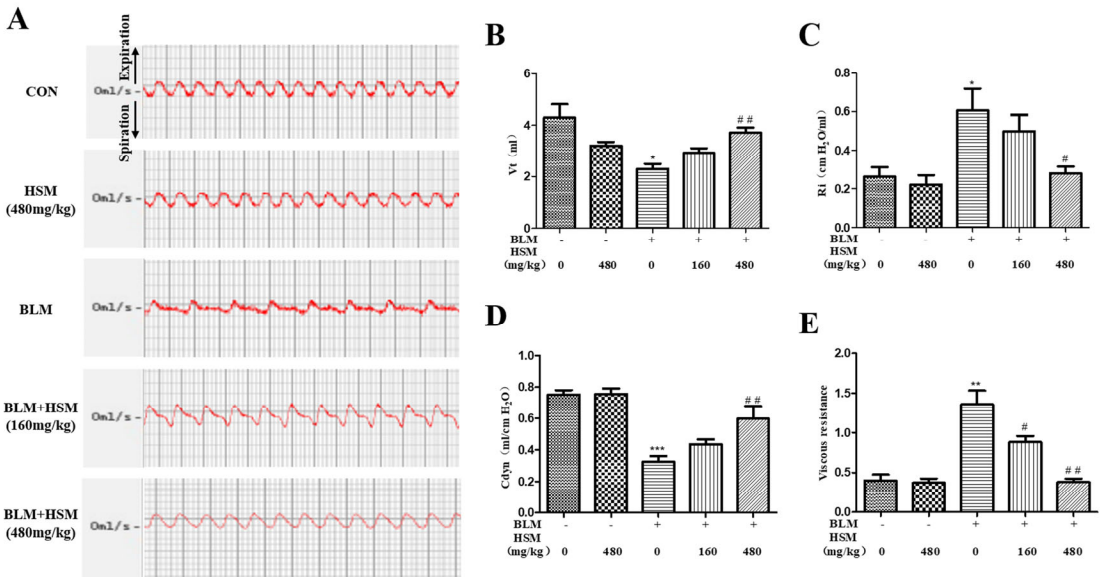
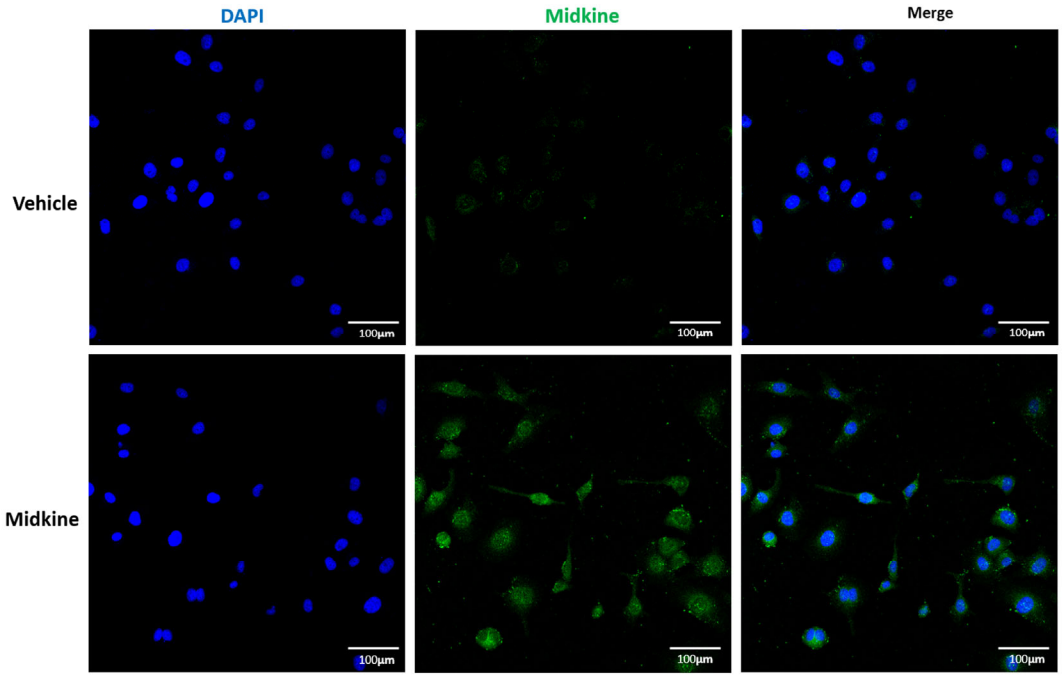
Supplementary method 1. Pulmonary function testing

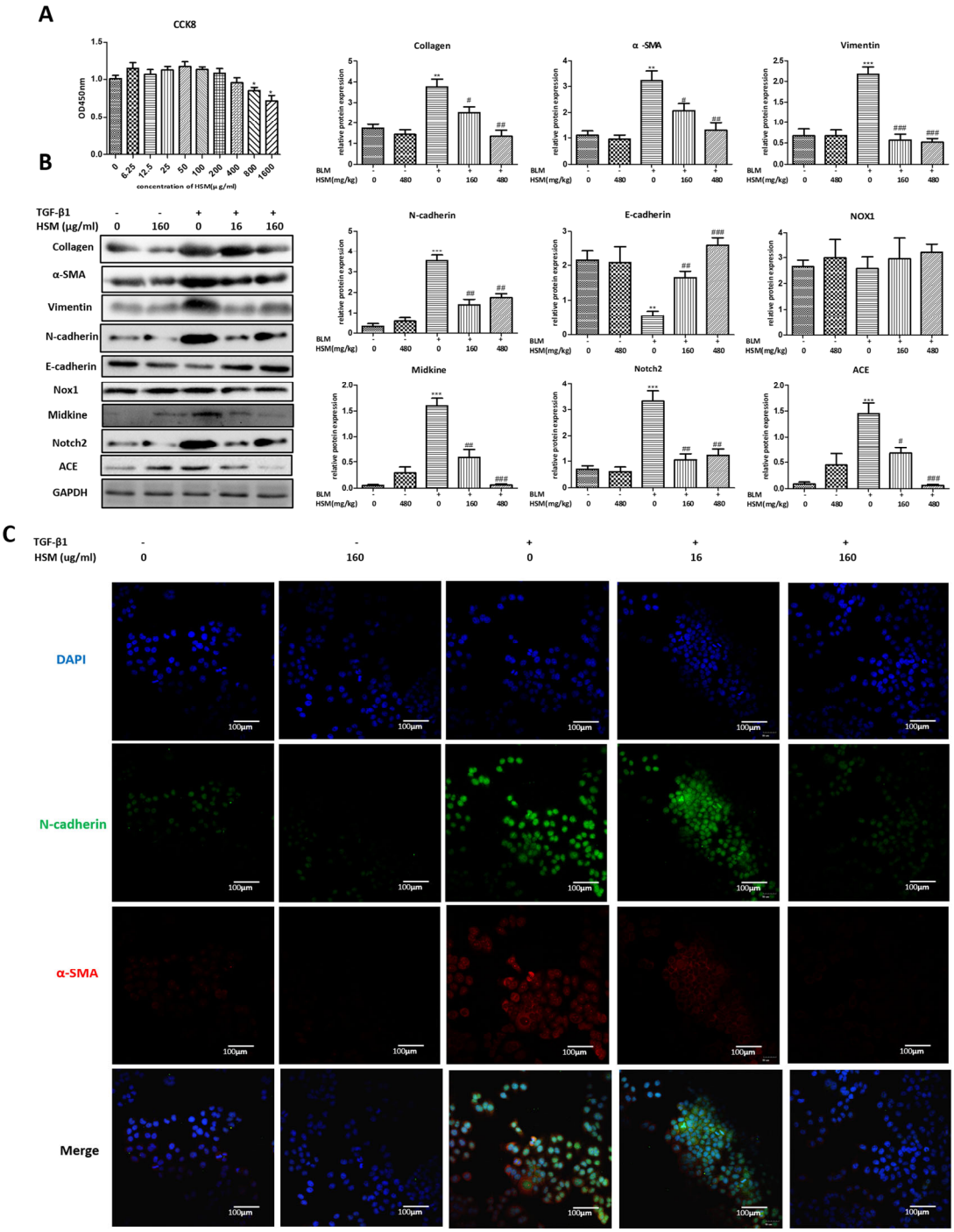
Male C57BL/6 mice were anesthetized with 6% chloral hydrate in saline (360 mg/kg, i.p.), tracheotomized below the larynx and intubated with a Y-type tracheal cannula (2.5 mm inner diameter). After surgery, the mice were placed in a supine position with their body inside the plethysmographic chamber (4665 ml volume) in order to analyze the pulmonary function by the Anires 2005 system (Beijing Biolab, Beijing, China). One branch of the Y-type tracheal cannula was connected to a venthole on the chamber wall and the venthole was connected to a ventilator from the outside of the chamber by a polyethylene tubing (8 mm inner diameter, 10 cm length). Natural air was provided to the animal through the ventilator with a rate of 80 breaths/min. The other branch of the cannula was connected to the pressure-detecting channel of the Anires 2005 system, and the peak inspiratory pressure was maintained at 10-16cm H_2O. By detecting the ventilation-associated pressure change inside the chamber, the Anires 2005 system automatically calculated and displayed pulmonary function parameters such as tidal volume (Vt), inspiratory resistance (Ri), viscous resistance and dynamic compliance (Cdyn).



