NEW AGONISTS AND ANTAGONISTS OF THE A_{2B} ADENOSINE RECEPTOR

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Selective adenosine A_{2B} receptor antagonists may have potential in the treatment of allergic diseases such as asthma. In the search for improved selective antagonist ligands of the A_{2B} adenosine receptor, we have synthesized and screened a variety of new 1,3-dipropyl-8-heterocyclic-substituted xanthines as potent and selective A_{2B} adenosine receptor antagonists derivatives as A_{2B}-AR antagonists.(1) The synthesized compounds showed A_{2B} adenosine receptor affinity in the nanomolar range and good levels of selectivity evaluated in radioligand binding assays at human A_1, A_{2A}, A_{2B}, and A_3 ARs. This study allowed us to prepare [^{3}H]-MRE 2029-F20 a selective antagonist radioligand for the human A_{2B} adenosine receptors.(2) The lack of molecules endowed with selective and potent agonistic activity toward the hA_{2B} adenosine receptors has limited the studies on this pharmacological target and consequently the evaluation of its therapeutic potential. In this lecture, we report the design and synthesis of two series of compounds as potent and selective hA_{2B} adenosine receptor agonists consisting of 1-deoxy-1-[6-[((hetero)aryl-carbonyl)-hydrazino]-9*H*-purin-9-yl]-N-ethyl-*β*-D-ribofuranuronamide (3) and N^6-[hetero)aryl/(cyclo)alkyl-carbamoyl-methoxy-phenyl]-(2-chloro)-5'-*N*-ethylcarboxamido-adenosines (4) derivatives.

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