The antimigraine butterbur ingredient, isopetasin, desensitizes peptidergic nociceptors via the transient receptor potential ankyrin 1 channel.

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Background and Purpose

The mechanism of the antimigraine action of butterbur [Petasites hybridus (L.) Gaertn.] is unknown. Here, we investigated the ability of isopetasin, a major butterbur constituent, to specifically target the transient receptor ankyrin 1 (TRPA1) channel and to affect functional responses relevant to migraine.

Experimental Approach

Single cell calcium imaging and patch-clamp recordings in human and rodent TRPA1-expressing cells, neurogenic motor responses in isolated rat urinary bladder, release of calcitonin gene-related peptide (CGRP) from mouse spinal cord in vitro, and facial rubbing and dural artery vasodilation in vivo in rodents were examined.

Key Results

Isopetasin produced (i) calcium responses and currents in rat/mouse trigeminal ganglion (TG) neurons and in cells expressing the human TRPA1, (ii) substance P-mediated contractions of isolated rat urinary bladders and (iii) CGRP release from mouse dorsal spinal cord, responses that were selectively abolished by TRPA1 genetic deletion/pharmacological antagonism. Preexposure

to isopetasin produced marked desensitization of allyl isothiocyanate (AITC, TRPA1 agonist)- or capsaicin (TRPV1 agonist)-evoked currents in rat TG neurons, contractions of rat urinary bladder and CGRP release from central terminals of primary sensory neurons. Repeated intragastric administration of isopetasin attenuated mouse facial rubbing, evoked by local AITC or capsaicin, and dilation of rat meningeal arteries by acrolein or ethanol (TRPA1 and TRPV1 agonists, respectively).

Conclusion and Implications

TRPA1 agonism by isopetasin results in excitation of neuropeptide-containing nociceptors that is followed by remarkable neuronal desensitization. Such attenuation in pain and neurogenic inflammation may account for the antimigraine action of butterbur.