much smaller (1.5-1.6 folds) rise during hibernation, but those of α_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.

Original papers of this thesis appeared in "Comp. Biochem. Physiol.", Vol. 110B, 785–789 (1995) and "Comp. Biochem. Physiol.", Vol. 114A, 349–353 (1996).

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, Jusohonmach 2-chome,
Yodogawa-ku, Osaka, 532–8686 Japan

Original papers of this thesis appeared in "J. Pharmacol. Exp. Ther.", Vol. 277, 502–510 (1996), and "Thromb. Res.", Vol. 86, 275–285 (1997).

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 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_{ATP}) and a rise of intracellular Ca^{2+} concentration. ATP also showed the inhibition of Ca^{2+} current (I_{Ca}) dependently on the amplitude of I_{ATP}. However, when a high concentration of EGTA was used in the intracellular solution, the inhibitory effect became independent of the amplitude of I_{ATP}. This reduction was decreased by dialysis of cells with GDPβS or GTPγS, or by the application of a depolarizing prepulse. ADP, AMP and adenosine also reduced I_{Ca} and the effect of adenosine was the most potent. These results suggest that Ca^{2+} entry through ATP-activated channels results in the inactivation of Ca^{2+} channels, in addition, that

ATP modulates Ca^{2+} channels via the pathway related to GTP-binding protein. P_1 and 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 α,β-methylene ATP (α,β-meATP) each caused relaxation. Reactive blue 2 (RB2) and suramin inhibited the relaxant responses to ATP and α,β-meATP. PPADS and DIDS inhibited the relaxation caused by α,β-meATP but not by ATP. Both ATP- and α,β-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>> ATP≥UTP>> α,β-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 desensitizaiton with ATP. ATP- and UTP-induced contractions were inhibited by the removal of extracellular Ca^{2+} or the application of nifedipine. These results suggest that there are two purinoceptors mediating relaxation, and that apamin-sensitive K^+ channels are involved in the relaxant responses to these adenine nucleotide. In addition, it was suggested that ATP and UTP caused contractions via P_{2Y} receptors and pyrimidinoceptors, respectively, and that these contractions were caused by the Ca^{2+} entry through voltage-dependent 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.

Original papers of this thesis appeared in "Neurosci. Lett.", Vol. 187, 145–148 (1995), "Pflügers Arch. Eur. J. Physiol.", Vol. 431, 402–407 (1996) and " Eur. J. Pharmacol.", Vol. 317, 97–105 (1996).

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 Ca channels in porcine adrenal chromaffin cells, Ca currents (I_{Ca}), rise of intracellular Ca concentration ($[Ca^{2+}]_i$) and catecholamine release responses induced by stimulation with high 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_{Ca} indicated that porcine adrenal chromaffin cells possess only high voltage-activated type of Ca channels. The I_{Ca} was inhibited by ω-conotoxin GVIA (ω-CgTx), nifedipine and ω-agatoxin IVA (ω-AgTx) dose-dependently, though the magnitudes of inhibition were various. The degree of inhibition