Anti-inflammatory properties of TRPA1 antagonists. 
Pyrazine-fused triterpenoids as an example:

Pyrazine-fused triterpenoids block TRPA1 ion channel in vitro and inhibit TRPA1-mediated inflammation in vivo

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Background: TRPA1 is a cation channel expressed mostly in non-myelinated nerve endings. TRPA1 has a significant role in sensing chemical and mechanical pain and, according to the more recent findings, also in inflammation. We have recently shown that pharmacological blockade and genetic deletion of TRPA1 alleviates inflammation and pain in murine models of gout and (os-teo)arthritis. Furthermore, we have discovered that TRPA1 is expressed in human articular chondrocytes and synovial cells in inflammatory conditions, and mediates inflammatory and catabolic responses in vitro.

Triterpenoids are naturally occurring molecules, which have been discovered to have anti-inflammatory and anti-cancer properties. In the present study, we synthesized a series of derivatives of the triterpenoid betulin (which is a bioactive molecule from birch bark) and investigated their effects on TRPA1.

Methods and Results: In the initial screening based on Fluo 3-AM intracellular Ca2+ measurements, six of the fourteen tested triterpenoids had a significant blocking effect on TRPA1 at 10 uM concentration. In the further studies, the two most potent compounds (Compounds 8 and 9) were found to have dose-dependent, reversible and voltage-dependent blocking effects on TRPA1 at submicromolar concentrations based on whole-cell patch clamp recordings. Interestingly, the TRPA1 antagonistic activity of these two pyrazine-fused triterpenoid derivatives was also translated to in vivo, as Compounds 8 and 9 significantly attenuated TRPA1-mediated acute inflammatory paw edema in mice.

Conclusions: The results introduce pyrazine-fused triterpenoid derivatives as effective novel blockers of TRPA1 with lead potential for treatment of TRPA1 mediated adverse conditions, such as arthritis and arthritis-related pain.