Vol. 9, No. 9, Franks T. J. Human Pathology. 2003. Volume 34, No. 8, Liao M. (ePub ahead of print) https://doi.org/10.1101/2020.02.23.20026690, Tian S. Journal of Thoracic Oncology (ePub ahead of print) https://doi.org/10.1016/j.jtho.2020.02.010.

[0005] In models of acute lung disease, treatment with the potent SSAO inhibitor BI-1467335 (formerly, PX-4728A), reduced LPS-induced neutrophil lung migration and cytokine-induced cell migration by diminishing leukocyte rolling and adherence. Schilter, H. C. Respir. Res. 2015, 16, 42. A related SSAO inhibitor, PXS-4681A, also reduced leukocyte trafficking and cytokine production in both LPS- and carrageenan-induced mouse models of lung inflammation. Foot, J. J. Pharmacol. Exp. Ther. 2013 347(2) 365-374. In these studies, the effects of PXS-4681A were comparable to treatment with the anti-inflammatory glucocorticoid, dexamethasone. In models of chronic obstructive pulmonary disease (COPD) and acute cigarette smoke-induced lung disease, treatment with BI-1467335 suppressed airway infiltration of inflammatory immune cells, reduced pulmonary fibrosis, and improved lung function. Jarnicki, A. G. Br. J. Pharmacol. 2016, 173, 3161-3175. Finally, in a model to mimic viral exacerbation of asthmatic response, BI-1467335 treatment reduced inflammatory cellular infiltrates and airway hyperreactivity in mice sensitized with house dust mite (HDM) and subsequently challenged with HDM and rhinovirus infection. Schilter, H. C. Respir. Res. 2015, 16, 42. However, BI-1467335 retains off-target activity against MAO-B, which may present a safety concern in certain patients.

[0006] Accordingly, there is a need for an improved treatment of respiratory disorders, such as ARDS, using a SSAO inhibitor, such as a selective SSAO inhibitor over MAO-A/B.

~~BRIEF~~ SUMMARY

[0007] Provided herein are compositions and methods for the treatment of respiratory disorders, such as ARDS.

[0007a] In one aspect, the present disclosure refers to use of a compound of Formula 5, or a pharmaceutically acceptable salt thereof in the manufacture of a medicament for treating a respiratory disease in an individual in need thereof.

BRIEF DESCRIPTION OF THE FIGURES

[0008] FIG. 1A shows the plasma SSAO activity compared to baseline of healthy volunteers administered a single dose of placebo or 1, 3, 6, or 10 mg of the compound of Formula 5 at 4 hours and 168 hours post dose.

[0009] FIG. 1B shows a time course of SSAO activity compared to baseline of healthy volunteers administered a single dose of placebo or 1, 3, 6, or 10 mg of the compound of Formula 5.

CLAIMS

What is claimed is:

1. Use of ~~A method~~ a compound of Formula 5, or a pharmaceutically acceptable salt thereof in the manufacture of a medicament ~~of~~ for treating a respiratory disease ~~comprising administering an effective amount of a compound of Formula 5, or a pharmaceutically acceptable salt thereof to~~ in an individual in need thereof.

2. The ~~method~~ use of claim 1, wherein the respiratory disease is acute respiratory distress syndrome (ARDS).

3. The ~~method~~ use of claim 1 or 2, wherein inflammation in the lungs of the individual is reduced.

4. The ~~method~~ use of any one of claims 1-3, wherein the level of neutrophils in the individual is reduced.

5. The ~~method~~ use of any one of claims 2-4, wherein the individual has acute respiratory distress syndrome caused by a pathogen.

6. The ~~method~~ use of claim 5, wherein the pathogen is a virus or bacteria.

7. The ~~method~~ use of claim 5, wherein the pathogen is selected from the group consisting of SARS-CoV-2, SARS-CoV, MERS-CoV, Influenza virus, Metapneumovirus, Varicella zoster virus, Streptococcus pneumoniae, Haemophilus influenzae, mycobacterium tuberculosis, COVID-19 and Malaria.

8. The ~~method~~ use of any one of claims 1-7, wherein the compound is to be administered to the individual once daily.

9. The ~~method~~ use of any one of claims 1-8, wherein the compound is to be administered at a dose of about 1 mg to about 10 mg.

10. The ~~method~~ use of any one of claims 1-9, wherein MAO-A and MAO-B are not inhibited.

11. The ~~method~~ use of any one of claims 1-10, wherein the compound is to be delivered intranasally or via inhalation.