TRICYCLIC CYCLOALKYLPURINEDIONES: POTENCY AS ADENOSINE RECEPTOR LIGANDS AND ANTICONVULSANTS

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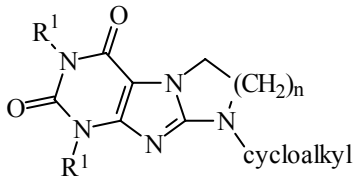
The xanthine alkaloids caffeine and theophylline were the first antagonists for adenosine receptors (AR). During the past 20 years a large number of AR antagonists have been developed including xanthine bi- or tricyclic derivatives.

As a continuation of our studies [1, 2] tricyclic purinediones with cycloalkyl substituents were synthesized and their biological activity was evaluated *in vitro* and *in vivo*.

In order to investigate SARs the lead structure was modified by enlarging of the annelated ring (from 5 to 7 membered), by variation of the cycloalkyl moiety and by elongation of the substituents at the pyrimidinedione ring nitrogen atoms.



n = 1, 2, 3
R^1 = methyl, propyl

Compounds were tested *in vitro* for their affinity towards rat A_1 and A_{2A} AR, with [^{3}H] CCPA and [^{3}H] MSX-2 as radioligands, respectively. Pyrimidine as the third annelated ring and propyl as substituent R^1 were beneficial for high potency at both receptor subtypes.

Cycloalkyl derivatives were also investigated *in vitro* as anticonvulsants. Some of them have shown anticonvulsive protection mainly in chemical seizures (ScMet).

Supported in part by Polish State Committee for Scientific Research (Grant No 2 P05F 022 26)

[1] K. Kieć-Kononowicz, A. Drabczyńska, E. Pękala, B. Michalak, C.E. Müller, B. Schumacher, J. Karolak-Wojciechowska, H. Duddeck, S. Rockitt, R. Wartchow. *Pure. Appl. Chem* **2001**, *73*, 1411–1420.

[2] A. Drabczyńska, C.E. Müller, B. Schumacher, S. Hinz, J. Karolak-Wojciechowska, B. Michalak, E. Pękala, K. Kieć-Kononowicz. *Bioorg. Med. Chem.* **2004**, *12*, 4895–4908.