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New helicase-primase inhibitors as drug candidates for the treatment of herpes simplex disease.

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Abstract

The vast majority of the world population is infected with at least one member of the human herpesvirus family. Herpes simplex virus (HSV) infections are the cause of cold sores and genital herpes as well as life-threatening or sight-impairing disease mainly in immunocompromized patients, pregnant women and newborns. Since the milestone development in the late 1970s of acyclovir (Zovirax), a nucleosidic inhibitor of the herpes DNA polymerase, no new non-nucleosidic anti-herpes drugs have been introduced. Here we report new inhibitors of the HSV helicase-primase with potent in vitro anti-herpes activity, a novel mechanism of action, a low resistance rate and superior efficacy against HSV in animal models. BAY 57-1293 (N-[5-(aminosulfonyl)-4-methyl-1,3-thiazol-2-yl]-N-methyl-2-[4-(2-pyridinyl)phenyl]acetamide), a well-tolerated member of this class of compounds, significantly reduces time to healing, prevents rebound of disease after cessation of treatment and, most importantly, reduces frequency and severity of recurrent disease. Thus, this class of drugs has significant potential for the treatment of HSV disease in humans, including those resistant to current medications.

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