THE GASTRIC EFFECTS OF UFP 112, A NEW NOP RECEPTOR AGONIST, IN PHYSIOLOGICAL AND PATHOLOGICAL CONDITIONS

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Nociceptin /orphanin FQ (N/OFQ), the endogenous ligand of the NOP receptor, has been reported to centrally modulate gastric motor and secretory functions, and to prevent ethanol-induced gastric lesions in rats. Recently, a novel N/OFQ analog, [(pF)Phe^{4}Aib^{7}Arg^{14}Lys^{15}]N/OFQ-NH_2 (UFP-112), was synthesized and demonstrated to behave as a highly potent and selective peptide agonist for NOP receptors and to produce long-lasting effects in mice compared with the natural ligand N/OFQ. The present study was aimed at evaluating the effects of centrally (intracerebroventricularly/icv) and peripherally (intraperitoneally/ip) administered UFP 112 on gastric emptying and gastric acid secretion, and on the development of gastric mucosal lesions induced by 50% ethanol in the rat.
UFP 112 mimicked the effects of N/OFQ, inducing, after icv injection, dose-related and significant delay (up to 70%) in the gastric emptying of a phenol red meal, decrease (up to 90%) of gastric acid secretion in water loaded rats after 90 min-pylorus ligature and reduction (up to 87 %) of gastric lesions caused by ethanol. In all these assays, UFP 112 was more effective than N/OFQ and its effective doses were at least 30-100 fold lower than N/OFQ effective doses. The highly selective NOP receptor antagonist, UFP-101, decreased the efficacy of UFP 112 in the assays above reported, thus confirming that central NOP receptors mediate an inhibitory control on these functional and pathological conditions in rats.
The ip injection of N/OFQ and UFP 112 induced not dose related gastric ipersecretory and antiulcer effects, partially abolished by UFP-101. When ip injected, both UFP 112 and N/OFQ failed to modify gastric emptying in rats, suggesting that peripheral NOP receptors play a role in mediating gastric hypersecretory and antiulcer effects but are not involved in the control of gastric motility.
In addition, this novel NOP receptor agonist has been shown to produce longer lasting inhibitory effects than N/OFQ on gastric emptying and ulcers.
In conclusion, UFP 112, which acts as potent NOP receptor ligand and is able to produce full and long lasting activation of NOP receptors, represents a new pharmacological tool to study the functional roles of the central and peripheral N/OFQ receptor system.