NEW PHARMACOLOGICAL INTERVENTIONS INFLUENCING FOOD INTAKE REGULATION

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ABSTRACT

Prolactin-releasing peptide (PrRP) identified as an endogenous ligand of the orphan receptor GPR10 was originally found to stimulate the secretion of prolactin (PRL) both *in vitro* and *in vivo*. PrRP-mediated PRL secretion was later questioned and is not currently considered to be the primary function of PrRP. The fact that both PrRP and GPR10 knock-out mice are hyperphagic and develop late-onset obesity proves the unique anorexigenic properties of PrRP. Designing and evaluation of PrRP analog(s) with selective anorexigenic properties and searching for PrRP antagonists would contribute to finding the mechanism and possible treatment of obesity and metabolic syndrome. In our recent published study (Maixnerová et al., Peptides (2011)), the PrRP receptor was immunodetected and characterized by saturation binding in three rodent tumor pituitary cell lines. Two naturally occurring analogs, PrRP31 and PrRP20, showed comparable potency in binding, cell signaling and prolactin release in pituitary RC-4B/C cells, as well as caused food intake decrease after intracerebroventricular administration in fasted mice. In the present study, analogs of PrRP20 with C-terminal Phe amide derivatives with modified aromatic ring were used. Analogs with deleted Phe or containing Phe derivatives with bulky side chain or halogenated aromatic ring showed high binding potency and cell signaling in RC-4B/C cells. Moreover, their anorexigenic effect after central administration in fasted mice was long lasting.

KEY WORDS:

Prolactin-releasing peptide

Analogs PrRP20

Receptor GPR10