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The role of cannabinoid CB_1 receptor agonists in gastric mucosal protection in rats and mice

Nashwan Shujaa[1], Zoltán S Zádori[1], Mahmoud Al-Khrasani[1], Susanna Fürst[1], Tibor Wenger[2] and Klára Gyires[1]

[1]Department of Pharmacology and Pharmacotherapy, Semmelweis University, Budapest, Hungary

[2]Department of Human Morphology, Semmelweis University, Budapest, Hungary

E-Mail: gyirkla@pharma.sote.hu

CB_1 receptor agonists inhibit stimulated gastric acid secretion and exert an anti-ulcer activity in acid-dependent ulcer models. The aims of this study were to investigate the gastroprotective effect of cannabinoids in an acid-independent ulcer model and to analyze the role of opioid and vanilloid receptors in this effect. Gastric mucosal damage was induced by acidified ethanol in rats and in $CB_1^{+/+}$ and $CB_1^{-/-}$ mice. Anandamide, methanandamide and WIN-55,212-2 inhibited the ethanol-induced gastric mucosal damage significantly after peripheral and central administration, and their effects were reversed by the CB_1 receptor antagonist SR141716A. The gastroprotective effect of cannabinoid agonists was significantly decreased by naloxone and partially by capsazepine (TPRV1 receptor antagonist). The gastroprotective effect of opioid peptides DAGO and deltorphin II was significantly reduced in $CB_1^{-/-}$ mice. In conclusion, cannabinoid CB_1 receptors are likely to be involved in gastric mucosal defense. The effect seems to be central, and correlation between opioid and cannabinoid system in gastric mucosal protection may be raised.

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