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Molecular docking and synthesis of 8-substituted 3,4-dihydro-6-methyl-4-(2,4-dinitrophenyl)imidazo[1,5-*b*][1,2,4]triazin-2(8*H*)-one derivatives as novel antiasthmatic agents

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ABSTRACT

In the last few years there has been a growing interest for the therapeutic applications of phosphodiesterase4 (PDE4) inhibitors. PDE4 inhibitors are currently under development for the treatment of respiratory diseases including asthma and COPD. The rationale for the development of this drug class stems from our understanding of the role of PDE4 in suppressing the function of a range of inflammatory and resident cells thought to contribute toward the pathogenesis of these diseases. Similarly, numerous preclinical in vivo studies have shown that PDE4 inhibitors suppress characteristic features of these diseases, namely, cell recruitment, activation of inflammatory cells and physiological changes in lung function in response to a range of insults to the airways. The ability of the PDE4 inhibitors to relax airway smooth muscle on one hand and to suppress the function of a range of inflammatory cells on the other hand, led to concentration of the research efforts on drugs of this class. We synthesized new class of PDE4 inhibitors, 6-methyl-3,4-dihydroimidazo[1,5-b][1,2,4]triazin-2(8H)-one structurally unrelated to rolipram as promising agents for treatment of asthma and investigated antiasthmatic activity using guinea pig tracheal chain method. Results shows that synthesized compounds have prominent antiasthmatic activity.

Keywords: Phosphodiesterase4, Asthma, Imidazole[1,5-*b*][1,2,4]triazine, Guinea pig trachea.