분류번호	II-P-44

제목	Studies on the Analgesic Mechanism of Capsaicin - capsaicin-evoked adenosine release and metabolism of capsaicin
연구자	유은숙, 박영호, 이상섭
소속	서울대학교 약학대학

내용

To investigate analgesic mechanism of capsaicin and its analogues (capsaicinoids), release of adenosine was measured by high performance liquid chromatography from dorsal spinal cord synaptosomes. Exposure of synaptosomes to K^+ and morphine produced a dose dependent release of adenosine in the presence of Ca^{++}. Capsaicin (0.1, 1, 10 M), and its analogues ; 6-paradol (1, 10 M), NE-19550 (1, 10, 100 M), DMNE (1, 10, 100 M) and KR 25018 (0.1, 1, 10 M) produced a dose dependent release of adenosine in the presence of Ca^{++}. Nifedipine, L-type voltage sensitive calcium channel blocker, inhibited K^+ (6, 12 mM)- and morphine (10 M)-evoked release of adenosine completely, but inhibited capsaicin, and capsaicinoids-evoked release of adenosine partially. Capsazepine, a novel capsaicin selective antagonist, blocked only capsaicin and capsaicinoids induced release of adenosine. Therefore, the adenosine release by capsaicin and capsaicinoids having antinociceptive effects involve activation of capsaicin specific receptor and capsaicin sensitive Ca^{++} channel.

Capsaicin-hydrolyzing enzyme plays a key role in the most important process of capsaicin metabolism. Its subcellular location and orientation in the membrane, lumen of endoplasmic reticulum, was elucidated by marker enzyme assays and solubilization procedures. The enzyme was extracted from microsomes with Triton X-100 and purified by DEAE-cellulose, Sephadex G-200(superfine), and isoelectrofocusing chromatography. The enzyme was eluted from a gel filtration column as peaks with relative molecular mass of 60,000 and 180,000. Isoelectrofocusing using Rotofor Cell showed that isoelectric points of these enzymes are around 5.6 and 6.1, respectively. The pI 5.6 enzyme showed much higher activity compared with the p*I* 6.1 enzyme. This p*I* 5.6 enzyme proved to be serine hydrolase type by inhibition study and to have the pH optima at pH 8.0 - 9.0. With these and other criteria, these enzymes were verified to be previously known hydrolase p*I* 5.6 and hydrolase p*I* 6.1 which belong to carboxylesterase(EC 3.1.1.1).