κB activity were increased in the embolized lungs. In contrast, pretreatment with baicalin attenuated the increase in these parameters and significantly improved histological appearance. The protective effect of baicalin was accompanied by down-regulation of the production of proinflammatory cytokines and oxygen radicals, and a suppression of NF-κB activity.

The increase in PAP is a prominent outcome of pulmonary air embolism. The mechanism has been considered as mechanical vascular obstruction by the air bubbles first, followed by the release of inflammatory mediators (Souders, 2000). In this study, pulmonary hypertension was a consequence of elevation in vascular resistance, because the flow rate was constant. Vascular obstruction undoubtedly plays an important role in the increased vascular resistance. Our results showed that baicalin reduced the increase in vascular permeability without decreasing the PAP. Therefore, vascular obstruction and subsequent hypoxaemia are not responsible for the major mechanism of air embolism-induced lung injury in our model.

Multiple factors initiate air embolism-induced lung injury, including complement activation, reactive oxygen species, cytokines and chemokines. The pulmonary vascular endothelium acts as a barrier to prevent entry of fluids and proteins into the interstitium of the lung. Gas emboli have been demonstrated to disrupt or injure the endothelial lining and lead to increased pulmonary vascular permeability, which is the major feature of acute lung injury (Souders, 2000). Neutrophils play an important role in the pathogenesis of acute lung injury. During air embolism, neutrophils interact with the air emboli and damage endothelial cells and initiate intravascular inflammatory responses. The activated neutrophils that infiltrated the lung release reactive oxygen species, proteases, cytokines, vasoconstricting lipids, and up-regulate adhesion molecules and damage the lung. Depletion of neutrophils with nitrogen mustard or using antioxidants can attenuate air embolism-induced lung injury (Flick *et al.*, 1981; 1988). Baicalin has been reported to have radical scavenging capability to protect against ischaemia–reperfusion injury in cardiomyocytes (Chang *et al.*, 2007b). The anti-inflammatory effect of baicalin is thought to decrease MPO activity in carrageenan-injected paw (Chou *et al.*, 2003). In this study, pretreatment with baicalin attenuated neutrophil infiltration, MPO activity and lipid peroxidation. Therefore, endothelial damage may be attenuated. Moreover, this attenuation was associated with a decrease in pulmonary oedema indicated by K_f, wet/dry weight ratio and protein concentrations in the bronchoalveolar lavage fluid.

Overproduction of TNF-α and CINC-1 were involved in the development of various models of acute lung injury (Goodman *et al.*, 2003; Chu *et al.*, 2005b). CINC-1, a member of the C-X-C chemokines in rats, is a functional homologue of human IL-8 and is known to have potent chemotactic activity for neutrophils. Previous investigations have reported that anti-TNF-α and anti-CINC-1 antibodies can significantly attenuate the LPS-induced acute lung injury (Ulich *et al.*, 1995; Arbibe *et al.*, 1997). This study was first to demonstrate that TNF-α and CINC-1 levels were significantly increased in air embolism-induced lung injury

Baicalin has been reported to suppress the increase of plasma level of TNF-α in LPS-exposed rat lung, experimental heatstroke, severe acute pancreatitis and concanavalin A-induced liver injury (Lo *et al.*, 2005; Chang *et al.*, 2007a; Liu *et al.*, 2007). Our present study also showed that baicalin decreased the perfusate level of TNF-α and CINC-1 in air embolism-induced lung injury. Early-response TNF-α will induce later elevation of chemokines such as CINC-1 in rats (Luster, 1998). Therefore, inhibition of TNF-α production may lead to decrease CINC-1 production induced by air embolism.

Although many studies on anti-inflammatory effects of baicalin have been investigated, the protective mechanism of baicalin was still not well known. NF-κB is an important transcription factor required for regulation of gene expression of cytokines, chemokines and adhesion molecules (Liu and Malik, 2006). In a previous study, baicalin showed no effect on LPS-induced NF-κB DNA binding activity in Raw 264.7 cells (Woo *et al.*, 2006). Other investigators reported that baicalin inhibited *Helicobacter pylori*-induced inflammation in human gastric epithelial cells, caerulein-induced acute pancreatitis and age-associated gene expression by suppressing NF-κB activation (Kim *et al.*, 2006; Xue *et al.*, 2006; Shih *et al.*, 2007). The reason for this difference was not clear. In our study, baicalin decreased the inflammation response by inhibiting NF-κB activation.

In conclusion, our study showed that baicalin significantly attenuated the acute lung injury induced by air embolism in rat isolated lungs. So far, no severe adverse effects of baicalin have been reported. Administration of baicalin may be a useful prophylactic or adjunct drug therapy for air embolism-induced lung injury, and studies in human models would be required to further assess these effects.

Acknowledgements

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Conflict of interest

None.

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