ACS Medicinal Chemistry Letters

In This Issue

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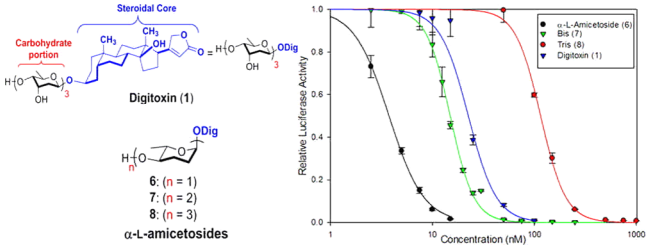
IMPROVED ANTI-HCMV ACTIVITY OF DIGITOXIN

Human cytomegalovirus (HCMV) is related to other herpesviruses, including the well-known herpes simplex viruses 1 and 2, varicella-zoster virus, and Epstein−Barr virus. Cardiac glycosides, which include digoxin and ouabain, reportedly inhibit herpes simplex virus 1 and human cytomegalovirus in nanomolar concentrations.

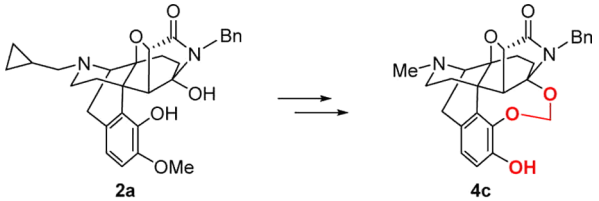
Here, Cai et al. (DOI: 10.1021/ml400529q) describe exciting SAR studies revealing that sugar type and length of cardiac glycosides affect CMV activity and showing that the bioactivities of these cardiac glycosides go beyond the indication for treating congestive heart failure and arrhythmias. The study shows cardiac glycosides' potential in drug repurposing. Further, sugar modification may be key in the discovery of new and safer digitoxin alternative for antiviral therapeutics.



NEW DELTA OPIOID RECEPTOR AGONISTS

Activation of the δ opioid receptor (DOR) is associated with various pharmacological effects such as antinociceptive, antidepressive, anxiolytic, and cardioprotective effects. Importantly, DOR is a promising medical target because it does not have addictive nor aversive effects. However, it is known that some DOR agonists produced convulsive behaviors, whereas others do not.

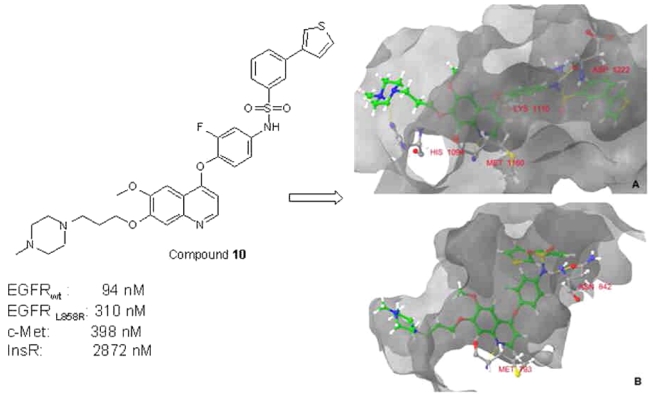
Here, Fujii et al. (DOI: 10.1021/ml400491k) describes the synthetic path for several new delta opioid receptor agonists with novel oxazatricyclodecane structure and their pharmacological properties. The identified lead compound mediated antinociception without inducing convulsions. One new DOR agonist serves as a promising lead compound with a novel chemotype.



DUAL EGFR/C-MET INHIBITORS

Non-small cell lung cancer (NSCLC) is one of the leading cancers worldwide. Epidermal growth factor receptor (EGFR) related signaling pathways play an important role in NSCLC and have been proven to be potential therapeutic targets. Another important player is receptor tyrosine kinase c-Met, which is implicated in many cellular processes such as proliferation, survival, migration, invasion, and wound healing. Thus, simultaneous inhibition of EGFR and c-Met kinases is desirable.

In this issue, Szokol et al. (DOI: 10.1021/ml4003309) report the novel small-molecule kinase inhibitors of both EGFR and c-Met activity, which inhibit at nanomolar range and induce apoptosis in clinically relevant NSCLC cell lines.



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