
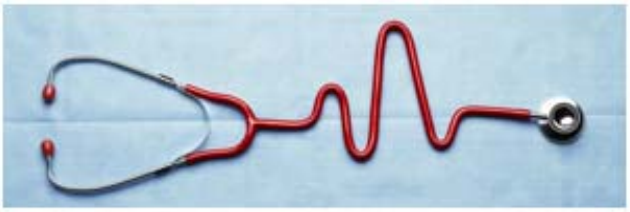

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Research Details :

Research Title : *An endogenous capsaicin-like substance with high potency at recombinant and native vanilloid VR1 rec*

An endogenous capsaicin-like substance with high potency at recombinant and native vanilloid VR1 rec

Descriptipn : The vanilloid receptor VR1 is a nonselective cation channel that is most abundant in peripheral sensory fibers but also is found in several brain nuclei. VR1 is gated by protons, heat, and the pungent ingredient of ‘‘hot’’ chili peppers, capsaicin. To date, no endogenous compound with potency at this receptor comparable to that of capsaicin has been identified. Here we examined the hypothesis, based on previous structure-activity relationship studies and the availability of biosynthetic precursors, that N-arachidonoyl-dopamine (NADA) is an endogenous ‘‘capsaicin-like’’ substance in mammalian nervous tissues. We found that NADA occurs in nervous tissues, with the highest concentrations being found in the striatum, hippocampus, and cerebellum and the lowest concentrations in the dorsal root ganglion. We also gained evidence for the existence of two possible routes for NADA biosynthesis and mechanisms for its inactivation in rat brain. NADA activates both human and rat VR1 overexpressed in human embryonic kidney (HEK)293 cells, with potency (EC50 50 nM) and efficacy similar to those of capsaicin. Furthermore, NADA potently activates native vanilloid receptors in neurons from rat dorsal root ganglion and hippocampus, thereby inducing the release of substance P and calcitonin gene-related peptide (CGRP) from dorsal spinal cord slices and enhancing hippocampal paired-pulse depression, respectively. Intradermal NADA also induces VR1-mediated thermal hyperalgesia (EC50 1.5 0.3 g). Our data demonstrate the existence of a brain substance similar to capsaicin not only with respect to its chemical structure but also to its potency at VR1 receptors

Research Type : Article

Added Date : Sunday, March 30, 2008

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