ACS Medicinal Chemistry Letters

IN THIS ISSUE

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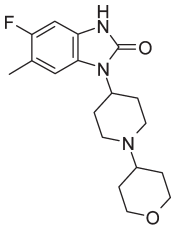
Muscarinic Acetylcholine Receptor Agonists

The muscarinic acetylcholine receptors are G-protein coupled receptors which are activated by the neurotransmitter acetylcholine. Now, Budzik et al. (DOI: 10.1021/ml100105x) describe the discovery and characterization of *N*-substituted benzimidazolone small molecules which are potent, subtype selective, orally bioavailable central nervous system-penetrant M1 muscarinic acetylcholine receptor agonists with demonstrated robust in vivo activity in several schizophrenia animal models. The results presented by the authors also suggest that selective M1 muscarinic acetylcholine receptor agonists are effective enhancers of cognitive abilities. In addition, these agonists are excellent tools for investigating and validating potential therapeutic benefits from selectively activating the M1 receptor. (This summary was corrected on September 21, 2010.)



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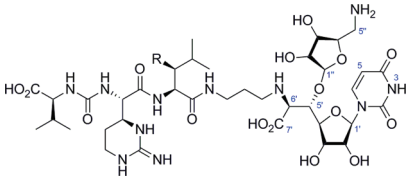
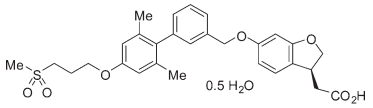
Muraymycin Analogues

Muraymycins are a class of nucleoside-lipopeptide natural product antibiotics isolated from species of *Streptomyces*. Tanino et al. (DOI: 10.1021/ml100057z) now report the synthesis of a series of muraymycin analogues. These analogues are active against many pathogenic bacteria such as methicillin-resistant *Staphylococcus aureus* and vancomycin-resistant *Enterococcus faecium*. The authors conclude that it might be possible to generate potential lead compounds with potent antibacterial activities based on the muraymycin analogues described in this study.



A New Diabetes Drug

The GPCR, GPR40, serves as a receptor for long-chain free fatty acids and is found in abundance in pancreatic β-cells. It has been postulated that a GPR40 agonist might serve as an effective antidiabetic compound. Now, Negoro et al. (DOI: 10.1021/ml1000855) present a compound that is the first orally bioavailable GPR40 agonist in clinical trials for type 2 diabetes mellitus. This compound is both specific and potent.



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