Raltegravir potassium salt

Cat. No.: HY-10353A
CAS No.: 871038-72-1
Molecular Formula: C₂₀H₂₀FKN₆O₅
Molecular Weight: 482.51
Target: HIV Integrase; HIV
Pathway: Metabolic Enzyme/Protease; Anti-infection
Storage: Powder
-20°C 3 years
4°C 2 years
In solvent
-80°C 6 months
-20°C 1 month

SOLVENT & SOLUBILITY

<table>
<thead>
<tr>
<th>In Vitro</th>
<th>H₂O : 25 mg/mL (51.81 mM; Need ultrasonic)</th>
</tr>
</thead>
<tbody>
<tr>
<td></td>
<td>DMSO : 6 mg/mL (12.43 mM; Need ultrasonic)</td>
</tr>
</tbody>
</table>

Preparing Stock Solutions

<table>
<thead>
<tr>
<th>Preparing Stock Solutions</th>
<th>Mass Concentration</th>
<th>1 mg</th>
<th>5 mg</th>
<th>10 mg</th>
</tr>
</thead>
<tbody>
<tr>
<td>1 mM</td>
<td>2.0725 mL</td>
<td>10.3625 mL</td>
<td>20.7250 mL</td>
<td></td>
</tr>
<tr>
<td>5 mM</td>
<td>0.4145 mL</td>
<td>2.0725 mL</td>
<td>4.1450 mL</td>
<td></td>
</tr>
<tr>
<td>10 mM</td>
<td>0.2072 mL</td>
<td>1.0362 mL</td>
<td>2.0725 mL</td>
<td></td>
</tr>
</tbody>
</table>

Please refer to the solubility information to select the appropriate solvent.

In Vivo

1. Add each solvent one by one: 10% DMSO >> 40% PEG300 >> 5% Tween-80 >> 45% saline
   Solubility: ≥ 0.6 mg/mL (1.24 mM); Clear solution
2. Add each solvent one by one: 10% DMSO >> 90% (20% SBE-β-CD in saline)
   Solubility: ≥ 0.6 mg/mL (1.24 mM); Clear solution
3. Add each solvent one by one: 10% DMSO >> 90% corn oil
   Solubility: ≥ 0.6 mg/mL (1.24 mM); Clear solution

BIOLOGICAL ACTIVITY

Description
Raltegravir potassium salt (MK 0518 potassium salt) is a potent integrase (IN) inhibitor, used to treat HIV infection.

In Vitro
PFV IN carrying the S217H substitution is 10-fold less susceptible to Raltegravir with IC₅₀ of 900 nM. PFV IN displays 10% of WT activity and is inhibited by Raltegravir with an IC₅₀ of 200 nM, indicating a appr twofold decrease in susceptibility to the IN strand transfer inhibitor (INSTI) compared with WT IN. S217Q PFV IN is as sensitive to
Raltegravir as the WT enzyme[1]. Raltegravir is metabolized by glucuronidation, not hepatically. Raltegravir has potent in vitro activity against HIV-1, with a 95% inhibitory concentration of 31±20 nM, in human T lymphoid cell cultures. Raltegravir is also active against HIV-2 when Raltegravir is tested in CEMx174 cells, with an IC\textsubscript{95} of 6 nM. Raltegravir metabolism occurs primarily through glucuronidation. Drugs that are strong inducers of the glucuronidation enzyme, UGT1A1, significantly reduce Raltegravir concentrations and should not be used. Raltegravir exhibits weak inhibitory effects on hepatic cytochrome P450 activity. Raltegravir does not induce CYP3A4 RNA expression or CYP3A4-dependent testosterone 6β-hydroxylase activity[2]. Raltegravir cellular permeativity is reduced in the presence of magnesium and calcium[3]. Raltegravir and related HIV-1 integrase (IN) strand transfer inhibitors (INSTIs) efficiently block viral replication[4]. In acutely infected human lymphoid CD4\textsuperscript{+} T-cell lines MT-4 and CEMx174, SIVmac251 replication is efficiently inhibited by Raltegravir, which shows an EC\textsubscript{90} in the low nanomolar range[5].

**In Vivo**

Raltegravir induces viro-immunological improvement of nonhuman primates with progressing SIVmac251 infection. One non-human primate shows an undetectable viral load following Raltegravir monotherapy[5].

### PROTOCOL

#### Cell Assay [5]

Human MT-4 cells are infected for 2 hours with the SIVmac251, HIV-1 (IIIB) and HIV-2 (CDC 77618) stocks at a multiplicity of infection of, approximately, 0.1. Cells are then washed three times in phosphate buffered saline, and suspended at 5 \times 10^5/mL in fresh culture medium (to primary cells 50 units/mL of IL-2 are added) in 96-well plates, in the presence or absence of a range of triplicate raltegravir concentrations (0.0001 \mu M-1 \mu M). Untreated infected and mock-infected controls are prepared too, in order to allow comparison of the data derived from the different treatments. Viral cytopathogenicity in MT-4 cells is quantitated by the methyl tetrazolium (MTT) method (MT-4/MTT assay) when extensive cell death in control virus-infected cell cultures is detectable microscopically as lack of capacity to re-cluster. The capability of MT-4 cells to form clusters after infection. Briefly, clusters are disrupted by pipetting; and, after 2 hours of incubation at 37°C, the formation of new clusters is assessed by light microscopy (100× magnification). Cell culture supernatants are collected for HIV-1 p24 and HIV-2/SIVmac251 p27 core antigen measurement by ELISA. In CEMx174-infected cell cultures, which show a propensity to form syncytia induced by the virus envelope glycoproteins, syncytia are counted, in blinded fashion, by light microscopy for each well at 5 days following infection.

MCE has not independently confirmed the accuracy of these methods. They are for reference only.

### CUSTOMER VALIDATION

- Bioorg Med Chem. 2019 Sep 1;27(17):3836-3845.

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### REFERENCES


