medical sciences forum

MDPI

Abstract

F- and OH-Containing Isopulegol-Derived Octahydro-2*H*-Chromenes as Agents against Influenza A Virus †

Irina V. Ilyina [1,*], Oksana S. Patrusheva [1], Vladimir V. Zarubaev [2], Konstantin P. Volcho [1], Nariman F. Salakhutdinov [1]

[1] Novosibirsk Institute of Organic Chemistry, Siberian Branch of the Russian Academy of Sciences, Lavrentjev av.9, 630090, Novosibirsk, Russia
[2] Pasteur Institute of Epidemiology and Microbiology, 14 Mira str., 197101 St. Petersburg, Russia
* Correspondence: ilyina@nioch.nsc.ru
† Presented at the 1st International Electronic Conference on Molecular Sciences: Druggable Targets of Emerging Infectious Diseases, online, 01-14 September 2021.

Academic Editor: Clemente Capasso

Published: 31 August 2021

Abstract: Monoterpenes, which have a unique diverse structure and are inexpensive, available and often enantiomerically pure, are an attractive renewable raw material for the development of physiologically active agents. One of the important methods to the utilization of monoterpenes is their interaction with carbonyl compounds resulting in heterocyclic compounds. Often these products exhibit analgesic, antiviral or neuroprotective properties. Earlier, we discovered anti-influenza A (H1N1) virus activity of several compounds with a hydro-2H-chromene scaffold, which were synthesized by the Prins reaction using p-menthane alcohols and carbonyl compounds; montmorillonite K10 or nanosized halloysite catalyst were used as the reaction catalysts [1]. Chromenols produced from an (–)-isopulegol and aliphatic ketones (acetone and cyclopentanone) demonstrated high activity in combination with low toxicity against the influenza virus [1]. The introduction of the fluorine atom into the molecule is an important strategy in the development of new biologically active compounds, which enables changing lipophilicity and electrostatic interactions and increasing the metabolic stability of compounds and, so affects their physiological activity. Here we synthesized fluoro- and hydroxy-containing octahydro-2*H*-chromenes by the Prins reaction starting from an (–)-isopulegol and a wide range of aromatic aldehydes in the presence of the $BF_3 \cdot Et_2O/H_2O$ system acting as both an acid catalyst and a fluorine source. Activity of the synthesized compounds against the influenza A/Puerto Rico/8/34 (H1N1) virus was studied. The highest activity was demonstrated by fluoro- and hydroxy-containing 2,4,6-trimethoxybenzaldehyde derivatives. These compounds were supposed to be capable of binding to viral hemagglutinin, which is an agreement with data on the effect of compounds on the viral fusogenic activity as well as with molecular docking studies.

[1] N.Salakhutdinov, K.Volcho, O.Yarovaya, Pure Appl. Chem., 2017;89:1105-1117.

Keywords: Influenza; Antiviral; Fluorine; Monoterpene; Chromene