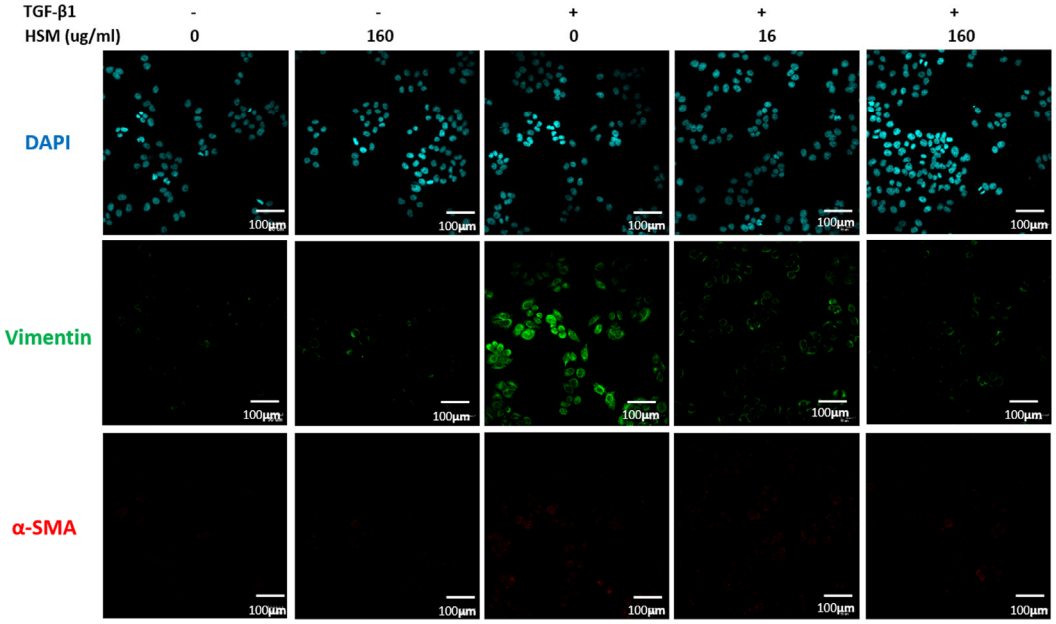
Supplementary Fig. S1 HSM alleviated abnormal lung function in BLM-induced mice. Pulmonary function between different groups were calculated, including representative respiratory waves (A), tidal volume (Vt) (B), inspiratory resistance (Ri) (C), dynamic compliance (Cdyn) (D) and expiratory resistance (Re) (E). Data represent the mean ± SD of three separate experiments. n=6 *P < 0.05, **P < 0.01, *** P < 0.005, vs. control group. #P < 0.05, ##P < 0.01, ### P < 0.005, vs. BLM group.



