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A STUDY ON THE INFLUENCE OF PERIPHERAL OR CENTRAL ADMINISTRATION OF ONDANSETRON ON STRESS-INDUCED GASTRIC ULCERATION.

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5-Hydroxytryptamine$_3$ (5-HT$_3$) is present in the gastrointestinal tract and brain. The amine has been shown to have mucosal ulcerogenic properties. The effects of ondansetron (Glaxo), a specific 5-HT$_3$ receptor blocker, on stress-induced gastric ulcers in rats were, therefore, studied. Female Sprague-Dawley rats (170-190 g) were injected s.c. with ondansetron (0.04, 0.08, 0.15 or 0.3 mg/kg) once every 12 h, with the fourth dose given 0.5 h before 2-h cold (4°C) and restraint (stress). Another group of rats had guide cannulae implanted surgically, using a stereotaxic technique, in the nucleus amygdaloideus centralis (ACE) or nucleus accumbens (ACE); cannulae positions were confirmed histologically on completion of experiments. The animals were allowed a 10-day period for recovery and then intracerebrally injected, via the indwelling guide cannulae, with ondansetron (0.1, 0.5 or 1 μg) once every 12 h with the fourth dose given 0.5 h before stress. Ondansetron s.c. dose-dependently and markedly reduced stress-induced gastric ulcer formation. Administration of ondansetron in the ACE also significantly decreased, whereas injection of the drug in the ACB significantly intensified, stress-evoked ulcers when given in higher doses (1 μg). The associated stomach wall mast cell degranulation was, however, not prevented by all doses of ondansetron given s.c. or intracerebrally. The findings indicate that 5-HT$_3$ block in different areas of the brain have dissimilar gastric effects; on the other hand, systemic administration consistently antagonises stress-evoked ulceration. It is likely that 5-HT$_3$ receptors at a peripheral post-vagal site are mainly involved in stress-induced gastric glandular mucosal damage, and that ondansetron exerts its antiulcer action through blockade of these receptors.