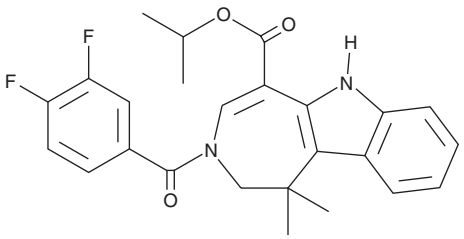
PRODUCT INFORMATION

XL335

Item No. 23350

CAS Registry No.:	629664-81-9
Formal Name:	3-(3,4-difluorobenzoyl)-1,2,3,6-tetrahydro-1,1-dimethyl-azepino[4,5-b]indole-5-carboxylic acid, 1-methylethyl ester
Synonyms:	Turofexorate isopropyl, WAY-362450
MF:	$C_{25}H_{24}F_2N_2O_3$
FW:	438.5
Purity:	≥98%
UV/Vis.:	λ_{max}: 216, 262, 340 nm
Supplied as:	A crystalline solid
Storage:	-20°C
Stability:	≥4 years



Information represents the product specifications. Batch specific analytical results are provided on each certificate of analysis.

Laboratory Procedures

XL335 is supplied as a crystalline solid. A stock solution may be made by dissolving the XL335 in the solvent of choice, which should be purged with an inert gas. XL335 is soluble in organic solvents such as ethanol, DMSO, and dimethyl formamide (DMF). The solubility of XL335 in these solvents is approximately 0.2, 5, and 10 mg/ml, respectively.

XL335 is sparingly soluble in aqueous buffers. For maximum solubility in aqueous buffers, XL335 should first be dissolved in DMF and then diluted with the aqueous buffer of choice. XL335 has a solubility of approximately 0.5 mg/ml in a 1:1 solution of DMF:PBS (pH 7.2) using this method. We do not recommend storing the aqueous solution for more than one day.

Description

XL335 is an orally bioavailable and potent agonist of the farnesoid X receptor (FXR) with an EC_{50} value of 4 nM in CV-1 cells transfected with human FXR.[1] It is selective for FXR over a panel of 15 nuclear receptors at concentrations up to 10 µM. XL335 induces expression of mouse intestinal bile acid binding protein (IBABP), human bile salt excretory pump (BSEP), and small heterodimer partner (SHP) genes in reporter gene assays. It also induces a 20-, 13-, and 2-fold increase in mRNA expression for IBABP, BSEP, and SHP, respectively, at a concentration of 1 µM. XL335 (3 mg/kg) reduces plasma cholesterol and triglycerides by 39 and 50%, respectively, and decreases the area of pre-atherosclerotic lesions in $LDLR^{-/-}$ mice fed a Western diet. It also decreases hepatic fibrosis in a mouse model of non-alcoholic steatohepatitis.[2]

References

1. Flatt, B., Martin, R., Wang, T.L., *et al.* Discovery of XL335 (WAY-362450), a highly potent, selective, and orally active agonist of the farnesoid X receptor (FXR). *J. Med. Chem.* **52(4)**, 904-907 (2009).
2. Zhang, S., Wang, J., Liu, Q., *et al.* Farnesoid X receptor agonist WAY-362450 attenuates liver inflammation and fibrosis in murine model of non-alcoholic steatohepatitis. *J. Hepatol.* **51(2)**, 380-388 (2009).

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