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Mechanism of Action of SCH 47802, an Antipicornavirus Molecule

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SCH 47802 represents a class of structures with potent in vitro and in vivo activities against picornaviruses. SCH 47802 and its active analogs stabilize poliovirus to thermal inactivation indicating that the compounds bind to the virus capsid. The binding of SCH 47802 to poliovirus appears to be largely reversible by dilution, with only an incremental enhancement of virus recovery occurring after chloroform extraction. Mechanistic studies with poliovirus type 2 indicate that SCH 47802 does not block virus attachment to HeLa cells. Studies investigating virus recovery in an infectious center assay and recovery of intact virions on linear sucrose gradients support the notion that SCH 47802 blocks poliovirus uncoating. Mechanistic studies with other viruses indicate that SCH 47802 blocks the attachment of human rhinovirus 14.

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Anti-Picornavirus Activity of New Substituted Flavons and Flavanones

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Chloro-, cyano-, amidino- and oxazolinyl- flavans, isoflavans, and isoflavenes, synthesized by us, significantly inhibited the *in vitro* replication of several picornaviruses (Desideri N. *et al.*,1992, Antiviral Chem. Chemother. 3: 195-202). Flavones, belonging to a broad group of natural compounds, have also been found active against a wide range of picornaviruses (Y. Tsuchiya *et al.*, 1985, Chem. Pharm. Bull. 33: 3881-3886). With the aim of preparing substances with improved antiviral efficacy, a series of new analogues, bearing the more suitable substituents of the previously investigated compounds on a flavon or flavanon skeleton, have been synthesized. The antiviral potency of the new compounds has been evaluated against rhinovirus type 1B (HRV 1B) and poliovirus type 2 (PV 2) by a plaque reduction assay in HeLa cell cultures. A comparison of the activities of substituted flavons indicated that a chlorine atom and a 3-methoxy group were both necessary for a good anti HRV 1B activity. A chlorine and a 3-hydroxyl group were instead required for an anti PV 2 effect, indicating different binding specificities. Flavanones, with a less restricted conformation, were generally much less effective than the planar flavons: only 6-chloro-4'-oxazolinylflavanon exhibited a significant inhibitory effect towards both viruses (HRV 1B IC_{50}= 5.16 μM; PV 2 IC_{50}= 2.79 μM), further stressing the importance of these substituents for antipicornavirus activity. However, the overall analysis of the antipicornavirus activity of all these drugs indicates that substituted flavons and flavanones are much less effective and more toxic to uninfected cultures than the previously studied flavanoids.