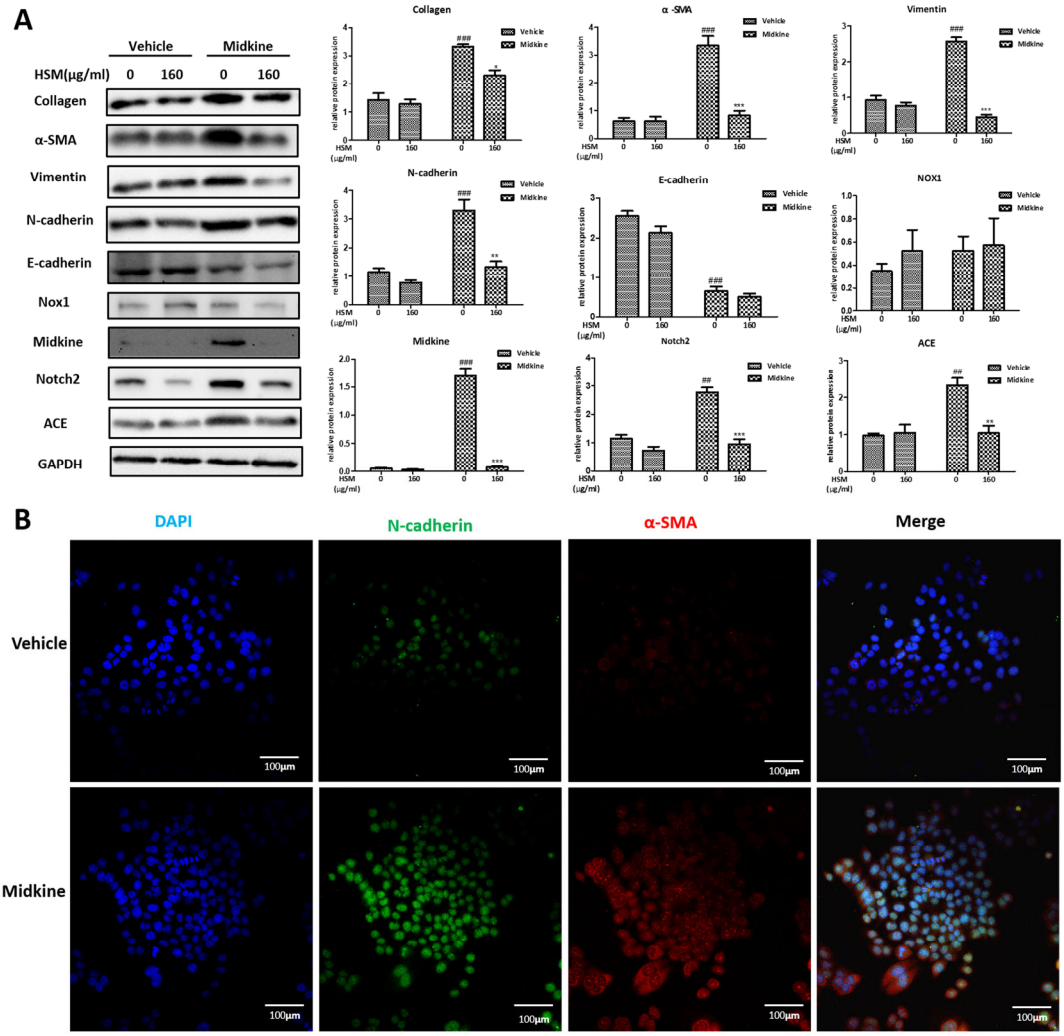
Supplementary Fig. S2 The expression of midkine was increased after transfecting with pcDNA3.1/Midkine in A549 cells. The expression of Midkine was analyzed by immunofluorescence staining. The scale bar indicated 100 μm in the images (40×).



