上海源叶生物科技有限公司
Shanghai yuanye Bio-Technology Co., Ltd
电话：021-61312973　　传真：021-55068248
网址：www.shyuanye.com
邮箱：shyysw@sina.com

# 产品名称：Ko 143
# 产品别名：Ko 143

## 生物活性：

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| **Description** | Ko 143 is a potent and selective ATP-binding cassette sub-family G member 2 (ABCG2; BCRP) inhibitor. |
| **$IC_{50}$ & Target** | EC90: 26 nM (BCRP) |
| **In Vitro** | Ko143 (10 nM) significantly decreases (2.5-fold) the IC50 of MTX for HEK G2 cells and mouse G2 cells. Ko143 (1-100 μM) metabolite does not inhibit the function of ABC Transporters[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 EC90 concentration of 25 nM[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[3]. |
| **In Vivo** | Ko143 (10 mg/kg, p.o.) increases the oral availability of SKF 104864A in mice[2]. Ko143 significantly affects the pharmacokinetics of ZD 4522 in rats[3]. |
| **Solvent&Solubility** | ***In Vitro:***<br>**DMSO : ≥ 50 mg/mL (106.48 mM)**<br>**$H_2O$ : < 0.1 mg/mL** (insoluble)<br>* "≥" means soluble, but saturation unknown. |

**Preparing Stock Solutions**

| Solvent / Mass / Concentration | 1 mg | 5 mg | 10 mg |
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| 1 mM | 2.1296 mL | 10.6480 mL | 21.2961 mL |
| 5 mM | 0.4259 mL | 2.1296 mL | 4.2592 mL |
| 10 mM | 0.2130 mL | 1.0648 mL | 2.1296 mL |

*请根据产品在不同溶剂中的溶解度选择合适的溶剂配制储备液；一旦配成溶液，请分装保存，避免反复冻融造成的产品失效。

储备液的保存方式和期限：-80°C, 6 months; -20°C, 1 month。-80°C 储存时，请在 6 个月内使用，-20°C 储存时，请在 1 个月内使用。

***In Vivo:***

请根据您的实验动物和给药方式选择适当的溶解方案。以下溶解方案都请先按照 In Vitro 方式配制澄清的储备液，再依次添加助溶剂：

——为保证实验结果的可靠性，澄清的储备液可以根据储存条件，适当保存；体内实验的工作液，建议您现用现配，当天使用； 以下溶剂前显示的百分比是指该溶剂在您配制终溶液中的体积占比；如在配制过程中出现沉淀、析出现象，可以通过加热和/或超声的方式助溶

1.请依序添加每种溶剂： 10% DMSO→40% PEG300 →5% Tween-80 → 45% saline

Solubility: ≥ 2.5 mg/mL (5.32 mM); Clear solution

此方案可获得 ≥ 2.5 mg/mL (5.32 mM，饱和度未知) 的澄清溶液。

以 1 mL 工作液为例，取 100 μL 25.0 mg/mL 的澄清 DMSO 储备液加到 400 μL PEG300 中，混合均匀；向上述体系中加入 50 μL Tween-80，混合均匀；然后继续加入 450 μL 生理盐水定容至 1 mL。

2.请依序添加每种溶剂： 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

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| | 此方案可获得 2.5 mg/mL (5.32 mM)的均匀悬浊液，悬浊液可用于口服和腹腔注射。<br>以 1 mL 工作液为例，取 100 μL 25.0 mg/mL 的澄清 DMSO 储备液加到 900 μL 20% 的 SBE-β-CD 生理盐水水溶液中，混合均匀。<br><br>3.请依序添加每种溶剂： 10% DMSO →90% corn oil<br>Solubility: ≥ 2.5 mg/mL (5.32 mM); Clear solution<br>此方案可获得 ≥ 2.5 mg/mL (5.32 mM，饱和度未知) 的澄清溶液，此方案不适用于实验周期在半个月以上的实验。<br>以 1 mL 工作液为例，取 100 μL 25.0 mg/mL 的澄清 DMSO 储备液加到 900 μL 玉米油中，混合均匀。 |
| **References** | [1]. Weidner LD, et al. The Inhibitor Ko143 Is Not Specific for ABCG2. J Pharmacol Exp Ther. 2015 Sep;354(3):384-93.<br>[2]. JD Allen et al. Potent and Specific Inhibition of the Breast Cancer Resistance Protein Multidrug Transporter in Vitro and in Mouse Intestine by a Novel Analogue of Fumitremorgin C. Mol. Cancer Ther. 2002, 1, 417-425.<br>[3]. Wen JH, et al. Effect of Ursolic Acid on Breast Cancer Resistance Protein-mediated Transport of ZD 4522 In Vivo and Vitro. Chin Med Sci J. 2015 Dec;30(4):218-25.<br>[4]. Hou J, et al. Quantitative determination and pharmacokinetic study of the novel anti-Parkinson's disease candidate drug FLZ in rat brain by high performance liquid chromatography-tandem mass spectrometry. J Pharm Biomed Anal. 2012 Jul;66:232-9.<br>[5]. Liu K, et al. Metabolism of KO143, an ABCG2 inhibitor. Drug Metab Pharmacokinet. 2017 Aug;32(4):193-200. |

**实验参考：**

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| **Cell Assay** | 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. [2] |
| **Animal Administration** | 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, |

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| | lungs, liver, adrenal glands, kidneys, urinary tract, spleen, thymus, bone marrow, pancreas, stomach, intestines, cecum, colon, testes, epididymus, skin, head, trunk, and limbs. [2] |
| **References** | [1]. Weidner LD, et al. The Inhibitor Ko143 Is Not Specific for ABCG2. J Pharmacol Exp Ther. 2015 Sep;354(3):384-93.<br>[2]. JD Allen et al. Potent and Specific Inhibition of the Breast Cancer Resistance Protein Multidrug Transporter in Vitro and in Mouse Intestine by a Novel Analogue of Fumitremorgin C. Mol. Cancer Ther. 2002, 1, 417-425.<br>[3]. Wen JH, et al. Effect of Ursolic Acid on Breast Cancer Resistance Protein-mediated Transport of ZD 4522 In Vivo and Vitro. Chin Med Sci J. 2015 Dec;30(4):218-25.<br>[4]. Hou J, et al. Quantitative determination and pharmacokinetic study of the novel anti-Parkinson's disease candidate drug FLZ in rat brain by high performance liquid chromatography-tandem mass spectrometry. J Pharm Biomed Anal. 2012 Jul;66:232-9.<br>[5]. Liu K, et al. Metabolism of KO143, an ABCG2 inhibitor. Drug Metab Pharmacokinet. 2017 Aug;32(4):193-200. |