**Ko 143**

**Cat. No.:** HY-10010  
**CAS No.:** 461054-93-3  
**Molecular Formula:** C₂₆H₃₅N₃O₅  
**Molecular Weight:** 469.57  
**Target:** BCRP  
**Pathway:** Membrane Transporter/Ion Channel  
**Storage:**  
- Powder: -20°C 3 years  
- 4°C 2 years  
- In solvent: -80°C 6 months  
- -20°C 1 month

**SOLVENT & SOLUBILITY**

**In Vitro**  
DMSO: ≥ 50 mg/mL (106.48 mM)  
H₂O: < 0.1 mg/mL (insoluble)  
*"≥" means soluble, but saturation unknown.*

**Preparing Stock Solutions**

<table>
<thead>
<tr>
<th>Solvent Concentration</th>
<th>1 mg</th>
<th>5 mg</th>
<th>10 mg</th>
</tr>
</thead>
<tbody>
<tr>
<td>1 mM</td>
<td>2.1296 mL</td>
<td>10.6480 mL</td>
<td>21.2961 mL</td>
</tr>
<tr>
<td>5 mM</td>
<td>0.4259 mL</td>
<td>2.1296 mL</td>
<td>4.2592 mL</td>
</tr>
<tr>
<td>10 mM</td>
<td>0.2130 mL</td>
<td>1.0648 mL</td>
<td>2.1296 mL</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: ≥ 2.5 mg/mL (5.32 mM); Clear solution
2. Add each solvent one by one: 10% DMSO >> 90% (20% SBE-β-CD in saline)  
   Solubility: 2.5 mg/mL (5.32 mM); Suspended solution; Need ultrasonic and warming and heat to 50°C
3. Add each solvent one by one: 10% DMSO >> 90% corn oil  
   Solubility: ≥ 2.5 mg/mL (5.32 mM); Clear solution

**BIOLOGICAL ACTIVITY**

**Description**  
Ko 143 is a potent and selective ATP-binding cassette sub-family G member 2 (ABCG2; BCRP) inhibitor.

**IC₅₀ & Target**  
EC90: 26 nM (BCRP)
In Vitro

Ko143 (10 nM) significantly decreases (2.5-fold) the IC\textsubscript{50} of MTX for HEK G2 cells and mouse G2 cells. Ko143 (1-100 μM) metabolite does not inhibit the function of ABC Transporters\textsuperscript{[1]}. Reversal of drug resistance in SKF 104864A-selected mouse MEF3.8/T6400 cells and human IGROV1/T8 cells by FTC analogue Ko143. Ko143 is applied at zero, one, or eight times the EC\textsubscript{90} concentration of 25 nM\textsuperscript{[2]}. Ko143 inhibits BCRP-mediated transport of ZD 4522 in Madin-Darby Canine Kidney (MDCK) 2-BCRP421CC (wild type) cells and MDCK2-BCRP421AA (mutant type) cells\textsuperscript{[3]}.

In Vivo

Ko143 (10 mg/kg, p.o.) increases the oral availability of SKF 104864A in mice\textsuperscript{[2]}. Ko143 significantly affects the pharmacokinetics of ZD 4522 in rats\textsuperscript{[3]}.

PROTOCOL

Cell Assay \textsuperscript{[2]}

Cells are plated at 400 or 1000/well in 96-well plates the night before addition of drugs. A concentration series of drug is applied along one plate axis and left for the duration of the assay. Plates are harvested after 4-5 days while untreated wells are still subconfluent. Relative cell proliferation is quantified with CyQuant or Sybr Green I fluorescent nucleic acid stains. Assays with human cell lines are performed in the presence of 0.1 μm PSC833 to inhibit confounding P-gp activity.

Animal Administration \textsuperscript{[2]}

Oral toxicity of FTC analogues in mice is tested by mixing 50 mg/mL stocks in DMSO 1:1 with Tween 80 (polyoxyethylene sorbitan mono-oleate) and diluting with 5% w/v glucose such that the final volume administered by oral gavage is 10 μL/g of body weight. Pairs of mice are administered oral doses of 50 mg/kg Ko132, Ko134, Ko143, or vehicle under light methoxyflurane anesthesia. Final tests of 50 mg/kg Ko134 or Ko143 are performed on additional pairs of unanesthetized animals to observe any behavioral effects. Further, another pair of mice receive the higher dose of 100 mg/kg Ko134. For i.p. toxicity tests, the FTC analogue stocks in DMSO are dispersed in at least 10 volumes of sterile corn oil such that the injected volume is 5 μL/g of body weight. After pilot tests at lower doses show no adverse effects, mice (4 per group) are administered vehicle or 10 mg/kg i.p. of Ko132, Ko134, or Ko143. The mice are observed continuously during the first hour after administration and then at increasing intervals for 2 weeks, after which they are sacrificed for histological examination of major organs and structures including brain, salivary glands, heart, lungs, liver, adrenal glands, kidneys, urinary tract, spleen, thymus, bone marrow, pancreas, stomach, intestines, cecum, colon, testes, epididymus, skin, head, trunk, and limbs.

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REFERENCES