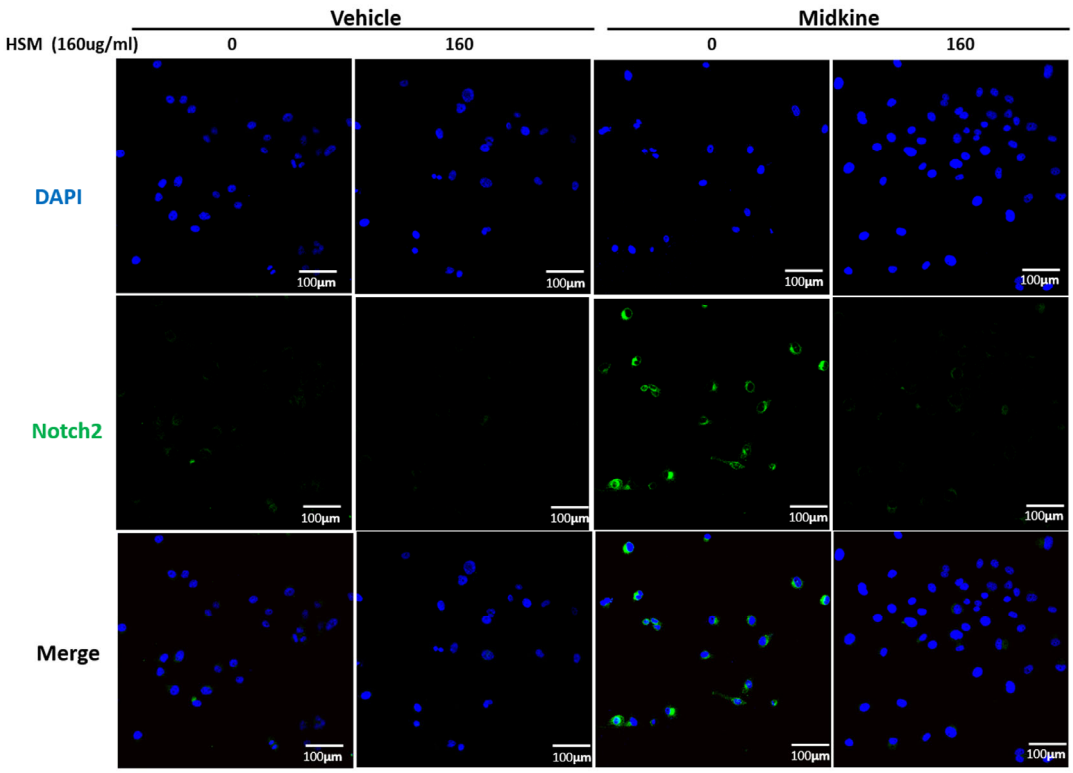
Supplementary Fig. S3 Primary mouse type II AECs were treated with various concentrations of HSM and cultured for 24 hours. The cell viability was analyzed by the CCK8 assay (A). Primary mouse type II AECs were pretreated with HSM for 2 hours and then treated with or without TGF-β1. Western blotting was used to assess the proteins expression of collagen, α-SMA, vimentin, N-cadherin, E-cadherin, NOX1, Midkine, Notch2 and ACE (B). The expression of N-cadherin and α-SMA in primary mouse type II AECs were analyzed by immunofluorescence staining. The scale bar indicated 100 μm in the images (40×). Data represent the mean ± SD of three separate experiments. *P < 0.05, **P < 0.01, *** P < 0.005, vs. control group. #P < 0.05, ##P < 0.01, ### P < 0.005, vs. BLM group.



Supplementary Fig. 4 HSM inhibited TGF-β1-induced EMT in A549 cells. The expression of vimrntin and α-SMA were analyzed by immunofluorescence staining. The scale bar indicated 100 μm in the images (40×).



Supplementary Fig. 5 Primary mouse type II AECs were pretreated with HSM for 2 hours and were subsequently transfected with pcDNA3.1/midkine plasmid. Western blotting was used to assess the proteins expression of collagen, α-SMA, vimentin, N-cadherin, E-cadherin, NOX1, Midkine, Notch2 and ACE (A). The expression of N-cadherin and α-SMA were analyzed by immunofluorescence staining (B). The scale bar indicated 100 μm in the images (40×). Data represent the mean ± SD of three separate experiments. *P < 0.05, **P < 0.01, *** P < 0.005, vs. control group. #P < 0.05, ##P < 0.01, ### P < 0.005, vs. BLM group.



Supplementary Fig. 6 HSM alleviated EMT by affecting the midkine signaling pathway in vitro. A549 cells were pretreated with HSM for 2 hours and were subsequently transfected with pcDNA3.1/midkine plasmid. The expression of EMT markers (vimentin and α-SMA) were analyzed by immunofluorescence staining (E). The scale bar indicated 100 μm in the images (40×).