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Autor(en) des Beitrags: Ziemba, Paul M.; Schreiner, Benjamin S. P.; Flegel, Caroline; Herbrechter, Robin; Stark, Timo D.; Hofmann, Thomas; Hatt, Hanns; Werner, Markus; Gisselmann, Gunter
Titel des Beitrags: Activation and modulation of recombinantly expressed serotonin receptor type 3A by terpenes and pungent substances
Abstract: Serotonin receptor type 3 (5-HT3 receptor) is a ligand-gated ion channel that is expressed in the central nervous system (CNS) as well as in the peripheral nervous system (PNS). The receptor plays an important role in regulating peristalsis of the gastrointestinal tract and in functions such as emesis, cognition and anxiety. Therefore, a variety of pharmacologically active substances target the 5-HT3 receptor to treat chemotherapy-induced nausea and vomiting. The 5-HT3 receptors are activated, antagonized, or modulated by a wide range of chemically different substances, such as 2-methyl-serotonin, phenylbiguanide, setrones, or cannabinoids. Whereas the action of all of these substances is well described, less is known about the effect of terpenoids or fragrances on 5-HT3A receptors. In this study, we screened a large number of natural odorous and pungent substances for their pharmacological action on recombinantly expressed human 5-HT3A receptors. The receptors were functionally expressed in Xenopus oocytes and characterized by electrophysiological recordings using the two-electrode voltage-clamp technique. A screening of two odorous mixes containing a total of 200 substances revealed that the monoterpenes, thymol and carvacrol, act as both weak partial
agonists and positive modulators on the 5-HT3A receptor. In contrast, the most effective blockers were the terpenes, citronellol and geraniol, as well as the pungent substances gingerol, capsaicin and polygodial. In our study, we identified new modulators of 5-HT3A receptors out of the classes of monoterpenes and vanilloid substances that frequently occur in various plants.