Melanin-concentrating hormone receptor 1 antagonists: a new perspective for the pharmacologic treatment of obesity.

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Abstract

Obesity is a chronic disease characterized by the accumulation of excess adipose tissue associated with an increased risk of multiple morbidities and mortality. At the present time, only three drugs have been approved by the Food and Drug Administration (FDA) for the treatment of obesity. Agonists and antagonists of some of the substances implicated in the regulation of energy homeostasis represent opportunities for anti-obesity drug development. The most promising targets are alpha-melanocyte stimulating hormone (alpha-MSH) receptors, cannabinoid receptors, the 5-hydroxytryptamine (5-HT) receptors and melanin-concentrating hormone (MCH) receptors. MCH receptors could be major potential targets for the treatment of obesity. Many pharmaceutical companies have described MCH-R1 antagonists that have appeared over the past year. Recently, two compounds went into phase I clinical trials that evaluate MCH receptor antagonists as a new perspective for the pharmacologic treatment of obesity. In this review, structure-activity relationships (SAR) in the development of MCH-R1 antagonists are provided.