Adenosine is a modulator of many physiological and pathophysiological processes in the central nervous system (CNS). Blockade of the adenosine receptors A1ARs and A2AARs has shown beneficial neuroprotective effects in animal models and in clinical studies of Parkinson's disease (PD) and Alzheimer's disease (AD).

Furthermore, selective inhibitors of the monoamine oxidase A (MAO-A) are applied as adjunctive therapeutics for PD, as they protect the brains of PD patients from oxidative stress.

Nevertheless, there is still no satisfactory multitarget drug approach which inhibits MAO-A and the two adenosine receptors A1ARs and A2AARs.

This invention provides newly designed tricyclic xanthine derivatives which allow overcoming this problem. A variety of 69 derivatives were prepared and evaluated in radioligand binding studies at adenosine receptors and for their ability to inhibit monoamine oxidases. Potent dual-target-directed A1/A2A adenosine receptor antagonists were identified. Several compounds even showed triple-target inhibition.

Together, these observations position tricyclic xanthine derivatives as ideal candidates for the treatment of neurodegenerative diseases such as PD and AD, but might also be suitable for the treatment of depression, addiction and restless legs syndrome.
PUBLIKATIONEN & VERWEISE


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