

9TH ANNUAL EUROPEAN PHARMA CONGRESS

June 26-28, 2017 Madrid, Spain



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Potential Benefits of Roflumilast in Bronchial Asthma

Statement of the Problem: Bronchial asthma affects about 150 million people all over the world. The inflammatory mediators released from eosinophils, T-helper 2 lymphocytes, airway epithelium, and airway smooth muscle contribute to chronic inflammation and remodeling. Airway remodeling leads to progressive decline of lung functions and it is steroid resistant, thus there is a need for new medications with better anti-remodeling effect. Phosphodiesterase (PDE)-4 inhibitors have anti-inflammatory and anti-remodeling properties. Roflumilast; a selective PDE-4 inhibitor; is approved as an add-on therapy for chronic obstructive pulmonary disease (COPD). The inflammation in COPD and severe asthma is neutrophilic while in asthma it is eosinophilic. Consequently, investigating effects of roflumilast in eosinophilic inflammation is beneficial. During exacerbation of murine acute asthma, roflumilast (oral and intratracheal) decreased airway macrophages, eosinophils, neutrophils, T-helper 2 cytokines, and hyperresponsiveness (AHR). In contrast, steroids failed to affect AHR or neutrophil numbers which are considered important parameters for exacerbations of human asthma. Addition of roflumilast to high-dose fluticasone in patients with uncontrolled asthma improved asthma possibly through affecting the neutrophilic component of the disease. Ability of roflumilast to reduce sputum eosinophils, neutrophils, and macrophages makes it of potential off-label use in asthma. In a lipopolysaccharide-induced inflammation model in Wistar rats, "inhaled" roflumilast N-oxide decreased neutrophils in the bronchoalveolar lavage fluid (BALF). Thus "inhaled" roflumilast N-oxide could be as a useful alternative to oral roflumilast in airway disorders. **Conclusion & Significance:** Roflumilast (oral or inhalational) significantly decreases airway hyperresponsiveness, the elevated inflammatory mediators, the elevated BALF levels of matrix metalloproteinase-9 and its inhibitor (TIMP-1), and remodeling in both human asthma and animal asthma models. These benefits are due to its anti-inflammatory and anti-fibrotic effects. Investigating the effects of a triple inhalation therapy consisting of roflumilast, corticosteroids, and long acting β_2 agonists in chronic asthma models is a point for research.

Biography

Hussam AS Murad worked as a Professor at Pharmacology and Clinical Pharmacy Departments in a number of universities in Egypt and Saudi Arabia. He has an experience of about 25 years in teaching and research. Murad has worked in 10 research projects as a principal investigator and as a first co-investigator in another four. He has got funds from King Abdulaziz City for Science and Technology (KACST), Riyadh, SA, and Deanship of Scientific Research, King Abdulaziz University (KAU), Jeddah, SA. He received the award of scientific publication from KAU, in 2015 and in 2017.

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