The anti-inflammatory and bronchodilating properties of the novel pharmacological compound Sul-121.

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Introduction

Chronic obstructive pulmonary disease (COPD) is characterized by airway obstruction and chronic inflammation [1]. Although most patients can be treated with (combinations of) bronchodilating agents and anti-inflammatory glucocorticosteroids, a subset of patients responds poorly to these drugs leading to increased hospitalizations [2].

Aim

In the present study, we explored the anti-inflammatory and bronchodilating properties of a novel pharmacological compound Sul-121 *in vitro* and *in vivo*.

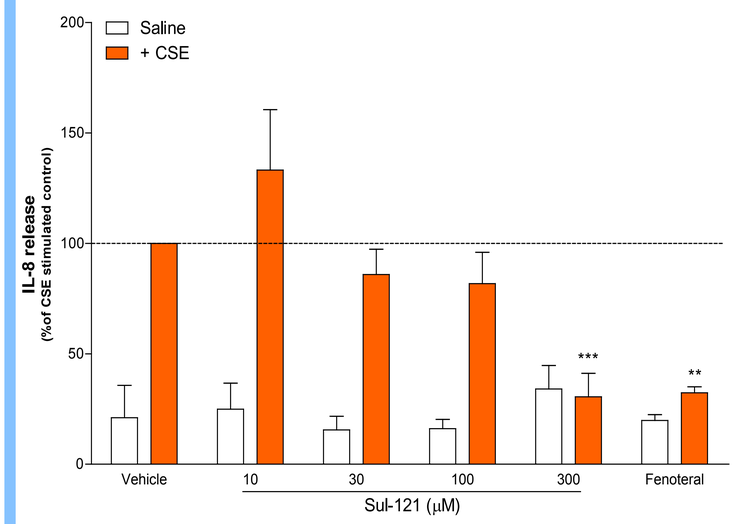

Figure 1. Sul-121 dose-dependently altered CSE-induced IL-8 release.
Cells were treated with the indicated concentrations of Sul-121 in the presence or absence of cigarette smoke extract (CSE) for 24 h. Cell supernatants were collected for IL-8 ELISA. **: p<0.01, ***:p<0.001, compared with CSE control. Fenoterol served as a positive control. Data represent as mean±SEM of n=6-8.

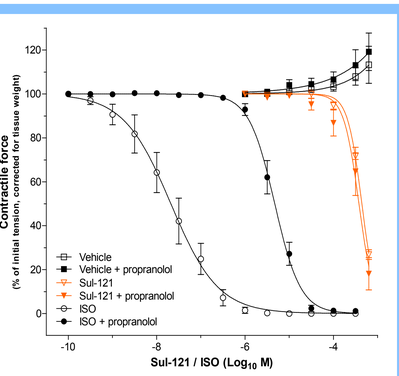

Figure 3. Sul-121 induced BTSM relaxation independent of the β_2-adrenoreceptor.
Bovine airway smooth muscle (BTSM) strips were precontracted with methacholine (MCh, 1 X $10^{-3.5}$ μM). After a 30 min incubation with/without the β-adrenoreceptor antagonist propranolol (1 μM) , the indicated concentrations of Sul-121 were added to build up a accumulated dose response curve. Isoprenaline (ISO) served as the positive control. Data represent as mean±SEM of n=3.

