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★令和7年度（2025年） 卒業生 「矢島宙 君」の研究成果が、「栄養学」の国際的専門誌”Nutrients“に掲載されました!!!

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Article

Naringenin Suppresses the Hyperexcitability of Trigeminal Nociceptive Neurons Associated with Inflammatory Hyperalgesia: Replacement of NSAIDs with Phytochemicals

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Abstract: The present study examines whether the systemic application of naringenin (NRG) reduces inflammation-induced hyperexcitability in the spinal trigeminal nucleus caudalis (SpVc) related to hyperalgesia, and compares its impact with that of diclofenac (DIC). To provoke inflammation, the whisker pads of rats were injected with complete Freund's adjuvant, and subsequently, mechanical stimuli were administered to the orofacial region to determine the escape threshold. Compared to naïve rats, the inflamed rats showed a significantly lower mechanical threshold, and this reduced threshold returned to normal levels two days post-administration of NRG, DIC, and half-dose DIC plus half-dose NRG (1/2 DIC + 1/2 NRG). Using extracellular single-unit recordings, the activity of SpVc wide-dynamic range neurons was measured in response to mechanical stimulation of the orofacial area under anesthesia. The average firing rate of SpVc neurons when exposed to both non-painful and painful mechanical stimuli was significantly reduced in inflamed rats following NRG, DIC, and 1/2 DIC + 1/2 NRG administration. The heightened average spontaneous activity of SpVc neurons in rats with inflammation was significantly reduced following NRG, DIC, and 1/2 DIC + 1/2 NRG administration. The increased average receptive field size observed in inflamed rats reverted to normal levels after either NRG, DIC, or 1/2 DIC + 1/2 NRG treatment. These findings indicate that NRG administration can reduce inflammatory hyperalgesia linked to the heightened excitability of SpVc wide-dynamic range neurons.

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Keywords: inflammation; trigeminal nociceptive neuron; hyperalgesia; pathological pain; extracellular single-unit recording; diclofenac; NSAIDs; naringenin; phytochemical; complementary alternative medicine

ハイライト：これまでに、グレープフルーツなどの柑橘類に含まれるファイトケミカルであるナリンゲニンは非ステロイド性消炎鎮痛薬（NSAIDs）の標的分子であるシクロオキシゲナーゼ２の作用を抑制することは in vitroの実験で示唆されていたが、in vivo での効果は不明であった。今回、我々は末梢組織の炎症に伴い生じる“痛覚過敏の症状”とこの発症に重要な役割を果たす広作動域ニューロンの興奮性の変化が「ナリンゲニン」の慢性投与により抑制されることを明らかとした。さらにナリンゲニンとNSAIDｓの疼痛緩和効果が同等であることが確認され,ＮＳＡＩＤｓの半量をナリンゲニンで代替できたため、ナリンゲニンが副作用を伴わない臨床における「補完代替医療」に貢献する可能性が推定された。この成果は新規NSAIDs、特に“特異的Cox-2 阻害薬”の開発や“新たな鎮痛薬”などの創薬への応用が期待される重要性の高い知見と考えられる。