



Title	Responses and pharmacological classification of purinoceptors : Studies in guinea-pig adrenal chromaffin cells and rat gastric circular smooth muscle
Author(s)	OTSUGURO, Ken-ichi
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much smaller (1.5-1.6 folds) rise during hibernation, but those of  $\alpha_1$ -AT and C-reactive protein, the other APPs, did not show any seasonal variations. It was concluded that the increase in

serum Hp concentration during hibernation in the brown bear is independent of acute phase response, but associated with a hibernation-specific mechanism.

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Pharmacological profiles of TAK-029, a novel antagonist to platelet GPIIb/IIIa, and its antithrombotic effects

Masaki Kawamura

*Pharmaceutical Research Laboratories II,  
Pharmaceutical Research Division,  
Pharmaceutical Research Group,  
Takeda Chemical Industries, LTD.  
17-85, Jusohonmachi 2-chome,  
Yodogawa-ku, Osaka, 532-8686 Japan*

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Responses and pharmacological classification of purinoceptors  
— Studies in guinea-pig adrenal chromaffin cells and rat gastric circular smooth muscle

Ken-ichi OTSUGURO

*Laboratory of Pharmacology  
Department of Biomedical Sciences  
Graduate School of Veterinary Medicine  
Hokkaido University, Sapporo 060-0818, Japan*

The effects of extracellular ATP on voltage-dependent  $\text{Ca}^{2+}$  channels were examined using guinea-pig isolated adrenal chromaffin cells, and those of ATP on contractile responses were studied using rat gastric circular smooth muscle.

In the chromaffin cells, ATP evoked an inward current ( $I_{\text{ATP}}$ ) and a rise of intracellular  $\text{Ca}^{2+}$  concentration. ATP also showed the inhibition of  $\text{Ca}^{2+}$  current ( $I_{\text{Ca}}$ ) dependently on the amplitude of  $I_{\text{ATP}}$ . However, when a high con-

centration of EGTA was used in the intracellular solution, the inhibitory effect became independent of the amplitude of  $I_{\text{ATP}}$ . This reduction was decreased by dialysis of cells with  $\text{GDP}\beta\text{S}$  or  $\text{GTP}\gamma\text{S}$ , or by the application of a depolarizing prepulse. ADP, AMP and adenosine also reduced  $I_{\text{Ca}}$  and the effect of adenosine was the most potent. These results suggest that  $\text{Ca}^{2+}$  entry through ATP-activated channels results in the inactivation of  $\text{Ca}^{2+}$  channels, in addition, that

ATP modulates  $\text{Ca}^{2+}$  channels via the pathway related to GTP-binding protein.  $\text{P}_1$  and  $\text{P}_2$  receptors seem to coexist in guinea-pig adrenal chromaffin cells.

In the smooth muscle tissues contracted by acetylcholine, ATP, 2-methylthio ATP (2MeSATP) and  $\alpha, \beta$ -methylene ATP ( $\alpha, \beta$ -meATP) each caused relaxation. Reactive blue 2 (RB2) and suramin inhibited the relaxant responses to ATP and  $\alpha, \beta$ -meATP. PPADS and DIDS inhibited the relaxation caused by  $\alpha, \beta$ -meATP but not by ATP. Both ATP- and  $\alpha, \beta$ -meATP-induced relaxations were inhibited by apamin.

In tissues at resting tone, ATP and its related compounds caused contractions with the rank order of potency; 2MeSATP  $\gg$  ATP  $\geq$  UTP  $\gg$   $\alpha, \beta$ -meATP. RB2 and suramin inhibited both ATP- and UTP-induced contractions. PPADS inhibited the contraction

caused by UTP but not by ATP. Desensitization with UTP slightly decreased ATP-induced contraction. UTP-induced contraction was not inhibited by desensitization with ATP. ATP- and UTP-induced contractions were inhibited by the removal of extracellular  $\text{Ca}^{2+}$  or the application of nifedipine. These results suggest that there are two purinoceptors mediating relaxation, and that apamin-sensitive  $\text{K}^+$  channels are involved in the relaxant responses to these adenine nucleotide. In addition, it was suggested that ATP and UTP caused contractions via  $\text{P}_{2Y}$  receptors and pyrimidinoceptors, respectively, and that these contractions were caused by the  $\text{Ca}^{2+}$  entry through voltage-dependent  $\text{Ca}^{2+}$  channels. In summary, there are some purino- and pyrimidinoceptors in both chromaffin cells and smooth muscle cells. ATP and its related compounds may play a role as a transmitter in these tissues.

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Voltage-dependent calcium channels in porcine adrenal chromaffin cells:  
Channel subtypes and mechanisms of their facilitation.

Naoki KITAMURA

Laboratory of Pharmacology,  
Department of Biomedical Sciences,  
Graduate School of Veterinary Medicine,  
Hokkaido University,  
Sapporo 0600818, Japan

To study the characteristics of voltage-dependent  $\text{Ca}$  channels in porcine adrenal chromaffin cells,  $\text{Ca}$  currents ( $I_{\text{Ca}}$ ), rise of intracellular  $\text{Ca}$  concentration ( $[\text{Ca}^{2+}]_i$ ) and catecholamine release responses induced by stimulation with high  $\text{K}^+$  (60 mM) were measured by whole-cell voltage clamp technique, microfluorometry and HPLC-ECD method, respectively. The results

obtained were as follows:

Voltage-current relationship of  $I_{\text{Ca}}$  indicated that porcine adrenal chromaffin cells possess only high voltage-activated type of  $\text{Ca}$  channels. The  $I_{\text{Ca}}$  was inhibited by  $\omega$ -conotoxin GVIA ( $\omega$ -CgTx), nifedipine and  $\omega$ -agatoxin IVA ( $\omega$ -AgTx) dose-dependently, though the magnitudes of inhibition were various. The degree of inhibition