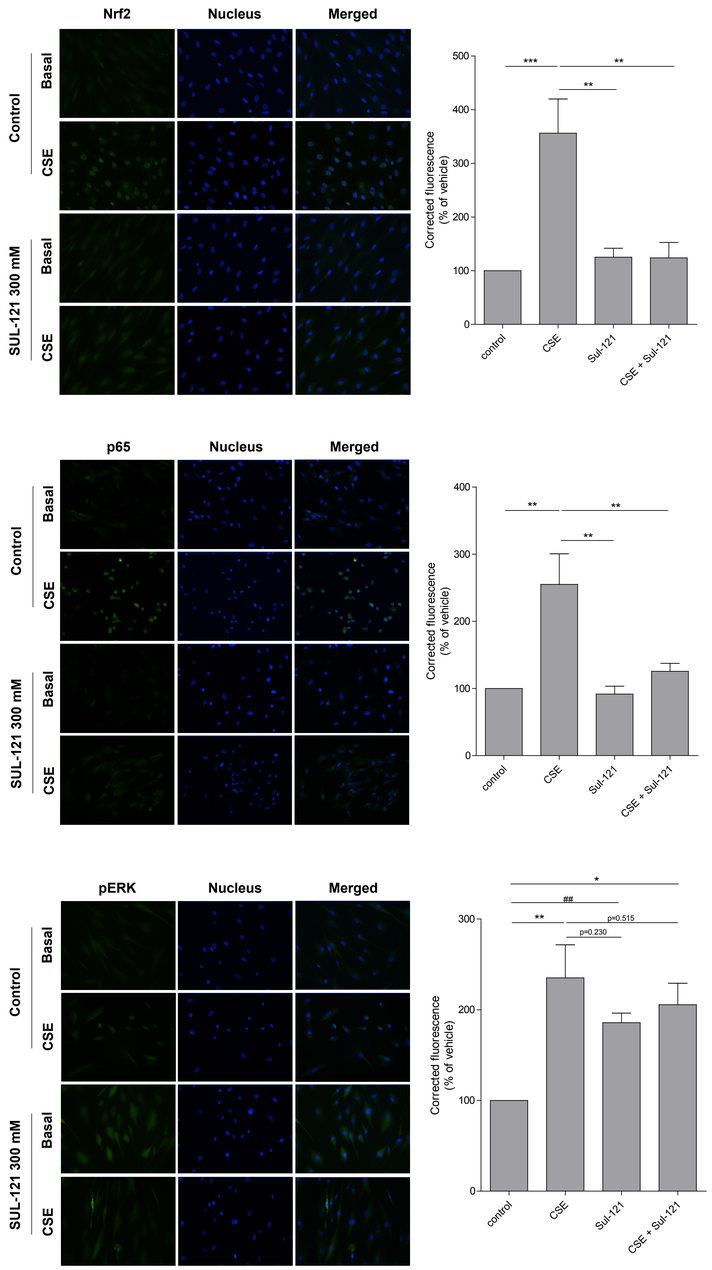

Figure 2. Sul-121 prevented CSE-induced nuclear translocation of Nrf2 and p65, without significantly affecting phospho-ERK1/2 nuclear translocation.
Cells were treated with the indicated concentrations of Sul-121 in the presence or absence of cigarette smoke extract (CSE) for 2 h. Cells were fixed for immunofluorescence of Nrf2, p65 or pERK. The corrected fluorescence was acquired by using ImageJ 1.48v. *: p<0.05, **: p<0.01, ***: p<0.001, One way ANOVA with Bonferroni post hoc test. ##: p<0.01, p=0.515, p=0.230, T test. Data represent as mean±SEM of n=4-5.

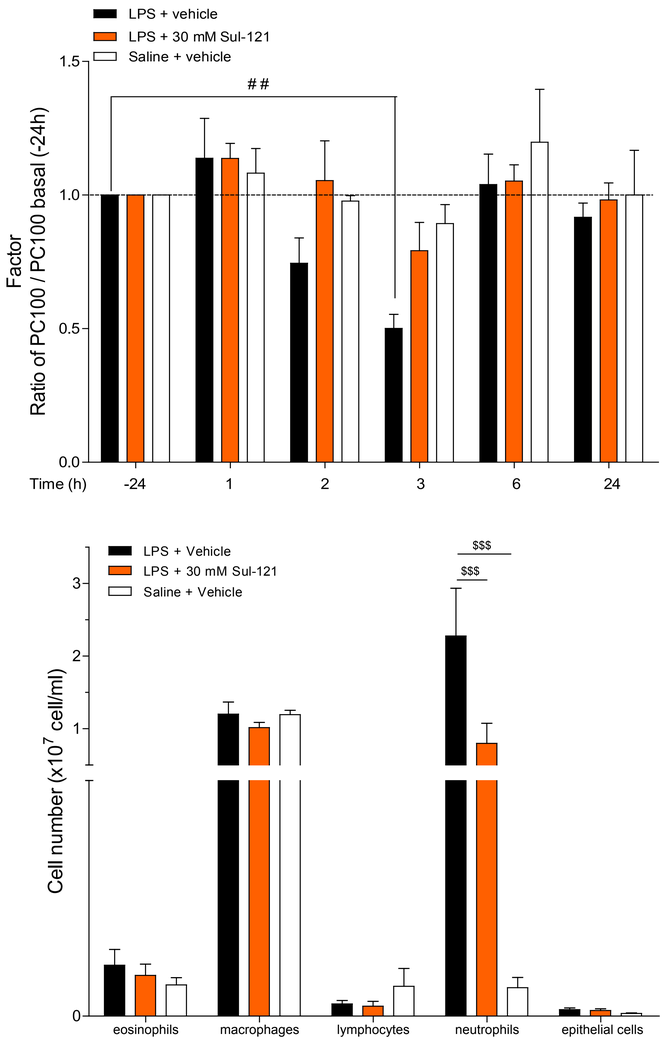

Figure 4. Sul-121 prevented LPS-induced airway hyperresponsiveness as well as BAL neutrophilia in a guinea pig model of acute LPS-induced COPD.
(A) Airway responsiveness to inhaled histamine was assessed as PC100 (provocative concentration causing a 100% increase in pleural pressure). Data were expressed as PC100 factor (ratio of PC100 / PC100 basal). (B) BAL leukocytes counting. With 2 way ANOVA, LPS + Vehicle treatment is significantly different from the other groups in PC100 factor. ##: p<0.01, 1 way ANOVA with repeated measurement. $$$: p<0.001, 2 way ANOVA with Bonferroni post-tests. Data represent as mean±SEM, n=3-7.

Conclusion

Our data show that Sul-121 has both anti-inflammatory and (non-receptor mediated) bronchodilating properties *in vitro* and *in vivo*. Therefore, Sul-121 may represent a novel approach in the pharmacological treatment of COPD.

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1. Broadley KJ. Eur J Pharmacol. 2006 Mar 8;533(1-3):15-27. Epub 2006 Feb 15.
2. Barnes PJ. Nat Rev Immunol. 2008 Mar;8(3):183-92. Epub 2008 Feb 15.